NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of sutureless aortic valve replacement for aortic stenosis

Aortic stenosis happens when the aortic valve, which lets blood flow out of the heart, becomes narrowed (stenosed). This reduces blood flow from the heart. This puts strain on the heart and can cause an enlarged heart, irregular heartbeat, chest pain and sudden collapse. In this procedure, a cut is made in the chest. The heart is then connected to a heart-lung bypass machine. The narrowed aortic valve is removed and replaced with an artificial valve that holds itself in place.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety

and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2018.

Procedure name

- Sutureless aortic valve replacement for aortic stenosis

Specialist societies

- Society for Cardiothoracic Surgery in Great Britain and Ireland
- British Cardiovascular Society
- Royal College of Surgeons.

Description of the procedure

Indications and current treatment

Aortic stenosis causes impaired blood flow out of the heart and is usually progressive. The increased cardiac workload leads to left ventricular hypertrophy, arrhythmias, and may lead to life-threatening heart failure. Symptoms of aortic stenosis typically include shortness of breath and chest pain on exertion.

Conventional treatment for patients with severe symptomatic aortic stenosis is surgical aortic valve replacement. Surgical aortic valve replacement may not be suitable for some patients because of their medical comorbidities or technical considerations such as a calcified aorta or scarring from previous cardiac surgery. Continued medical care may be the only option for some patients. Transcatheter aortic valve implantation (TAVI) for aortic stenosis is an alternative for patients for whom surgery is unsuitable, but it does not allow for concomitant coronary artery bypass grafting.

What the procedure involves

Sutureless aortic valve replacement (S-AVR) for aortic stenosis is an alternative to both conventional surgical aortic valve replacement and TAVI. The potential benefits of the procedure are that the diseased valve is removed, combined pathologies of the aortic valve and the coronary arteries can be treated. Also the

procedure may be quicker because the valve does not need to be sewn in, which reduces cardiopulmonary and aortic cross-clamp times.

With the patient under general anaesthesia, access to the heart is usually made through a full- or mini-sternotomy. Once cardiopulmonary bypass and cardioplegia are established, the diseased aortic valve is accessed and removed through a cut in the aorta. Bulky calcifications around the native aortic annulus are removed to achieve a smooth round annulus for valve implantation. One or more stitches may be needed to guide correct positioning of the new valve. The valve prosthesis, loaded into a delivery device, is inserted into the native annulus. The valve is then released and guide stitches are removed. Balloon dilatation of the new valve may be used to maximise the area of contact between the prosthesis and the aortic annulus. The position and function of the valve are assessed intraoperatively by transoesophageal echocardiography.

Different devices are available for this procedure, all of which contain material derived from animal sources.

Outcome measures

Clinical assessment of severity of aortic stenosis

New York Heart Association (NYHA) heart failure classification: this is used to classify the severity of breathlessness from class I, in which the patient has no limitation in daily physical activity, to class IV, in which the patient is breathless at rest.

Haemodynamic assessment (usually by echocardiography and Doppler): aortic valve area (cm^2) or aortic valve area index (relative to body surface area; cm^2/m^2). An aortic valve area of less than 0.6 cm^2/m^2 indicates severe aortic stenosis.

Transaortic gradient (mmHg): Peak transaortic valve gradient of more than 64 mmHg and mean transaortic valve gradient of more than 40 mmHg indicates severe aortic stenosis.

The logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE); measures patient risk at the time of surgery using a logistic-

regression equation on a 0 to 100% scale (higher scores indicating greater risk; a score higher than 20% indicates very high surgical risk).

Efficacy summary

Aortic cross-clamp time

A systematic review and meta-analysis of 1,037 patients in 12 observational studies on sutureless aortic valve replacement (SU-AVR) reported that the weighted pooled aortic cross-clamping (ACC) time was 46.5 minutes (95% confidence interval [CI] 38.9 to 54.0 minutes, I^2=98%; p<0.001). In patients having isolated SU-AVR, ACC time was 33.1 minutes (95% CI 25.5 to 40.8 minutes; I^2=99%; p<0.001). A subgroup analysis suggested that ACC time was comparable for full sternotomy (weighted mean 53.6 minutes; 95% CI 45.6 to 91.6) compared with minimally invasive SU-AVR approach (weighted mean 59.3 minutes; 95% CI 56.1 to 62.4).[1]

A systematic review of SU-AVR using Perceval valves reported that in 15 studies on 9 different cohorts, overall mean ACC time ranged from 32 to 50.7 minutes. For isolated SU-AVR, mean ACC times ranged from 17.8 to 40.5 minutes, whereas concomitant SU-AVR mean ACC times ranged from 44.2 to 69.6 minutes[5].

In a case series of 731 patients with SU-AVR, the mean ACC was 30.8 minutes for full sternotomy, and 37.6 minutes for the minimally invasive approach, respectively in patients who had isolated SU-AVR (n=498)[7].

<u>SU-AVR compared with conventional aortic stented valve replacement (C-AVR)</u>
In the systematic review of SU-AVR with Perceval valves, when compared with C-AVR, pooled analysis from 7 retrospective observational cohort studies showed a statistically significant reduction in ACC time (38.6 compared with 66.3 minutes, mean difference [MD]= -20.71, 95% CI -24.81 to -16.60, p<0.00001)[5].

Cardiopulmonary bypass (CBP) time

The systematic review and meta-analysis of 1,037 patients in 12 observational studies on SU-AVR reported that the weighted pooled CBP time was 73.1 minutes (95% CI 63.2 to 83.1, I^2=97%; p<0.001). In patients having isolated SU-AVR, CBP time was 56.7 minutes (95% CI 45.2 to 68.2; I^2=98%; p<0.001). A subgroup analysis suggested that CBP time has a trend towards being lower with full sternotomy (weighted mean 78.2 minutes; 95% CI 14.5 to 141.9) compared with minimally invasive approach (weighted mean 92.3 minutes; 95% CI 87.7 to 96.8)[1].

The systematic review of SU-AVR with Perceval valves reported that in 15 studies on 9 different cohorts, overall CBP time ranged from 44 .7 to 78.9 minutes. For isolated SU-AVR, mean CPB times ranged from 46.4 to 66.0 minutes, whereas for concomitant SU-AVR, CBP times ranged from 67.6 to 88.7 minutes[5].

In the case series of 731 patients the mean CBP time was 50.8 minutes for full sternotomy, and 64.4 minutes for the minimally invasive approach, respectively in patients who had isolated SU-AVR[7].

SU-AVR compared with C-AVR

In the systematic review of SU-AVR with Perceval valves when compared with C-AVR, pooled analysis from 7 retrospective observational cohort studies showed a statistically significant reduction in CBP time (61.4 compared with 84.9 minutes, MD= -22.83, 95% CI -27.39 to -18.26, p<0.00001)[5].

Length of hospital/intensive care unit (ICU) stay (days)

The systematic review of SU-AVR with Perceval valves reported that in 15 studies on 9 different cohorts, overall ICU stay ranged from 2.0 to 3.7 days and hospital stay ranged from mean 11.4 to 15.0 days[5].

SU-AVR compared with transcatheter aortic valve replacement (TAVI)

In a systematic review and meta-analysis of 12 studies comparing SU-AVR with C-AVR and TAVI, analysis of 1 propensity-matched comparative study (with 204 patients) reported that SU-AVR was associated with shorter length of hospital stay (−2.0, 95% CI −3.65 to −0.35, p=0.02) and ICU stay (−1.0; 95% CI −1.86 to −0.14, p=0.02) compared with TAVI[2].

In the systematic review of SU-AVR with Perceval valves when compared with TAVI, pooled analysis from 8 retrospective observational cohort studies showed no statistically significant difference in ICU stay (1.73 compared with 1.54 days, OR= −0.16, 95% CI −0.67 to 0.99, p=0.71)[5].

SU-AVR compared with C-AVR

In the systematic review and meta-analysis of 12 studies comparing SU-AVR with C-AVR and TAVI, analysis of 3 propensity-matched comparative studies (with 204 patients) reported that SU-AVR was associated with shorter ICU stay (0.11 days; 95% CI −0.17 to −0.38, p=0.44, I^2=79%, p=0.010) compared with C-AVR and analysis of 1 propensity matched study showed that SU-AVR is associated with shorter length of hospital stay (−1.50 days, 95% CI −2.62 to −0.38, p=0.009)[2].

In the systematic review of SU-AVR with Perceval valves when compared with C-AVR, pooled analysis from 7 retrospective observational cohort studies showed no significant reduction in ICU stay (MD= −0.30, 95% CI −0.73 to 0.14, p=0.18)[5].

Haemodynamic outcomes

The systematic review and meta-analysis of 1,037 patients in 12 observational studies on SU-AVR reported that the pooled weighted mean transaortic valve gradient (reported in 8 studies) was 11.13 mmHg (95% CI 9.8 to 12.4 mmHg, I^2=94%; p<0.001) at discharge, 9.0 mmHg (95% CI 8.7 to 9.3 mmHg; I^2=0%; p=0.663) at 6 months and 9.6 mmHg (95% CI 8.7 to 10.6 mmHg, I^2=86%; p<0.001) at 12 months follow-up (reported in 6 studies). Pooled weighted peak transaortic valve gradient (reported in 5 studies) at discharge was 19.6 mmHg (95% CI 16.6 to 22.7 mmHg; I^2=95%; p<0.001), 17.8 mmHg (95% CI 16.0 to 19.5 mmHg; I^2=86%; p<0.001) at 6 months and 17.3 mmHg (95% CI 16.1 to 18.4 mmHg, I^2=69%; p=0.007) at 12 months follow-up. The effective orifice area (EOA, reported in 6 studies) was similar at discharge (1.77 cm^2; 95% CI 16.2 to 2.0 cm^2; I^2=98%; p<0.001), 6 months (1.75 cm^2; 95% CI 1.5 to 2.0 cm^2; I^2=97%; p<0.001) and 12 months follow-up (1.73 cm^2; 95% CI 1.5 to 1.9 cm^2; I^2=97%; p<0.001)[1].

In the case series of 731 patients with SU-AVR, mean and peak transaortic valve gradients decreased from 42.9 and 74.0 mmHg preoperatively, to 7.8 and 16 mmHg at 3 years follow-up. At 5 years follow-up, the mean and peak transaortic valve gradients changed to 8.8 and 21.1 mmHg respectively. There was an increase in the EOA (from 0.75 cm^2 preoperatively to 1.80 cm^2 at 5 years), and regression in left ventricle mass (from 254.5 to 177.4 g at 3 years)[7].

In a case series of 287 patients with SU-AVR, the mean transaortic valve gradient was 10.6 ± 4.2 mmHg at discharge, 9.0 ± 3.5 mmHg at 1 year, 9.6 ± 4.3 mmHg at 3 years, 10.5 ± 5.4 mmHg at 5 years (p=0.188 compared to discharge) respectively, across all valve sizes. The peak gradient was 20.0 ± 7.6 mmHg at discharge, 16.9 ± 6.1 mmHg at 1 year, 17.6 ± 7.4 mmHg at 3 years and 18.9± 9.3 mmHg at 5 years (p=0.42 compared to discharge) respectively. The EOA at discharge, 3 and 5 years was 1.7 ± 0.2 cm^2, 1.7 ± 0.2 cm^2 and 1.6 ± 0.3 cm^2, respectively. Left ventricular mass was 217.8 ± 62.5 g at discharge, 184 ± 48 g at 1 year, 187 ± 48 g at 3 years and 192 ± 44 g at 5 years respectively.[8]

Patient prosthesis mismatch

In the case series of 287 patients with SU-AVR, 64.7% (33/51) of patients were free from patient-prosthesis mismatch (PPM as defined by EOA index >0.85 cm^2/m^2), 27.5% (14/51) of patients had moderate PPM (defined by EOA index 0.65 to 0.85 cm^2/m^2) and 7.8% (4/51) of patients had a severe PPM (defined by EOA index <0.65 cm^2/m^2)[8].

Improvement in clinical status

The case series of 287 patients reported that at 5 years follow-up, NYHA status improved in 63.2% of patients while 25.3% of them stayed in the same NYHA class and 11.5% worsened[8].

Survival

The systematic review of SU-AVR with Perceval valve reported that survival rates ranged from 86.4 to 91.7% at 1 year (in 5 cohort studies), 82.4 to 87% at 2 years (3 cohort studies) and 71.3 to 85.5% (in 2 cohort studies) at 5 years follow-up[5]. In the same study, 4 retrospective observational cohort studies comparing SU-AVR with TAVI showed that 2 year survival rates were higher in the SU-AVR group than TAVI (91.6 compared with 66.2%, p=0.1, 90.6 compared with 87.3%, p=0.46, 97.3 compared with 86.5%, p=0.015, 94.9% compared with 79.5%, p=0.028)[5]. Three studies comparing SU-AVR with C-AVR showed that 2 year survival rates were not significantly different among the groups (92% compared with 91%, p=0.463, 92% compared with 92%, 97.5% compared with 96.2%, p=0.646)[5].

In the case series of 731 patients with SU-AVR, overall survival rates at 1 and 5 years were 92.1% and 74.7%, respectively[7].

In the case series of 287 patients with SU-AVR, the overall survival rate was 81.1% (95% CI 75.5 to 86.8%) at 5 years follow-up. The survival rates were 85.7 ± 3.4% (95% CI 79.2 to 92.3%) and 75.2 ± 4.9% (95% CI 65.6 to 84.8%) for isolated SU-AVR and concomitant SU-AVR, respectively (p=0.085)[8].

Safety summary

Mortality

Pooled 30 day mortality (in 10 studies) and 1 year mortality rates (in 11 studies) were 2.1% (95% confidence interval [CI], 1.1 to 3.3%; I^2=11%; p=0.341) and 4.9% (95% CI 2.7 to 7.7%; I^2=59%; p=0.007) respectively, in a meta-analysis of 1,037 patients in 12 observational studies on sutureless aortic valve replacement (SU-AVR)[1].

30 day mortality ranged from 0 to 4.9% (in 2 studies) in a systematic review of SU-AVR with Perceval valves[5]. 30-day mortality rate was 2.3 (pooled weighted mean, 95% CI 1.44 to 3.25%) in another systematic review and meta-analysis of SU-AVR with Perceval valves[6].

Early (less than 30 days) all-cause and cardiac mortality rates were 3.4% (25/731) and 1.9 (14/731) respectively, in a case series of 731 patients with SU-AVR. Late (more than 30 days) all-cause and cardiac mortality rates were 7.0% (51/729) and 1.4% (10/729) respectively[7]. Early all-cause mortality rate was 1.7%

(5/287) and late all-cause mortality rate was 3.5% per patient year (37 events) in a case series of 287 patients. 3 of the early deaths and 2 of the late deaths were valve related[8].

SU-AVR compared with transcatheter aortic valve replacement (TAVI)

Pooled analysis of 6 matched comparative studies (with 1,223 patients) reported that SU-AVR was associated with at least 30% reduction in 30 day mortality compared with TAVI (odds ratio [OR] 0.40, 95% CI 0.25 to 0.62, p<0.001, I^2=0%, p=0.79) primarily in the low and intermediate risk groups in a meta-analysis of 12 studies comparing SU-AVR with conventional AVR (C-AVR) and TAVI[2].

Meta-analysis of 7 observational comparative studies showed a statistically significant reduction in mortality with SU-AVR compared with TAVI (2.5% [9/354] compared with 7.3% [39/531]; OR 0.33; 95% CI 0.16 to 0.69; p value for overall effect =0.003, I^2=0%, p value for heterogeneity =0.93; risk difference [RD] −5.23%, 95% CI −8.12 to −2.33%; p=0.0004)[3].

Pooled analysis of 8 retrospective observational cohort studies comparing SU-AVR with TAVI demonstrated statistically significant reduction in early mortality with SU-AVR over TAVI (2.98% [19/636] compared with 6.9% [44/636], RR=0.48, 95% CI =0.28 to 0.82, p=0.007) in the systematic review of SU-AVR with Perceval valves[5].

SU-AVR compared with C-AVR

Pooled analysis of 5 matched comparative studies (with 1,323 patients) shows no significant effect was seen in the risk for 30 day mortality in the SU-AVR group compared with C-AVR (OR 1.03, 95% CI 0.56 to 1.88, I^2=0%; p=0.93) in a meta-analysis of 12 studies comparing SU-AVR with C-AVR and TAVI[2].

Pooled analysis of 8 retrospective observational cohort studies comparing SU-AVR with C-AVR showed no statistically significant difference in early (30 day) mortality with SU-AVR over C-AVR (3.39% [23/678] compared with 3.91% [40/1,022], OR=0.99, 95% CI =0.58 to 1.70, p=0.98) in the systematic review of SU-AVR with Perceval valves[5].

All comparisons

Direct-comparison meta-analyses (DC-MA-[A] of SU-AVR compared with TAVI in 6 propensity-score matched [PSM] studies, a DC-MA-[B] of SU-AVR compared with C-AVR in 6 studies [1RCT and 5 PSM studies], and a DC-MA-[C] TAVI compared with C-AVR in 24 studies) and an adjusted indirect-comparison meta-analysis (IDC-MA-[A] of TAVI compared with SU-AVR from the results of the DC-MA-[B] and the DC-MA-[C] done for severe aortic stenosis show that the 3 DC-MAs showed significantly lower perioperative (30 day or in-hospital) all-cause

mortality after SU-AVR than after TAVI (odds ratio [OR], 0.48; 95% CI 0.28 to 0.80; p=0.005) and no significant differences between SU-AVR and C-AVR (OR, 1.07; 95% CI, 0.60 to 1.94; p=0.81) and between TAVI and C-AVR (1.07; 95% CI, 0.90 to 1.27; p=0.45). The computed IDC-MA-[A] (6 RCTs and 30 PSM studies with 15,887 patients) indicated no statistically significant difference in mortality between SU-AVR and TAVI (1.01; 95% CI, 0.54 to 1.86). Combining the results of the DC-MA-[A] and IDC-MA [A] showed statistically significantly lower mortality after SU-AVR than after TAVI (OR, 0.65; 95% CI 0.44 to 0.97; p=0.03)[4].

Pacemaker implantation

Weighted pooled estimate of pacemaker implantation over mean 1 year follow-up (in 5 studies) was 5.6% (38/627; 95% CI, 3.5 to 8.0%; I^2=25%; p=0.252) in a meta-analysis of 1,037 patients in 12 observational studies on sutureless aortic valve replacement (SU-AVR)[1].

Pacemaker implantation rates within 30 days ranged from 3.1 to 17% (in 2 cohort studies) in a systematic review of SU-AVR with Perceval valves[5].

New occurrence of early atrioventricular block III leading to pacemaker implantation in patients with no history of cardiac rhythm disorders was 7.4% (54/731) in the case series of 731 patients[7]. New pacemakers were implanted in 7% (19/287) of patients before 30 days follow-up and in 1.6% per patient year (17) during the late follow-up in the case series of 287 patients with SU-AVR[8].

SU-AVR compared with TAVI

Pooled analysis of 6 matched comparative studies (with 1,228 patients) for permanent pacemaker reported that no significant effect was seen in SU-AVR group compared with TAVI (OR 0.74, 95% CI 0.50 to 1.08, I^2=0%; p=0.51) in a meta-analysis of 12 studies comparing SU-AVR with SAVR and TAVI[2].

Meta-analysis of 7 observational comparative studies showed no statistically significant difference in post-operative conduction disturbance among patients between SU-AVR and TAVI (6.9% [26/376] compared with 11% [43/380]; OR 0.66; 95% CI 0.24 to 1.78%, p value for overall effect =0.41; I^2=44%, p value for heterogeneity =0.10)[3].

Pooled analysis of 8 retrospective observational cohort studies comparing SU-AVR with TAVI showed no statistically significant difference in pacemaker implantation with SU-AVR over TAVI (9.75% [62/636] compared with 9.28% [59/636], risk ratio [RR]=1.36, 95% CI=0.62 to 2.98, p=0.45) in the systematic review of SU-AVR with Perceval valves[5].

SU-AVR compared with C-AVR

In the pooled analysis of 5 matched comparative studies (with 1,323patients) and 2 unadjusted studies (n=648), the risk of pacemaker implantation was significantly increased in the SU-AVR group compared with C-AVR group (OR 2.16, 95% CI 1.34 to 3.47, p=0.002, I^2=16%; p=0.31; and OR 5.72, 95% CI 2.65 to 12.36%, p<0.001, I^2=0%) in a meta-analysis of 12 studies comparing SU-AVR with SAVR and TAVI[2].

In the systematic review of SU-AVR with Perceval valves, 4 studies comparing SU-AVR with C-AVR demonstrated that early (less than 30 days) pacemaker implantation rates were significantly higher using SU-AVR and 4 studies showed no significant difference among both groups[5].

Myocardial infarction and cerebrovascular accident

SU-AVR compared with TAVI

Pooled analysis of 6 matched comparative studies (with 1,228 patients), for risk of cerebrovascular accident and 2 studies (n=582) for the risk of myocardial infarction shows that no significant effect was seen in the SU-AVR group compared with TAVI for the outcomes (cerebrovascular accident: OR 0.53, 95% CI 0.26 to 1.05; I^2=6%, p=0.38; myocardial infarction: OR 0.29, 95% CI 0.07 to 1.20, I^2=0%, p=0.98) in a meta-analysis of 12 studies comparing SU-AVR with SAVR and TAVI[2].

SU-AVR compared with C-AVR

Meta-analysis of 5 adjusted matched comparative studies (with 1,323 patients), 1 RCT (n=94), and 2 observational studies (n=648) for risk of stroke and 3 matched comparative studies (with 817 patients) and 1 RCT (n=94) for the risk of myocardial infarction shows that no significant effect was seen in the SU-AVR group compared with C-AVR for the outcomes (stroke: OR 0.89, 95% CI 0.45 to 1.75; I^2=35%, p=0.20; myocardial infarction: OR 1.22, 95% CI 0.24 to 6.35, I^2=22%, p=0.28) in a meta-analysis of 12 studies comparing SU-AVR with SAVR and TAVI[2].

Endocarditis

Weighted pooled estimate of endocarditis over mean 1 year follow-up (in 10 studies) was 2.2% (26/1032, 95% CI 0.8 to 4.1; I^2=58%; p=0.012) in the meta-analysis of 1,037 patients in 12 observational studies on SU-AVR[1].

Weighted pooled estimate of endocarditis (in 7 studies) was less than 1% (95% CI 0.5 to 6.7) in the meta-analysis of 2,505 patients in 14 observational studies on SU-AVR[6].

Endocarditis was reported in 1.9% (14/731) of patients in the case series of 731 patients with SU-AVR[7]. Two events of endocarditis were reported at late

follow-up in the case series of 287 patients with SU-AVR. One event lead to valve explant and the other one was successfully treated by medication[8].

Bleeding

Pooled analysis of 5 observational comparative studies showed no statistically significant difference in bleeding complications among patients between SU-AVR and TAVI (4.8% [15/312] compared with 0.9% [3/329]; OR 3.18; 95% CI 0.91 to 11.18%, p value for overall effect=0.07; I^2=1%, p value for heterogeneity =0.40)[3].

Major bleeding was reported early in 7.3% (20/287) of patients and late in 2.2% per patient year (n=23) in the case series of 287 patients. Half of these events were anticoagulation related[8].

Structural valve deterioration/degeneration

Weighted pooled estimate of structural valve degeneration or dislocation at 30 days follow-up (in 6 studies) was 2.3% (12/504, 95% CI 0.5 to 5.1, I^2=52%, p=0.062) and over mean 1 year follow-up (in 4 studies) was 0.4% (95% CI 0 to 1.4; I^2=0%; p=0.79) in the meta-analysis of 1,037 patients in 12 observational studies on SU-AVR[1].

Structural valve deterioration was reported as 0% at 30 days, 1 year and 5 year follow-up in 2 studies in the systematic review of SU-AVR with Perceval valve[5]. Two case reports of structural valve deterioration (stiffened leaflets, valvular thrombosis) were reported in the same review. The degenerated prosthesis was removed and a mechanical prosthesis was implanted in both cases[5].

Structural valve deterioration presenting as prosthesis stenosis was reported in less than 1% (n=4) of patients (2 in isolated SU-AVR and 2 in C-AVR) at late follow-up in the case series of 287 patients[8].

Paravalvular leakage (PVL)

Weighted pooled estimate of PVL at 30 days follow-up (in 10 studies) was 4.3% (41/940, 95% CI 2.2 to 6.9%, I^2=60%, p=0.007) and over mean 1 year follow-up (in 10 studies) was 3.0% (95% CI 1.0 to 5.8; I^2=72%; p<0.001) in the meta-analysis of 1,037 patients in 12 observational studies on SU-AVR[1].

Moderate and severe PVL rates at discharge ranged from 0 to 3.4% (in 15 studies on 9 different cohorts) in the systematic review of SU-AVR with Perceval valves[5]. Another systematic review of SU-AVR with Perceval valves reported that PVL ranged from 0.6 to 3.85% in 2 studies at 1 year follow-up[5]. Major PVL (defined as PVL of grade +3/+4), was reported early (within 30 days) in less than 1% (n=2) and late (more than 30 days and up to 5 years) in less than 1% per patient year (n=7)[8].

SU-AVR compared with TAVI

Analysis of 6 matched comparative studies (with 1,228 patients) shows that the risk of PVL in SU-AVR group was statistically significantly lower than in the TAVI group (OR 0.13; 95% CI 0.90 to 0.17; I^2=79%, p=0.0002) in a meta-analysis of 12 studies comparing SU-AVR with C-AVR and TAVI[2].

Meta-analysis of 7 observational comparative studies showed a statistically significant reduction in post-operative PVL among patients with SU-AVR compared with TAVI (3.4% [13/376] compared with 33.1% [126/380]; OR 0.09; 95% CI 0.04 to 0.23%, p value for overall effect <0.00001; I^2=41%, p value for heterogeneity=0.12; mean difference −22.56%, 95% CI −36.59 to −8.53%; p=0.002)[3].

Pooled analysis of 8 retrospective observational cohort studies comparing SU-AVR with TAVI showed statistically significant reduction in early (less than 30 days) moderate or severe PVL with SU-AVR over TAVI (0.94% [6/636] compared with 10.22% [65/636], risk ratio [RR]=0.13, 95% CI=0.06 to 0.28, p<0.0001) in the systematic review of SU-AVR with Perceval valves[5].

Major PVL happened in 1.4% and 1% at early (less than 30 days) and late (more than 30 days) follow-up, respectively in the case series of 731 patients[7].

SU-AVR compared with C-AVR

Analysis of 4 matched comparative studies (with 1,057 patients), 3 unadjusted studies (n=768) and 1 RCT (n=94) shows that the risk of PVL in SU-AVR group was not significant compared with C-AVR (OR 2.13; 95% CI 0.89 to 5.14; p=0.09, I^2=75%) in a meta-analysis of 12 studies comparing SU-AVR with SAVR and TAVI[2].

Thromboembolic events

Weighted pooled estimate of stroke at 30 days follow-up (in 7 studies) was 1.9% 12/562, 95% CI 0.8 to 3.4%, I^2=0%, p=0.632) and over mean 1 year follow-up (in 8 studies) was 1.5% (95% CI 0.4 to 3.1%, I^2=43%; p=0.092) in the meta-analysis of 1,037 patients in 12 observational studies on SU-AVR[1].

Pooled analysis of 8 retrospective observational cohort studies comparing SU-AVR with TAVI showed no statistically significant difference in stroke rates with SU-AVR over TAVI (1.57% [10/636] compared with 2.83% [18/636], risk ratio [RR]=0.63, 95% CI=0.29 to 1.36, p=0.24) in the systematic review of SU-AVR with Perceval valves[5]. At 1 year stroke rates ranged from 0 to 3% in 2 studies.[5]

Early thromboembolic events in 4.5% (13/287) and late thromboembolic events in 1.7% per patient year (n=18) were reported in the case series of 287 patients. The majority of these events were stroke (11/18 events)[8].

Renal failure

Weighted pooled estimate of renal failure at 30 days follow-up (in 4 studies) was 3.1% (8/244, 95% CI 1.0 to 6.0%, I^2=0%, p=0.856) and over mean 1 year follow-up was 1.2% (95% CI 0 to 4.1%; I^2=52%; p=0.012) in the meta-analysis of 1,037 patients in 12 observational studies on SU-AVR[1].

SU-AVR compared with TAVI

Analysis of 5 matched comparative studies (with 1,024 patients) reported that acute kidney injury and need for renal replacement in SU-AVR group was not significant compared with TAVI (OR 0.80, 95% CI 0.49 to 1.32, I^2=68%, p=0.01) in a meta-analysis of 12 studies comparing SU-AVR with C-AVR and TAVI[2].

Pooled analysis of 6 observational comparative studies showed no statistically significant difference in post-operative acute kidney injury among patients between SU-AVR and TAVI (5.7% [20/349] compared with 4% [14/351]; OR 1.36; 95% CI 0.50 to 3.74%, p value for overall effect=0.55; I^2=30%, p value for heterogeneity=0.21)[3].

SU-AVR compared with C-AVR

Analysis of 2 matched comparative studies (with 551 patients) and 1 RCT (n=94) reported that acute kidney injury and need for renal replacement in SU-AVR group was not significant compared with C-AVR (OR 0.40, 95% CI 0.21 to 0.75, I^2=81%, p=0.02) in a meta-analysis of 12 studies comparing SU-AVR with C-AVR and TAVI[2].

Overall events

Pooled analysis of 8 retrospective observational cohort studies comparing SU-AVR with TAVI showed statistically significant reduction in overall events with SU-AVR over TAVI (1.26% [8/636] compared with 14.31% [91/636], risk ratio [RR]=0.12, 95% CI =0.06 to 0.25, p<0.0001) in the systematic review of SU-AVR with Perceval valves[5].

Reoperation rates

Reoperation rates within 30 days for bleeding or valve explantation ranged from 2.5 to 5% (in 15 studies on 9 different cohorts) in the systematic review of SU-AVR with Perceval valves[5]. At 1 year rate of reoperation was 4.2% in 2 studies[5].

Weighted pooled estimate of reoperation for bleeding (in 10 studies) was 1.4% (95% CI 0 to 3.6%; I^2=52%; p=0.103) in the meta-analysis of 1,037 patients in 12 observational studies on sutureless aortic valve replacement (SU-AVR)[1].

Valve explantation

Valve explantation ranged from 0 to 2% in 2 studies in the systematic review of SU-AVR with Perceval valves [5].

Valve explantation was reported early (within 30 days) in 1.4% (4/287) of patients (3 in isolated SU-AVR and 1 in C-AVR) and late (more than 30 days and up to 5 years) in less than 1% per patient year (n=5) (1 in isolated SU-AVR and 3 in C-AVR) in the case series of 287 patients. All of these cases were non-fatal. The reasons for the early explants were because of procedural bleeding (n=1), cardiac arrest (n=1) after 2 days and PVL (n=2) at 19 and 26 days. The reasons for the late explants were because of endocarditis (n=1), pseudoaneurysm at the annulus (n=1) and PVL (n=3)[8].

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers listed the following anecdotal adverse events: inadequate decalcification leading to paravalvular leak and redeployment valve problems. They considered that the following were theoretical adverse events: anchoring mechanism problems with new designs and valve failure.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to sutureless aortic valve replacement for aortic stenosis. The following databases were searched, covering the period from their start to 30.10.2017: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with aortic stenosis.
Intervention/test	Sutureless aortic valve replacement.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on approximately 21,393 patients from 6 systematic reviews and meta-analysis and 2 case series. There is an overlap of studies included in systematic reviews and some of the studies did not specify the number of patients included.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on sutureless aortic valve replacement for aortic stenosis

Study 1 Phan K [2015]

Details

Study type	Systematic review and meta-analysis
Country	Centres within Europe (Germany, Italy, Sweden, Belgium, Finland), Canada (1 study) USA (1 study).
Study period	Inception to 2014
Study population and number	n=**1037 patients in 12 observational studies (10 prospective, 2 retrospective and 2 propensity matched studies).** Pooled logistic EuroSCORE 11.7%, mean LVEF 58.9%
Age and sex	Mean age 77.3 years; 61.1% female
Study selection criteria	Relevant studies with patients who underwent aortic valve replacement using a sutureless valve, published in English were included. Studies were excluded if they did not report mortality or any complications, if they were duplicate publications, case reports, abstracts, reviews or conference presentations. Databases searched: 6 databases (Medline, PubMed, Cochrane central register of controlled trials, Cochrane database of systematic reviews, ACP journal club, and Database of Abstracts of Review of Effectiveness) from inception to January 2014, reference lists in relevant studies were reviewed and experts were consulted.
Technique	Sutureless aortic valve replacement (SU-AVR) using any type of sutureless valves such as Perceval S, 3f Enable, Triology or Edwards Intuity valve. Perceval was the most widely used (6 studies, n=502), 3f Enable (4 studies, n=316), Triology valve (1 study, n=32) and Edwards Intuity (1 study, n=146). Minimally invasive approach was used in 40% of included patients (20% mini-sternotomy and 20% mini-thoracotomy), conventional sternotomy in 60%, while 28.4% underwent concomitant coronary bypass surgery (CABG). Valve sizes used: 19mm in 1%, 21mm in 23.6%, 23mm in 46.3%, 25mm in 24.7%, 27mm in 5.7% of patients
Follow-up	**Varied (range in-hospital to 4 years);** **Mean 1 year (5 studies), mean 10 months (5 studies), up to 4 years (1 study), in-hospital (1 study).**
Conflict of interest/source of funding	Authors declared no conflicts of interest

Analysis

Follow-up issues: follow-up varied across studies (mean 1 year), long term data was reported only in 1 study. The meta-analysis mainly focused on short term outcomes.

Study design issues: comprehensive literature search was done, 2 investigators independently reviewed and any disagreement was resolved by discussion and consensus. Studies were appraised using a critical appraisal checklist of the Dutch Cochrane centre proposed by Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. Data were extracted and analysed according to predefined clinical endpoints. A meta-analysis was conducted and the methods were appropriate. Studies included were small with lack of randomisation and statistical power. There was significant heterogeneity in certain outcomes. The likelihood of publication bias was assessed.

Study population issues: 7 studies had 50 or more patients and 5 studies had fewer than 50 patients. Comorbidities such as hypertension (70%), diabetes (27%), coronary artery disease (35%), dyslipidaemia (57%), lung disease (14%), prior strokes (6%) and renal failure 10%) were reported in patients. Other problems such as atrial fibrillation, mitral and tricuspid insufficiency and peripheral vascular disease were reported in few studies.

Key efficacy and safety findings

Efficacy

Number of studies analysed: **12 studies**

Mean aortic cross clamp time and CBP duration (minutes)

ACC time	46.5 minutes (95% CI 38.9 to 54.0; I^2=98%; p<0.001)
CPB time	73.1 minutes (95% CI 63.2 to 83.1, I^2=97%; p<0.001)
Isolated SU-AVR CBP time	56.7 (95% CI 45.2 to 68.2; I^2=98%; p<0.001)
Isolated SU-AVR ACC time	33.1 (95% CI 25.5 to 40.8; I^2=99%; p<0.001)
Minimally invasive SU-AVR CBP time	92 .3 (95% CI 87.7 to 96.8; n=1)
Minimally invasive SU-AVR ACC time	59.3 (95% CI 56.1 to 62.4; n=1)
Full sternotomy CBP time	78.2 (95% CI 14.5 to 141.9; n=2)
Full sternotomy ACC time	53.6 (95% CI 45.6 to 91.6; n=3)

Haemodynamic outcomes

Haemodynamic outcome	**No of studies (patients)**	**Weighted pooled estimate (95% CI)**	**I^2, p value**
Mean gradient			
Discharge	8 (654)	11.128 (9.831 to 12.425)	94,<0.001
6 months	5 (529)	9.004 (8.697 to 9.311)	0, 0.663
12 months	6 (579)	9.644 (8.703 to 10.586)	86, <0.001
Peak gradient			
Discharge	5 (529)	19.61 (16.54 to 22.681)	95,<0.001
6 months	5 (529)	17.797 (16.046 to 19.547)	86, <0.001
12 months	5 (528)	17.286 (16.136 to 18.436)	69, 0.007
Effective orifice area (EOA)			
Discharge	6 (579)	1.772 (1.554 to 1.990)	98, <0.001
6 months	5 (529)	1.745 (1.499 to 1.991)	97, <0.001
12 months	6 (577)	1.731 (1.548 to 1.914)	97, <0.001

Safety

Safety outcomes

	% (95% CI, I^2; p value)
Mortality at 30 days (10 studies)	2.1 (1.1 to 3.3; 11%; p=0.341)
Mortality at 1 year (11 studies)	4.9 (2.7 to 7.7); 59%; p=0.007
Reoperation for bleeding (10 studies)	1.4 (0 to 3.6; 52%; p=0.013)
Stroke	1.5 (0.4 to 3.1)
Endocarditis	2.2 (0.8 to 4.1;58%; p=0.012)
Pacemaker implantation	5.6 (3.5 to 8.0; 25%; p=0.252)
PVR (10 studies)	3.0 (1.0 to 5.8; 72%; p<0.001)
Renal failure	1.2 (0 to 4.1; 52%; p=0.012)
Structural valve deterioration	0.4 (0 to 1.4; 0%; p=0.79)
Neurological events (early follow-up)	1.9 (0.8 to 3.4; 0%; p=0.632)
Neurological events (later follow-up)	1.5 (0.4 to 3.1; 43%; 0.092)

Abbreviations used: ACC, aortic cross clamp time; CBP, cardiopulmonary bypass; CI, confidence interval; PVR, paravalvular regurgitation; SU-AVR, sutureless aortic valve.

Study 2 Qureshi SH [2018]

Details

Study type	Systematic review and meta-analysis
Country	UK
Study period	Inception to January 2016
Study population and number	n= **12 studies (1 RCT and 11 observational studies)** **SU-AVR versus conventional SAVR (8 studies**- 1 RCT [Borger 2015], 7 observational studies [Gilmanov 2014, Pollari, 2014, Dalen 2016, Muneretto 2015, D'Onforio 2013, Vola 2015, Shrestha 2013] **SU-AVR versus TAVR (6 studies**-observational- Miceli 2016, Muneretto 2015, Binacari 2016, D'Onoforio, Kamperidis 2015, Santarpino 2015) Operative risk category: low (5 studies), intermediate (6 studies), and high risk (0).
Age and sex	Not reported
Study selection criteria	Published studies (observational or randomised) comparing sutureless aortic valve replacement (SU-AVR) with conventional surgical aortic valve replacement (SAVR) using a stentless or stented valve or with transcatheter aortic valve replacement (TAVR) of any prosthesis or approach were included. Non-comparative studies, reviews, how to do articles and feasibility and animal studies were excluded. Databases searched: Medline, Embase from inception to January 2016. Hand search of bibliographies of relevant articles was done and articles were restricted to English language.
Technique	Sutureless aortic valve implantation (SU-AVR) using Perceval S (8 studies), 3f Enable (2 studies) and Edwards Intuity valve (1 study). One study used a combination of all 3 valves (Gilmanov 2014). Minimally invasive approach in 5 studies, combined approach in 6 studies.
Follow-up	**30 days**
Conflict of interest/source of funding	None declared.

Analysis

Follow-up issues: only short term follow-up.

Study design issues: study was conducted according to a pre-specified protocol and adhered to the preferred Reporting Items for Systematic Reviews (PRISMA) guidelines. Comprehensive search strategy was used. The primary outcome was 30 day mortality. Methodological quality of observational studies was assessed using the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklist and the RCT was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. Studies were of moderate methodological quality; odds ratios were pooled using fixed and random effects models. Heterogeneity and the likelihood of publication bias was assessed. A trial sequential analysis (TSA) was done to assess the statistical reliability of cumulative evidence. Propensity matched and unadjusted evidence were pooled separately.

In the RCT, as methodological rigor for control of selection and performance bias was not established, it was considered among unmatched outcome analysis. The mean STROBE compliance score was 48%.

Authors state that there might be some potential overlapping of studies as some studies were from one centre but were considered separately for comparisons as each reported different outcomes (Gilmanov and Miceli; Pollar and Santarpino, Dallen and Pollari, Santarpino and Binacari).

Other issues: lack of separate subgroup analyses for isolated SU-AVR versus concomitant procedures, minimally invasive versus full sternotomy.

Key efficacy and safety findings

Safety

Number of patients analysed: **12 studies**

SU-AVR versus TAVI (propensity matched comparison) pooled analysis of primary and secondary outcomes.

Length of hospital stay and ICU stay

Analysis of 1 propensity-matched comparative study (with 204 patients) reported that SU-AVR was associated with shorter length of hospital stay (mean difference [MD] −2.0, 95% CI −3.65 to −0.35, p=0.02) and ICU stay (MD −1.0; 95% CI −1.86 to −0.14, p=0.02) compared with TAVI.

Outcomes	Studies	Effect estimate OR [95% CI], heterogeneity, p value
30 day-mortality	6 matched comparative studies (n=1223) SAVR3.9% (22/558) versus TAVI 9.4% (63/670)	0.40, [0.25 to 0.62], p<0.001, I^2=0%, p=0.79
Cerebrovascular accident	6 matched comparative studies (n=1223)	0.53, [0.26 to 1.05]; I^2=6%, p=0.38
Myocardial infarction	2 studies (n=582)	0.29, [0.07 to 1.20], I^2=0%, p=0.98
Need for pacemaker	6 matched comparative studies (n=1223)	0.74, [0.50 to 1.08], I^2=0%; p=0.51
Acute kidney injury and need for renal replacement	5 matched comparative studies (n=1024)	0.80, [0.49 to 1.32], I^2=68%, p=0.01
Paravalvular leak	6 matched comparative studies (n=1223)	0.13; [0.90 to 0.17]; I^2=79%, p=0.0002

SU-AVR versus conventional AVR (propensity matched comparison) pooled analysis of primary and secondary outcomes

Length of hospital stay and ICU stay

Analysis of 3 propensity-matched comparative studies (with 204 patients) reported that SU-AVR was associated with shorter ICU stay (0.11 days; 95% CI −0.17 to −0.38, p=0.44, I^2=79%, p=0.010) compared with C-AVR and analysis of 1 propensity matched study showed that SU-AVR is associated with shorter length of hospital stay (−1.50 days, 95% CI −2.62 to −0.38, p=0.009).

Outcomes	Studies	Effect estimate OR [95% CI], heterogeneity, p value
30 day-mortality	5 matched comparative studies (n=1323) SAVR 3.5% (22/621) versus CAVR 3.1% (22/702)	1.03, [0.56 to 1.88], I^2=0%; p=0.93
Cerebrovascular accident	5 matched comparative studies (n=1323), 1 RCT (n=94) and 2 observational studies (n=648)	0.89, [0.45 to 1.75]; I^2=35%, p=0.20
Myocardial infarction	3 matched comparative studies (n=817), 1 RCT (n=94)	1.22, [0.24 to 6.35], I^2=22%, p=0.28
Need for pacemaker	5 matched comparative studies (n=1323), 2 unadjusted studies (n=648)	2.16, [1.34 to 3.47], p=0.002, I^2=16%; p=0.31 5.72, [2.65 to 12.36], I^2=0%, p<0.001
Acute kidney injury and need for renal replacement	2 matched comparative studies (n=551), 1 RCT (n=94)	0.40, [0.21 to 0.75], I^2=81%, p=0.02
Paravalvular leak	4 matched comparative studies (n=1057), 3 unadjusted studies (n=768) and 1 RCT (n=94)	2.13; [0.89 to 5.14], I^2=75%, p=0.09

Abbreviations used: CI, confidence interval; Conv AVR, conventional aortic valve replacement; ICU, intensive care unit;; OR, odds ratio; SU-AVR, sutureless aortic valve replacement; TAVR, transcatheter aortic valve implantation.

Study 3 Takagi H [2016]

Details

Study type	Systematic review and meta-analysis
Country	Japan
Recruitment period	Inception to June 2015
Study population and number	n=**945 patients in 7 observational comparative studies of SU-AVR versus TAVI** (**5 propensity-score matched studies**- [Micelo 2015, Kamperidis 2015, Binacari 2015, D'Onofrio 2012, Santarpino 2014] **and 2 unadjusted studies** [Doss 2012 and Muneretto 2015)
Age and sex	SU-AVR age range 78 to 80.9 years; TAVI range 78.8 to 84.7 years SU-AVR range 59.3 to 84.2% female; TAVI range 51.5 to 78.9% female Logistic EuroSCORE: SU-AVR range 4.1 to 18.1%; TAVI range 6% to 35.3%
Study selection criteria	Comparative studies of patients with severe aortic valve stenosis, assigned to sutureless AVR versus TAVI and reporting early (in-hospital or 30 day) all-cause mortality were included. Medline and Embase were searched from inception through June 2015 using PubMed and Ovid search engines. Other relevant studies were identified through manual search of references in identified articles.
Technique	Sutureless-AVR (Perceval 5 studies, 3f Enable 2 studies) using either full sternotomy, mini thoracotomy, or mini sternotomy. TAVI –mainly transfemoral or transapical approaches, in few cases trans-aortic or trans-subclavian approaches were used (different bioprosthetic valves such as Sapien, CoreValve, Lotus and Portico were used in studies). Concomitant procedures (cardiopulmonary bypass or valve repairs or percutaneous coronary intervention) were done in some cases.
CV	**In-hospital and 30 day outcomes**
Conflict of interest/source of funding	No conflicts of interest.

Analysis

Study design issues: meta-analysis of 7 observational comparative studies with a small sample size of 945 patients. 5 of these were propensity score matched studies. Heterogeneity and the likelihood of publication bias were assessed. All analyses were done using Review Manager Version 5.3 and comprehensive meta-analysis version 2.

Study population issues: previous cardiac surgeries were done in some patients in both the groups in all studies. Comorbidities included hypertension and diabetes and there were no significant difference in rates in both groups.

Other issues: data for myocardial infarction and stroke were not pooled because of less than 4 studies.

Key efficacy and safety findings

Safety

Number of patients analysed: **7 studies**

SU-AVR versus TAVI:

Outcomes	**Studies**	**Effect estimate OR/RD/MD [95% CI], Heterogeneity, p value**
30 day-mortality	7 observational comparative studies (n=945) 2.5% (9/384) versus 7.3% (39/561)	OR 0.33, [0.16 to 0.69], I^2=0%; p=0.003, heterogeneity p=0.93 RD −5.23%, [−8.12 to −2.33]; p=0.0004
Post-operative bleeding complications	5 observational comparative studies (n=641) 4.8% (15/312) versus 0.9% (3/329)	OR 3.18, [0.91 to 11.18]; I^2=1%, p=0.07; heterogeneity p=0.40
Post-operative conduction disturbance	7 observational comparative studies (n=756) 6.9% (26/376) versus 11% (43/380)	OR 0.66; [0.24 to 1.78], p=0.41; I^2=44%, heterogeneity p=0.10
Acute kidney injury	6 observational comparative studies (n=700) 5.7% (20/349) versus 4% (14/351)	OR 1.36; [0.50 to 3.74], p=0.55; I^2=30%, heterogeneity p=0.21
Paravalvular leak	7 observational comparative studies (n=1057) 3.4% (13/376) versus 33.1% (126/380)	OR 0.09; [0.04 to 0.23], p<0.00001; I^2=41%, heterogeneity p=0.12 Mean difference −22.56%, [−36.59 to −8.53]; p=0.002

Abbreviations used: CI, confidence interval; IV, inverse variance; MD, mean difference; OR, odds ratio; SU-AVR, sutureless aortic valve replacement; RD, risk difference; TAVI, transcatheter aortic valve implantation.

Study 4 Tagaki H [2017]

Details

Study type	Systematic review and meta-analysis
Country	Japan
Study period	Inception to April 2016
Study population and number	n=**15,887 patients in 6 RCTs and 30 PSM studies** **SU-AVR versus TAVI** (n=1478 in 6 PSM studies), **SU-VAR versus C-AVR** (n=1469 in 6 studies-1 RCT, 5 PSM studies), **TAVI versus C-AVR** (n=12940 in 24 studies-5 RCTs, 19 PSM studies)
Age and sex	Mean age in SU-AVR studies: 77.5 years; C-AVR 77.9 years, TAVI 80.8 years. Sex: SU-AVR versus TAVI (female 60.5% versus 58.2%); SU-AVR versus C-AVR (52.2% versus 50.5%); C-AVR versus TAVI (50.1% versus 49.1%) Mean EuroSCORE: SU-AVR versus C-AVR studies [12.4 versus 12.2%}; TAVI versus C-AVR [18.5 vs 18.2%].
Study selection criteria	All randomised controlled trials (RCTs) and propensity score matched (PSM) studies of sutureless aortic valve replacement (SU-AVR) versus TAVI versus conventional aortic valve replacement (C-AVR) (SU-AVR versus TAVI, SU-AVR versus C-AVR, or TAVI versus C-AVR) for aortic stenosis with perioperative (30 day or in-hospital) all-cause mortality. Databases searched: Medline, Embase, and the Cochrane Central Register for Controlled Trials through PubMed and Ovid from inception to April 2016. Manual searching of references in relevant articles was also done.
Technique	Sutureless or rapid deployment aortic valve replacement (SU-AVR) with either Perceval, Intuity or Enable valves TAVI (with mainly Sapien or CoreValve): different access routes (transfemoral, transapical) were used. Conventional aortic valve replacement (C-AVR) with either mechanical, bioprosthesis, or biological prosthesis- eg Mitroflow, Perimount
Follow-up	**Perioperative (in-hospital and 30 day outcomes)**
Conflict of interest/source of funding	None

Analysis

Study design issues: data from different types of studies (RCTs and PSM studies) were extracted, odds ratios (OR) and 95% confidence intervals were generated for each individual study by use of data for mortality in both experimental and control groups. Study specific estimates were combined by means of inverse variance weighted averages of ORs in both fixed effect and random effects models. Between studies heterogeneity was assessed. Direct comparison meta-analysis (DC-MA of SU-AVR versus TAVI, SU-AVR versus C-AVR, and TAVI versus C-AVR) and an adjusted indirect comparison meta-analysis (IDC-MA of TAVI versus SU-AVR from the results of SU-AVR versus C-AVR and TAVI versus C-AVR) were performed first and then results of both direct and indirect comparisons were combined in a meta-analysis to compare SU-AVR with TAVI. All analyses were conducted using Review Manager Software. Moderate heterogeneity was noted between DC-MA and ID-MA as different devices, access route, valve sizes, and surgical approaches were used in studies.

The type of studies included in comparisons were different and could lead to different statistical power. DC-MA of SU-AVR versus TAVI was completely based on PSM studies while IDC-MA of SU-AVR versus TAVI was based on large number of patients receiving TAVI or C-AVR in RCTs.

Key efficacy and safety findings

Safety

Number of patients analysed: **15,887 (in 6 RCTs and 30 PSM studies)**

DC-MA of SU-AVR versus TAVI, SU-AVR versus C-AVR, TAVI versus C-AVR

Outcomes	Studies	Effect estimate OR (95% CI), p value, heterogeneity
DC-MA (A) SU-AVR versus TAVI		
All-cause mortality (30-day or in-hospital mortality)	6 propensity score matched [PSM] studies 2.9% (22/739) versus 6.4% (48/739)	0.48; (0.28 to 0.80); p=0.005; I^2=0%
DC-MA (B) SU-AVR versus C-AVR		
All-cause mortality (30-day or in-hospital mortality)	6 studies (1 RCT and 5 PSM studies 3.4% (24/701) versus 3.5% (27/768)	1.07; (0.60 to 1.94); p=0.81; I^2=0%
DC-MA (C) TAVI versus C-AVR		
All-cause mortality (30-day or in-hospital mortality)	24 studies 4.9% (290/5915) versus 4.2% (300/7025)	1.07; (0.90 to 1.27); p=0.45; I^2=14%

Pooled analysis of the results of DC-MA (SU-AVR versus TAVI) and adjusted IDC-MA (of SU-AVR versus TAVI from results of DC-MA [B] and DC-MA [C]) (36 studies, n=15,887))

Sub-group analysis	No of studies	OR, [95% CI]
DC-MA SU-AVR versus TAVI	6 propensity score matched [PSM] studies 2.9% (22/739) versus 6.4% (48/739)	0.48; [0.28 to 0.80]; p=0.005; I^2=0%
IDC-MA SU-AVR versus TAVI	6 RCTs and 30 propensity score matched [PSM] studies with 15,887 patients 2.9% (22/739) versus 6.4% (48/739)	1.01; [0.54 to 1.86]

In a sensitivity analysis, pooling the result of DC-MA and that of IDC-MA by random effects model produced no statistically significant difference in perioperative all-cause mortality between SU-AVR and TAVI: OR 0.68; 95% CI 0.33 to 1.41;p=0.30).

Summary of DC-MA [A,B,C], ICD-MA (SU-AVR versus TAVI), and combined DC-MA and IDC-MA (SU-AVR versus TAVI)

Sub-group analysis	OR, [95% CI]
DC-MA	
A) SU-AVR versus	0.48 [0.28, 0.80]
B) SU-AVR versus C-AVR	1.07 [0.60,1.94]
C) TAVI versus C-AVR	1.07 [0.90, 1.27]
IDC-MA SU-AVR versus TAVI	1.01, [0.54, 1.86]
DC-MA and IDC-MA	
DC-MA of SU-AVR versus TAVI	0.48, [0.28, 0.80]
IDC-MA of SU-AVR versus TAVI	1.01 [0.54, 1.86]
Combined DC-MA (of SU-AVR versus TAVI) ad IDC-MA (of SU-AVR versus TAVI)	0.65 [0.44,0.97], p=0.03, I^2=70%

Abbreviations used: C-AVR, conventional aortic valve replacement; CI, confidence interval; DC-MA, direct comparison meta-analysis; IDC-MA, adjusted indirect comparison meta-analysis; IV, inverse variance; OR, odds ratio; SU-AVR, sutureless aortic valve replacement; TAVI, transcatheter aortic valve replacement.

Study 5 Powell R [2017]

Details

Study type	Systematic review and meta-analysis
Country	Canada
Study period	2007 to October 2016
Study population and number	n=**89 studies** (**16 comparative case series** (SU-AVR versus TAVI=8, SU-AVR versus C-AVR=8; (**40 case series of SU-AVR** (of these 17 were cohort studies, 18 assessed complications, 1 study examined learning curve, 2 studies examined off label use, 2 studies performed cost analysis); a**nd 3 published recommendations for SU-AVR**).
Age and sex	Mean age range 69 to 82 years; sex: not reported
Study selection criteria	Studies with the Perceval bioprosthesis, those compared with other procedures, reported clinical outcomes, complications, off-label experience, learning curve analysis, cost analysis, and one or more cases of SAVR with the Perceval valve were included. Studies on other sutureless valves, studies that grouped outcomes of the Perceval with other prostheses in the same cohort, performed on cadaveric or animal subjects, non-English studies, not published in peer reviewed journals, conference abstracts and multiple publications of the same study were excluded. PubMED, Embase, and the Cochrane Library databases were searched.
Technique	Sutureless aortic valve replacement (SU-AVR) with the Perceval valve
Follow-up	**Varied across studies; minimum 30 days, maximum 5 years**
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: data was screened and extracted by one investigator and results were reviewed by senior investigators. Meta-analysis of summary statistics from individual studies was performed using Review Manager Software.

Study population issues: baseline characteristics were similar between groups in all comparative studies except 1, in which patients were older and had higher EuroSCORE risk.

Key efficacy and safety findings

Safety

Number of patients analysed: **89 studies**

Su-AVR versus C-AVR (8 retrospective observational cohort studies, 4 studies used PSM; n=range 14-204; maximum follow-up 2 years)

Overall ACC and CBP times were significantly shorter using SU-AVR than C-AVR valves in all studies.

Pooled analysis of SU-AVR with Perceval valve versus C-AVR

Outcomes	Studies	Effect estimate [95% CI], p value
Aortic cross clamping time (minutes)	7 studies, (n=642 versus 910) [38.6 minutes versus 66.3 minutes]	mean difference -20.71 [-24.81, -16.60], p<0.00001
CBP time (minutes)	7 studies, (n=642 versus 910) [61.4 minutes versus 84.9 minutes]	mean difference -22.83 [-27.39, -18.26], p<0.00001
ICU stay (days)	7 studies, (n=642 versus 910) [1.73 days versus 1.54 days]	mean difference −0.16, [−0.67 to 0.99, p=0.18
Early mortality (<30 days)	8 studies, (3.39% [23/678] versus 3.91% [40/1,022]	Risk ratio [RR] 0.99, [0.58 to 1.70], p=0.98
Pacemaker implantation	8 studies, 9.75% [62/636] versus 9.28% [59/636]	RR=1.36, [0.62 to 2.98], p=0.45

PPM implantation rates were significantly higher using SU-AVR in 4 studies and no significant difference was seen among both groups in another 4 studies.

Survival rates

	SU-AVR with Perceval valve through mini-sternotomy %	C-AVR through full sternotomy %	P value
Dalen 2015 (2 year follow-up)	92	91	0.463
Dalen 2016 (2 years follow-up)	92	92	NR
Konig 2014 (mean 13.6 months follow-up)	97.5	96.2	0.646

SU-AVR versus TAVI (8 studies of which 1 prospective observational cohort study and 7 retrospective observational cohort studies; 7 studies used PSM; n=range 31 to 314; maximum follow-up was 2 years)

Pooled analysis of SU-AVR with Perceval valve versus TAVI

Outcomes	Studies	Effect estimate [95% CI], p value
Aortic cross clamping time (minutes)	3 studies, (n=455 versus 455)	mean difference 0.16 [-1.16, -0.04] p=0.71
Early mortality (<30 days)	5 studies, (n=19/636 versus 44/636)	Risk ratio [RR] 0.48, [0.28 to 0.82], p=0.007
Mortality (maximum follow-up 29 months)	3 studies	Hazard ratio [HR] 0.21, [0.09, 0.48], p=0.0002
Moderate or severe paravalvular leak (<30 days)	5 studies, 0.9% [6/636] versus 10.2% [65/636]	RR 0.13, [0.06, 0.28], p<0.00001
Pacemaker implantation	5 studies, 9.75% [62/636] versus 9.28% [59/636],	RR 1.36, [0.62, 2.98], p=0.45
Stroke	5 studies, 1.5% [10/636] versus 2.8% [18/636]	RR 0.63, [0.29, 1.36], p=0.24
Overall events	5 studies, 1.2% [8/636] versus 14.3% [91/636]	RR 0.12, [0.06, 0.25], p<0.00001

Survival rates

Study	SU-AVR %	TAVI %	P value
1 year			
D'Onoforio 2016	94.2	90.6	0.16
Miceli 2016	91.6	78.6	0.1
2 years			
Miceli 2016	91.6	66.2	0.1
D'Onoforio 2016	90.6	87.3	0.46
Miceli 2016	97.3	86.5	0.015
Muneretto 2015	94.9	79.5	0.028

Minimally invasive SU-AVR (done through ministernotomy or right anterior minithoracotomy) n=5 retrospective observational cohort studies

Outcomes in minimally invasive case series (n=5 studies)

Author	n	Isolated AVR		Outcomes						
		ACC time, minutes	CPB time, minutes	30 day mortality %	Reoperation 30 days %	Stroke 30 days %	Explantation % 30 days	Pacemaker rate % 30 days	Paravalvular leak % 30 days	Endocarditis % 30 days

Miceli 2014	281	48	81	0.7	2.8	1.8	0	4.2	0.3	0
Fischlein 2015	145	35	NR	2.1	NR	NR	0	7.6	0	0
Gilmanov 2013	137	59.3± 19	92.3± 27	0	5.1	2.2	NR	3.6	1.45	0
Santarpino 2014	72	40± 13	68±18	1.4	0	0	0	5.5	0	0
Shrestha 2013	35	34± 10	70±24	0	0	0	0	8	0	2.9

Short term outcome (<30 days) data in case series (n=15 studies of 9 different cohorts)

Author	30 days mortality %	Reoperation * %	Stroke %	Explantation %	Pacemaker implantation %	Paravalvular leak %	Renal failure %	Endocarditis %
Santarpino 2011	3.7	4.5	2.2	0.9	8.1	0.5	0	0.2
Rubino 2014	3.2	2.5	1.9	0.0	8.0	0.6	1.6	-
Mazine 2015	4.0	5.0	3.0	0.0	17.0	0.0	2.0	0.0
Folliguet 2012	2.4	-	-	-	7.0	3.4	-	-
Zannis 2014	4.9	4.2	0.7	2.0	4.9	2.0	-	0.0
Flameng 2011	0	3.1	-	-	3.1	3.1	-	-
Shrestha 2008	3.3	-	-	0.0	3.3	0.0	-	0.0
Michelena 2014	0	12.5	0.0	-	37.5	0.0	0.0	0.0
Chang 2014	0	-	-	-	-	0.0	-	-
Shrestha 2014	2.1	6.2	1.3	2.1	5.9	1.7	-	0.0

*reasons for reoperation included bleeding and/or valve explantation.

Mid (>30 days to 2 years postoperatively) and long-term (>2 years) outcomes in case series (n=6 cohort studies, maximum follow-up 5 years)

		Survival					
Author	30 day mortality %	6 months %	1 year %	2 year %	3 year %	4 year %	5 year %
Santarpino 2011	3.7	93.3	91.7	NR	NR	NR	NR
Rubino 2014	3.2	92.6	90.5	87.0	NR	NR	NR
Folliguet 2012	2.4	NR	87.1	82.5	82.0	69.7	NR
Zannis 2014	4.9	NR	NR	NR	NR	NR	85.5
Flameng 2011	0.0	NR	90.7	NR	NR	NR	NR
Shrestha 2008	3.3	90.0	86.4	86.4	86.4	86.4	71.3

Complications in case series (n=6 cohort studies, maximum follow-up 5 years)

Reoperation	Stroke	Explantation	Pacemaker rate	Paravalvular leak	Endocarditis
4.% at 30-d	2.2% at 30-d, 2.9% at 6-mo, 3.0% at 1-y	0.9% at 30-d, 1.9% at 6-mo, 1.9% at 1-y	8.1% at 30-d, 8.8% at 6-mo, 9.6% at 1-y	0.5% at 30-d, 0.6% at 6-mo, 0.6% at 1-y	0.2% at 30-d, 1.1% at 6-mo, 1.4% at 1-y
2.5% at 30-d, 4.2% at 1-y, 4.2% at 2-y	1.9% at 30-d, 1.9% at 1-y, 1.9% at 2-y	0% at 30-d	8% at 30-d	0% at 30-d	0.8% at 1-y 0.8% at 2-y
NR	NR	NR	7% at 30-d	3.37% at 30-d, 3.85% at 1-y, 3.85% at 2-y	1.44% at 2-y
4.2% at 30-d, 4.2% at 1-y, 4.9% at 3-y	0.7% at 30-d	2.0% at 30-d, 2.0% at 1-y, 2.7% at 3-y	4.9% at 30-d	2.0% at 30-d	0% at 30-d, 0% at 1-y, 0.7% at 3-y
3.1% at 30-d 6.2% at 6-mo	0% at 30-d, 0% at 6-mo, 0% at 1-y	NR	3.1% at 30-d	0% at 30-d, 3.22% at 6-mo, 3.22% at 1-y	0% at 30-d, 3.1% at 6-mo, 3.1% at 1-y
3.33% at 30-d	NR	0% at 30-d 0% at 5-y	3.33% at 30-d	0% at 30-d, 3.33% at 1-y, 6.67% at 5-y	0% at 30-d, 3.33% at 1-y, 6.67% at 3-y

*reasons for reoperation included bleeding and/or valve explantation.

Special use and off-label procedures

Small aortic roots n=7 studies (1 prospective randomised study (Dedeilias 2016), 5 retrospective cohort studies (Shrestha 2016, Beckmann 2016, Shabi 2016, Ghoneim 2016, Villa 2015) and 1 case report [Biakoussis 2016])

Study	Aortic annulus size	Outcomes	SU-AVR	Stented valves	P value
Dedeilias 2016 (RCT)	<30mm	Post-operative EOA (cm^2)	1.5±0.3 (n=25)	1.1±0.5 (n=25)	0.002
Shrestha 2013	<20mm	Post-operative EOA (cm^2)	1.5±0.25 (n=50)	1.3 ±0.2 (n=70)	<0.001
		30 day mortality	0%	5.3%	NS
		5 year mortality	14%	17.4%	NS
Shabi 2016	<21mm	Post-operative EOA index (cm^2/m^2)	1.12 ±0.2 (n=22)	0.82±0.1 (n=22)	0.02
		Postoperative peak transvalvular gradient mmHg	15±7	20±11	0.02
Ghoneim 2016	<21mm		**SU-AVR (n=49)**	**Stented AVR (n=249), aortic root enlargement (n=20), stentless AVR (n=23)**	
		Post-operative gradient mmHg	10.9±6.2	NR	<0.001
Beckmann 2016			**SU-AVR (n=92)**	**Aortic root enlargement (n=36)**	
		Post-operative EOA index (cm^2/m^2)	0.83±0.14	0.91±0.2	0.040

One study (Villa 2015) reported no significant differences in complication rates and hemodynamic outcomes in patients receiving small valves (n=47) compared to those receiving medium and large valves (n=229).

Bicuspid aortic valves:
In a case series of 25 patients (Nguyen 2015) with SU-AVR in bicuspid aortic valve, rates of in-hospital mortality, PPM implantation, stroke and PVL were 4%, 20%, 8%, and 0%. In a case report (Santarpino 2012) SU-AVR was successful and postoperative course was uneventful.

Redo procedures

1 study reported that complication rates and hemodynamic outcomes were similar in SU-AVR (n=8) and ViV TAVI (n=6) patients undergoing redo procedures (Santarino 2016). Another study of 13 patients with redo SU-AVR reported that there were no major complications and all patients were alive at 8.5 months follow-up (Santarpino 2013).
SU-AVR was successfully done in 1 patient with severe TAVI prosthesis thrombosis (Poels 2015), in 1 patient with pannus overgrowth in bioprosthesis resulting in narrowed LV outflow (Chris 2016).

Redo for homograft (n=3, Capestro 2015, Canadyova 2015, Folliguet 2013)
3 case studies reported on the successful use of SU-AVR in calcified homograft replacement (severe AR was reported in all patients so valve leaflets were excised and SUAVR was done). Postoperative course was uneventful in all.

Redo for stentless prosthesis failure (n=5, Lio 2016, Kim 2015, Villa 2013, Repossini 2015))
5 cases have reported on the successful use of redo SU-AVR for stentless bioprosthesis failure (for root narrowing and rupture between coronary leaflets in 1, coronary leaflet tear causing severe AI in 1, low LVEF in 1, severe AR in 2). Postoperative course was uneventful in all.

Valve in valve TAVI (3 studies)
In 1 patient who had SU-AVR and severe PVL, Perceval valve collapsed at the non-coronary sinus and a ViV TAVI was done and postoperative course was uneventful (Eusanio 2015).
In 1 patient with severe aortic regurgitation and cardiogenic shock (who had SU-AVR plus CABG 3 years ago), ViV TAVI was done and patient was asymptomatic at 30 days (Durand 2015).
In another patient with deformed Perceval valve and severe AR, ViV TAVI was done and patient was asymptomatic at 6 months follow-up (Landes 2016)

Concomitant valve procedures (4 studies)
SU-AVR has been successfully used in patients who had triple valve surgery [tricuspid valve repair, aortotomy, and MVR] (Mazine 2015), with concomitant tricuspid valve repair in a patient who had previous MVR (Mazine 2013), with concomitant MVR in 10 patients (Minh 2014), with MVR in a patient who severe root calcification (Lio 2016), with MVR in a patient with small aortic root (Moriggia 2015).

Porcelain aorta (n=5, 2 studies)
In 5 patients with porcelain aorta SU-AVR with Perceval valve was successful and postoperative course was uneventful and asymptomatic at 6 months follow-up (Santarpino 2012, Gatti 2014).

Endocarditis (n=5, 1 study)
In a case series of 5 patients with prosthetic valve endocarditis, SU-AVR was successful in all patients with one in-hospital death due to septic shock and organ failure. At 30 days follow-up no complications were reported (Lio 2015).

Other complications

	n
Structural valve deterioration (Votsch 2016, Bouhout 2016)	n=2 (in 1 patient with SU-AVR, early structural valve deterioration [stiffened leaflets] was noted, prosthesis was removed and a mechanical prosthesis implanted; in another patient valvular thrombosis of the leaflet was noted after several months, prosthesis was removed and a mechanical valve implanted.
Stent distortion at the non-coronary sinus leading to PVL (Fleissner 2015)	N=2, patients developed moderate to severe leakage, one patient was re-operated and reimplanted with a C-AVR, another received balloon dilatation of the prosthesis.
Platelet count drop with no adverse events (Jiritano Stanger 2016, Flameng 2011)	Postoperative decrease in platelet count was seen in Perceval valves compared to other conventional or sutureless valves but it was associated with a lower need for red blood cell or platelet transfusions (p=0.001). In another study of 32 patients, a moderate decrease in platelet count was seen at 6-12 months (p<0.001). When compared to another sutureless valve (Intuity valve), platelet count was lower in Perceval valve group.

Abbreviations used: AR, aortic regurgitation; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; C-AVR, conventional aortic valve replacement; CC, cross-clamp; CI, confidence interval, CS, case series; CPB, cardiopulmonary bypass; EOA, effective orifice area; F/U, follow-up; ICU, intensive care unit; LAAC, left atrial appendage closure; LVEF, left ventricular ejection fraction; MS, ministernotomy; MVR, mitral valve replacement; NYHA, New York Heart Association; PNRCT, prospective non-randomised clinical trial; POC, prospective observational cohort, PSM, propensity score matched; PVL, paravalvular leak; RAMT, right anterior minithoracotomy; ROC, retrospective observational cohort; SU-AVR, sutureless aortic valve replacement; SD, standard deviation; TAVI, transcatheter aortic valve implantation; ViV, valve-in-valve.

Study 6 Sian K [2017]

Details

Study type	Systematic review and meta-analysis
Country	Australia
Study period	2000-2016
Study population and number	n=**2,505 patients in 14 observational studies** (7 prospective and 7 retrospective studies) Comparative studies (n=6): SU-AVR versus C-AVR versus TAVI (n=1); SU-AVR versus C-AVR (n=1); Minimally invasive surgery versus full sternotomy (n=3); SU-AVR with smaller valves versus larger valves (n=1)
Age and sex	Mean age 78.7 years (range 76.6 to 80.4 years); 61.5% female mean body surface area:1.78m^2; mean NYHA class III or IV: 70.9% (range 47.7 to 100%); mean LVEF:56.9%
Study selection criteria	Inclusion criteria: observational studies with patients undergoing Perceval valve implantation were included. Case series, case reports with less than 30 patients, abstracts, expert opinions and editorial reports were excluded. From 2000-2016 Medline, Embase, PubMed and Cochrane databases were searched. Further relevant studies were identified using reference lists of relevant articles and the company website.
Technique	SU-AVR using Perceval valves: despite minor variations, similar technique was performed at different centres. Surgical approach was via a thoracotomy, mini sternotomy or full sternotomy. Median sternotomy approach was used most frequently (mean 75.2% [1022/2505]). Minimally invasive surgery was done in 976 patients of which 336 were via the right anterior thoracotomy approach. Perceval valve sizes used: small in 22%, medium (22-23mm) in 46.4% (n=780), large (24-25mm) and XL in 40.3% (n=770) of patients. Additional cardiac procedures were done in 42.6% of patients.
Follow-up	**Mean 6 to 8 months (3 studies), 10 to 16 months (5 studies), and 18 to 24 months (3 studies).**
Conflict of interest/source of funding	No conflicts of interest

Analysis

Follow-up issues: loss to follow-up was inconsistently reported in studies. Loss to follow-up at 1 year was weighted mean 4.1% (95% CI 0 to13%).

Study design issues: studies were mainly observational, data extraction was done by 2 reviewers using standardised data extraction tables. Quality appraisal of studies was done using a critical review checklist from the Dutch Cochrane Centre as suggested by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. Any disagreements were resolved by discussion. Patient selection criteria for SU-AVR varied across studies. 7 studies reported multicentre data and 11 centres reported results in more than 100 patients. The majority of studies reported explicit inclusion criteria and operative technique. European score for Cardiac Operative risk Evaluation (EUROSCORE) was inconsistently reported in studies.

Study population issues: patients had various comorbidities and hyperlipidaemia and hypertension were mainly reported in the majority of patients.

Other issues: the majority of studies only reported early haemodynamic and survival outcomes. Long term data was only reported for a few patients. Studies might be prone to publication bias as they involved the same centres.

Key efficacy and safety findings

Efficacy and safety

Number of patients analysed: **14 studies**

Procedural outcomes

Weighted mean ACC time (minutes)	
Isolated SU-AVR	39.7 (range 35-92.3)
Combined procedures	45.6
Weighted mean CPB time (minutes)	
Isolated AVR	64.2 (range 35-92.3)
Combined procedures	66.5
Other	
Conversion to sternotomy % (range)	1.2 (0.6-1.4)
ICU stay (days)	2.3 (95% CI 1.0-3.2)
Hospital stay (days)	11.0 (95% CI 7.1-13.4)

Haemodynamic outcomes

	Preoperative	**postoperative**	**6 months**	**1 year**	**2 years**
Mean gradient (mmHg)	45.6 (95% CI 38.8-51.9)	12.1 (9-14.6)	10.1 (8.9-12.8)	10.1(8.9-12.5)	9.9 (8-11.8)
EOA (cm^2)	0.75 (range 0.7-0.8)	1.5 (range 1.4-1.6)			
EOA index (cm^2/m^2)		0.85 (range 0.80-0.90)			

Long term functional and survival outcomes

	1 year (6 studies)	**2 years (3 studies)**	**3 years (4 studies)**	**5 years (2 studies)**
Survival (weighted mean %, 95% CI)	86.8 (87.1-100)	85.6 (82.4-86.4)	72.4 (60.9-84.0)	83.0 (71.3-85.5)
NYHA class I,II at 1 year (weighted mean %, 95% CI)	90.0 (82.0-96.0)	NR	NR	NR

Safety pooled analyses data

Safety outcomes	**Weighted mean % (95% CI)**
30 day mortality rate	2.3 (1.44-3.25)
Pacemaker implantation	6.76 (4.68-8.86)
Cerebrovascular accidents	1.73 (1.23-2.22)
New onset of atrial fibrillation	24.6 (2.3-54.5)
Cardiac tamponade	4.6 ((3.3-5.4)
Myocardial infraction	0.6 (0-0.8)
Reoperation	1.4 (0-4.1)
Explantation of the SU valve	3.9 (2.5-10)
Infection	0.6 (0-6.7)
Mild PVL	4.7 (0-15.6)
Moderate to severe PVL	5.4 (0-8.7)
Endocarditis	0.8 (0.5-6.7)

Abbreviations used: ACC, aortic cross clamp; CPB, cardiopulmonary bypass; CI, confidence interval; EOA, effective orifice area; ICU, intensive care unit; NR, not reported; NYHA, New York Heart Association; PVL, paravalvular leak; SU-AVR, sutureless aortic valve replacement.

Study 7 Shrestha [2017]

Details

Study type	Case series (cumulative results of 3 trials Pilot, Pivotal, CAVALIER studies)
Country	Europe (25 centres)
Recruitment period	2007-2012
Study population and number	n=**731 patients** from 3 prospective European trials type of valve lesion: valve stenosis in 69.7% (509/731); steno-insufficiency in 30.2% (221/731)
Age and sex	Mean age 78.5 years (range 62-92 years, 40% >80 years old); 68.1% female Mean logistic EuroSCORE: 10.9±8.2%; mean STS score: 8.5±8.6%
Study selection criteria	Symptomatic patients aged 75 or older (in one study the age limit was lowered to 65 years or older), suitable for SUAVR and offered treatment if they fulfilled the selection criteria defined in each study protocol.
Technique	SU-AVR using Perceval aortic valve of different sizes (small-19-21mm [n=122], medium-21-23mm [n=383], large-23-25mm [n=226]) mainly in tricuspid valves (97.7%). minimally invasive approach in 25.9% (189/731), median sternotomy in 74.1% (542/731) Isolated AVR in 68.1% (498/731), concomitant procedures in 32.8% (242/731) patients, CABG in 26.3% (192/731) of patients with coronary artery disease. Patients received anticoagulant treatment as per standard protocol.
Follow-up	**Cumulative follow-up 729 years**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: follow-up was done at planned intervals (discharge, 30 days, 3-6 months, 12 months and then annually for up to 5 years.

Study design issues: multicentre large cohort study. Analysis of images were done by the core laboratory and an independent clinical events committee reviewed all complications. Statistical analyses were done using SAS software. Cumulative survival and freedom from events were assessed using Kaplan Meier method.

Study population issues: patients had multiple risk factors (mainly hypertension), only 2.3% patients had previous cardiac surgeries and 20% had rhythm disorders. Patients were mainly in NYHA class II (22%) and III (67%).

Key efficacy and safety findings

Efficacy and safety

Number of patients analysed: **731**

Procedure timings

	Isolated AVR (n=498)	Concomitant AVR (n=233)	Total (n=731)
Median sternotomy approach			
ACC time	30.8±10.8	51.5±23.6	39.2±19.9
CPB time	50.8±19.5	79.5±33.3	62.4±29.5
Minimally invasive approach			
ACC time	37.6±12.0	42.6±13.7	37.9±12.1
CPB time	64.4±19.2	68.5±23.1	64.719.5
Overall group			
ACC time	33.3±11.7	51.0±23.2	38.818.2
CPB time	55.8±20.5	78.9±32.9	63.0±27.2

Haemodynamic outcomes

	Pre-operative	Discharge/1 month	3-6 months	1 year	2 years	3 years	4 years	5 years
LVEF (%)	60.1±11.6	58.4±11.2	60.7±9.9	61.4±9.9	67.0±8.5	67.0±8.9	66.1±9.1	65.8±7.7
MPG (mmHg)	42.9±16.4	10.3±4.4	8.9±4.3	8.9±4.7	8.8±3.9	7.7±2.8	7.8±3.8	8.8±4.6
PPG (mmHg)	74.0±25.6	20.4±8.5	17.8±7.7	17.7±8.0	20.0±7.9	16.0±5.2	17.8±8.1	21.1±9.7
EOA (cm^2)	0.75±0.23	1.49±0.39	1.51±0.37	1.55±0.37	1.70±0.46	1.64±0.42	1.68±0.43	1.80±0.30
LV mass (g)	254.5±77.6	238.6±74.3	216.2±66.5	216.6±70.6	188.6±66.1	177.4±46.9	116.0±12.7	227.7±74.3

Functional status

Decrease in NYHA status was observed in majority of patients. 89 and 91% of patients were in classes I and II at 12 months and 2 years respectively.

Safety

	Early events (<30 days) % (n)	Late events (>30 days) % (n)	Total % (n)
Deaths (overall)	3.4 (25/731)*	7.0 (51/731)	10.4 (76/731)
Cardiac deaths	1.9 (14/731)	1.4 (10/731)	2.1 (24/731)
Non cardiac deaths	1.1 (8/731)	4.1 (30/731)	5.2 (38/731)
Sudden unexpected, unknown death	0.4 (3/731)	1.5 (11/731)	1.9 (14/731)
Explants	1.4 (10/731)^	1.5 (11/731)^^	2.9 (21/731)
Thromboembolism	4.0 (29/731)	2.3 (17/731)	6.3 (46/731)
Stroke	1.6 (12/731)	0.8 (6/731)	2.5 (18/731)
Non-structural valve dysfunction	2.0 (15/731)	1.5 (11/731)	3.6 (26/731)
Intra-prosthetic regurgitation	0.6 (4/731)	0.1 (1/731)	0.7 (5/731)
Paravalvular leak	1.4 (10/731)	1.2 (9/731)	2.6 (19/731)
Secondary paravalvular leak	0.1 (1/731)	0.1 (1/731)	0.3 (2/731)

Endocarditis	0.3 (2/731)	1.6 (12/731)	1.9 (14/731)
Valve thrombosis	0	0	0
Structural valve deterioration	0	0	0
Haemolysis	0.6 (4/731)	0.6 (4/731)	1.1 (8/731)
AV block III in patients without prior history of cardiac abnormalities leading to pacemaker implantation	6.0 (44/731)	1.4 (10/731)	7.4 (54/731)

*3 occurred in operating theatre (acute myocardial infarction in 1, annulus rupture during standard AVR for paravalvular leak after SU-AVR in 1 and myocardial failure during device removal for endocarditic lesion in 1).

^ 3 due to mis-sizing, 5 due to mis-positioning, 1 due to endocarditis, 1 due to bleeding from a tear below the right coronary ostium during decalcification of the annulus).

^^ 8 due to endocarditis, 1 due to left shunt between aorta and right ventricle, 1 to fibrous pannus overgrowth, 1 due to pseudo-aneurysm of the non-coronary sinus resulting in paravalvular regurgitation.

Abbreviations used: ACC, aortic cross clamp; CPB, cardiopulmonary bypass; CI, confidence interval; EOA, effective orifice area; ICU, intensive care unit; LV, left ventricle; LVEF, left ventricular ejection fraction; MPG, mean pressure gradient; NYHA, New York Heart Association; PPG, peak pressure gradient; PVL, paravalvular leak; SU-AVR, sutureless aortic valve replacement.

Study 8 Laufer G [2017]

Details

Study type	Case series (TRITON trial: NCT01445171)
Country	Germany & Austria (6 centres)
Recruitment period	2010-12
Study population and number	n=**287 patients** with aortic valve stenosis
Age and sex	Mean age 75.3 ± 6.7 years; 49.1% (139/287) female Mean logistic EuroSCORE (%):283: 8.4 ± 6.7; mean STS score (%): 282: 3.5 ± 3.5; LVEF (%): 188: 61.2 ± 11.1; left ventricular mass (g): 170: 233.3 ± 61.6 NYHA class I 4.9 (14/283), class II 41.7 (118/283), class III 50.2 (142/283), class IV 3.2 (9/283).
Study selection criteria	Patient selection was based upon an appropriate patient risk profile and surgeon preference.
Technique	Rapid deployment aortic valve replacement (AVR) with Edwards INTUITY valve system (generation I and II devices were used). valve sizes: 19mm (n=6), 21mm, (n=85), 23mm (n=99), 25mm (n=78) and 27mm (n=19). 55.1% (158/287) patients underwent isolated AVR and 44.9% (129/287) patients underwent AVR with concomitant procedures: coronary artery bypass grafting (n=78), or other procedures (n=51) such as atrial ablation (n=16), septal myectomy (n=4), aortic aneurysm/dissection repair (n=4). Anticoagulant therapy was given for 3 months after implantation in accordance to guidelines.
Follow-up	**Mean 3.7 ± 1.4 years; 5 years (in 89 patients) corresponding to a total of 1,050 late patient years of follow-up.**
Conflict of interest/source of funding	Study sponsored and data collected by Edwards Lifesciences; authors received consulting fees and/or honorarium from Edwards Lifesciences, Thoratec and Sorin.

Analysis

Follow-up issues: patients were followed up at 1 month, 3 months, and thereafter annually from 1 to 5 years.

Study design issues: prospective, multicentre study; haemodynamic outcomes were evaluated at planned intervals by an independent echocardiography core laboratory and safety events were assessed by an independent clinical events committee and freedom from events were assessed using Kaplan Meier method. Safety end-points were stratified by type of AVR surgery (isolated SU-AVR and C-AVR).

Key efficacy and safety findings

Efficacy and safety

Number of patients analysed: **287**

Haemodynamic outcomes (p valve to postoperative discharge)

	Postoperative discharge mean±SD (n)	**1 year mean±SD (n)**	**3 years mean±SD (n)**	**5 years mean±SD (n)**
EOA(cm^2)	1.7±0.2 (178)	1.7±0.2 (211) p=0.932	1.7±0.2 (177) p=0.205	1.6±0.3 (57) p=0.077
EAO index (cm^2/m^2)	0.9 ± 0.1 (165)	0.9 ± 0.1 (187) p= 0.253	0.9 ± 0.1 (154) p= 0.915	0.9 ± 0.2 (51) p= 0.686
Mean gradient (mmHg)	10.6 ± 4.2 (226)	9.0 ± 3.5 (230) p=0.326	9.6 ± 4.3 (185) p=0.389	10.5 ± 5.4 (59) p=0.188
Peak gradient (mmHg)	20.0 ± 7.6 (227)	16.9 ± 6.1 (230) p=0.242	17.6 ± 7.4 (185) p=0.776	18.9 ± 9.3 (59) p=0.426
LV mass (gms)	217.8 ± 62.5 (100)	184.3 ± 47.7 (178) p=0.107	186.9 ± 48.0 (135) p=0.397	191.6 ± 44.2 (37) p=0.583
LV mass index (gms/m^2)	117.6 ± 32.1 (93)	100.5 ± 23.5 (162)	100.8 ± 23.9 (123)	104.7 ± 23.4 (34)
Cardiac index $(l/min)/m^2$)	2.7 ± 0.6 (176)	2.6 ± 0.7 (191) p=0.344	2.6 ± 0.6 (157) p=0.608	2.6 ± 0.5 (52) p=0.567
LVEF (%)	62.0 ± 10.0 (134)	63.3 ± 9.3 (146) p=0.693	62.5 ± 8.1 (76) p=0.346	60.0 ± 12.5 (6) p=0.484

Patient prosthesis mismatch

	None [EOAI >0.85 cm^2/m^2]; % (n of events/n of patients)	**Moderate [EOAI 0.65–0.85 cm^2/m^2];% (n of events/n of patients)**	**Severe [EOAI <0.65 cm^2/m^2]; % (n of events/n of patients)**
Discharge	67.3% (111/165)	30.3% (50/165)	2.4% (4/165)
1 year	72.2% (135/187)	25.1% (47/187)	2.7% (5/187)
3 years	72.1% (111/154)	24.0% (37/154)	3.9% (6/154)
5 years	64.7% (33/51)	27.5% (14/51)	7.8% (4/51)

Functional outcomes

NYHA functional class: At 5 years, 63.2% of patients' substantially improved NYHA class from baseline, while 25.3% of the patients remained in the same NYHA class and 11.5% of the patients worsened.

Safety outcomes

	Early events			**Late events**		
	iAVR %(n=158)	**cAVR % (n=129)**	**P value**	**iAVR late patient years =588 %/ppy (n)**	**cAVR late patient years =462.2 %/ppy (n)**	**P value**
All-cause mortality	1.3 (2)	2.3 (3)	0.495	2.7 (16)	4.5 (25)	0.118
Valve related	1.3 (2)	0.8 (1)	0.684	0.2 (1)	0.2 (1)	0.865
Cardiac related	1.3 (2)	1.6 (2)	0.838	0.5 (3)	2.6 (12)	0.005
Thromboembolism	5.1 (8)	3.9 (5)	0.630	2.0 (12)	1.3 (6)	0.361
Stroke/TIA	4.4 (7)	3.1 (4)	0.560	1.7 (10)	1.1 (5)	0.405

Non-cerebral embolism	0.6 (1)	0.8 (1)	0.885	0.3(2)	0.2 (1)	0.710
All bleeding	9.5 (18)	8.5 (12)	0.777	3.2 (19)	2.8 (13)	0.700
Major bleeding	7.6 (13)	7 (9)	0.842	2.4 (14)	1.9 (9)	0.637
All paravalvular leak	11.4 (18)	8.5 (11)	0.423	4.1 (24)	4.5 (21)	0.720
Major paravalvular leak	0.6 (1)	0.8 (1)	0.885	0.5 (3)	0.9 (4)	0.484
Haemolysis	0	0	0	0.2 (1)	0	0.375
Endocarditis	0	0	0	0.2 (1)	0.2 (1)	0.865
Structural valve deterioration	0	0	0	0.3 (2)	0.4 (2)	0.809
Valve explant	1.9 (3)	0.8 (1)	0.419	0.2 (1)	0.9 (4)	0.105
Permanent pacemaker implant	5.3 (8)	9.0 (11)	0.224	1.2 (7)	2.3 (10)	0.200

Abbreviations used: ACC, aortic cross clamp; cAVR, concomitant aortic valve replacement; CPB, cardiopulmonary bypass; CI, confidence interval; EOA, effective orifice area; iEOA, effective orifice area index; iAVR, isolated aortic valve replacement; LV, left ventricle; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PPY, per patient year; PVL, paravalvular leak; SD, standard deviation; SU-AVR, sutureless aortic valve replacement; TIA, transient ischemic attack.

Validity and generalisability of the studies

- The overview has been restricted to bioprosthetic valves as sutureless mechanical valves appear to be no longer in use. Sutureless AVR can be performed using either a self-expanding bioprosthesis or a rapid-deployment valve.
- Currently 3 prostheses (3f Enable, Edwards Intuity and Sorin Perceval S) are marketed. Perceval has most studies with long term follow-up and Edwards Intuity has very few published studies.
- Most of the studies are observational (prospective and retrospective analyses) with short and mid-term follow-up.
- There is only one randomised controlled trial comparing SU-AVR with C-AVR.
- There are no randomised controlled studies comparing SU-AVR with other alternative methods such as TAVI.
- The comparative data is mainly from non-randomised comparative studies between SU-AVR and conventional surgical AVR or TAVI with propensity matching in different centres. Most of the meta-analysis focus on short term performance and safety.
- There is very limited long term evidence on safety, valve durability and haemodynamic performance.

Existing assessments of this procedure

The Canadian Agency for Drugs and Technologies in Health (CADTH) in 2015 assessed evidence on sutureless valves for the treatment of aortic stenosis and suggested that '*SU-AVR has comparable outcomes to surgical aortic valve replacement (SAVR), but results in higher rates of paravalvular leakage and pacemaker implantation. However, SU-AVR has lower rates of paravalvular leakage and pacemaker implantation than transcatheter aortic valve replacement (TAVR). It is currently unclear which patients are the best candidates for SU-AVR, or whether one valve type is superior to another in certain patients*'[9].

Another CADTH rapid response summary in 2015 focused on Perceval valve but reviewed all sutureless valves and suggested that *'sutureless AVR in aortic stensosis (AS) with Perceval valve is feasible, may enable less invasive surgical*

approaches and has short term safety and effectiveness in restoring aortic valve function. Longer term safety and effectiveness and determination of optimal surgical approaches is ongoing. There is no randomised evidence suggesting which strategy is optimal: SAVR, SU-AVR, or TAVI. Data comparing alternative strategies is limited, non-randomised comparisons are small and methodological quality is unclear. Currently patients are selected by individual case review and expert opinion[10].

An international valvular surgery study group (IVSSG) in 2015 assessed the evidence for SU-AVR and concluded that

- *'The introduction of multi-institutional databases, appropriate analyses from retrospective and prospective registry data will promote closer collaboration among all centers and allow sufficiently powered statistical analyses for risk factor prediction and indications for SU-AVR surgery based on patient risk profiles and predicted prognosis.*

- *Data and statistical analyses from the retrospective and prospective international registries will provide the basis for scientific publications on short- and long-term efficacy, complications and hemodynamic outcomes of SU-AVR, as well as potential risk factors and prognosis.*

- *The SU-AVR-International Registry initiated by the IVSSG will be the first independent global collaborative effort with the aim of providing the best evidence available for SU-AVR'[11].*

2 consensus papers on sutureless and rapid deployment valves in standard approach and minimally invasive approaches were published by expert groups[11, 12]. The first paper provided the following expert recommendations on the use of sutureless AVR and rapid deployment valves in comparison with conventional stented AVR[12].

Recommendation	Level of Evidence	Strength of Recommendation
1. Proctoring and education are necessary for the introduction of sutureless AVR on an institutional basis as well as for the individual training of surgeons	C	I
2. Consider sutureless AVR as an alternative to stented valves in patients requiring SAVR with a biological valve, especially for redo or delicate aortic wall conditions as calcified root, porcelain aorta or prior implantation of aortic homografts of stentless valves	C	IIa
3. Consider sutureless AVR as the valve prosthesis of first choice in cases requiring concomitant procedures and in case of small aortic annulus to reduce CC time	B	IIa
4. Preoperative CT recommended	C	I

5. Intraoperative TEE recommended	C	I
6. Suitable annular sizes (after decalcification) 19-27mm	C	I
7. Oversizing with sutureless valves is not beneficial and can have a negative impact	C	I
8. Contraindication for bicuspid valves type 1 and 2 if coronary ostia do not have 180-degree position, annulus round or uniform height of the commissures (type 2)	C	IIa
9. Contraindication for annular abscess or destruction due to infective endocarditis	C	III
10. Careful but not complete decalcification of the aortic root is recommended to avoid paravalvular leakage; extensive decalcification should be avoided not to create annular defect	C	I
11. Recommendation of proximal anastomoses of concomitant CABG during single aortic CC period	C	I

The second series focused on minimally invasive SU-AVR and the following recommendations were given[13]

Recommendation
1. Use of sutureless AVR with minimally invasive approaches in patients requiring biological valve replacement and not serving as candidates for TAVI
2. Use of sutureless AVR are recommended in order to reduce CC and CPB times
3. Suitable annular sizes (after decalcification) of 19-27mm
4. Oversizing with sutureless valves is not beneficial and can have negative impact
5. Contraindication for annular abscess or destruction due to infective endocarditis
6. Contraindication for bicuspid valve type 0
7. Contraindication for bicuspid valves type 1 and 2 if coronary ostia do not have 180-degree position, round annulus or uniform height of the commissures (type 2)
8. Use of sutureless AVR reduces early complications as prolonged ventilation, blood transfusions, atrial fibrillation, pleural effusions, paravalvular leakages and aortic regurgitation, and renal replacement therapy
9. Use of sutureless AVR results in reduced ICU and hospital stay
10. Use of sutureless AVR will lead to a higher adoption rate of minimally invasive approaches in SAVR
11. Take respect to necessary, brief learning curves for both sutureless and minimally invasive programs

The National Health Committee and Executive in 2015 recommended to the Ministry of Health in New Zealand that

1. *'Current evidence base on SU-AVR is limited. Randomised controlled trials with short follow-up time suggest that sutureless AVR is safe with low incidence of complications and comparable mortality, compared with conventional surgical AVR. This is supported by observational studies. Compared with TAVI, sutureless AVR may have lower rates of paravalvular leak.*

2. Sutureless AVR is a substitute procedure for conventional surgical AVR in high-risk patients; as such it is not expected to significantly expand the population pool receiving surgical AVR.

3. There may be between five and ten percent of AVR patients that could benefit from sutureless AVR; potential beneficiaries of the procedure include patients with anatomical features that make suturing difficult or risky such as a heavily calcified aortic annulus or a very small aortic root.

4. Sutureless AVR should not replace conventional surgical AVR as the standard of care for severe symptomatic AS. If clinicians would prefer to use sutureless valves, there seems to be sufficient justification in them doing so; providing the sutureless valve is a similar price to conventional bioprosthetic valves'[14].

A rapid HTA report in 2015 comparing sutureless aortic valve replacement (Su-AVR) to traditional aortic valve replacement (AVR) and to transcatheter aortic valve implantation (TAVI) concluded that '*available data show that the efficacy and safety on short term outcomes between SU-AVR and traditional valve implantation using sternotomy was substantially similar. However, large randomised controlled trials with long term outcome assessment are needed. The evidence regarding the effectiveness and safety of SU-AVR as an alternative to traditional AVR is limited. One randomised trial and three controlled clinical trials were identified and the overall quality of the evidence was moderate. No statistical difference in overall mortality and cause-specific mortality between the two groups were found. Clinical outcomes and safety events were similar between SU-AVR and conventional valves using traditional sternotomy approach'*[15].

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Transcatheter aortic valve implantation for aortic stenosis. Interventional procedures guidance 586 (2017). Available from https://www.nice.org.uk/guidance/ipg586

- Transcatheter valve-in-valve implantation for aortic bioprosthetic valve dysfunction. Interventional procedures guidance 504 (2014). Available from https://www.nice.org.uk/guidance/ipg504
- Percutaneous fetal balloon valvuloplasty for aortic stenosis. Interventional procedures guidance 175 (2006). Available from https://www.nice.org.uk/guidance/ipg175
- Balloon valvuloplasty for aortic valve stenosis in adults and children. Interventional procedures guidance 78(2004). Available from https://www.nice.org.uk/guidance/ipg78

NICE guidelines

- Acute heart failure: diagnosis and management. NICE guideline 187 (2014). Available from https://www.nice.org.uk/guidance/cg187

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. 4 Specialist Advisor Questionnaires for sutureless aortic valve replacement for aortic stenosis were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme sent 35 questionnaires to 2 NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 17 completed questionnaires. Overall, 16 respondents (94%) reported that the procedure did work and that it had a positive impacts on their quality of life. 5 respondents (29%) highlighted side effects following the procedure.

Company engagement

A structured information request was sent to 4 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- NCT02673697: Perceval Sutureless Implant Versus Standard-Aortic Valve Replacement A Controlled Randomized Trial in the Surgical Treatment of Aortic Valve Disease (PERSIST-AVR); RCT; multi-centre including the UK; estimated enrolment=1,234; study start date=March 2016; estimated study completion date=January 2023 , status: ongoing
- NCT01368666: Perceval S Valve Clinical Trial for Extended CE Mark; single group assignment; multi-centre; enrolment=658; study start date=February 2010; estimated study completion date=September 2018
- NCT02907463: Assessing Clinical Outcomes Using the EDWARDS INTUITY Elite Valve System in Isolated AVR Using Minimally InvaSive Surgery In a EurOpean Multi-ceNter, Active, Post-market Registry (MISSION); observational; multi-centre including the UK; enrolment=273; study start date=February 2016; estimated study completion date=December 2017
- NCT01636648: Enable I Long-term Follow-up Study; type: case series; location: Europe; estimated enrolment: 100; study start date: August 2012; estimated study completion date: December 2019.

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4. Tagaki H, Ando T et al (2017). Direct and indirect comparisons of perioperative mortality after sutureless or rapid deployment aortic valve replacement versus transcatheter aortic valve implantation. International Journal of Cardiology. 228:327-334.
5. Powell R, Pelletier MP et al (2017). The Perceval Sutureless Aortic Valve: Review of Outcomes, Complications, and Future Direction. Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery: Volume 12 (3): p 155–173
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14. National Health Committee. 2015. Sutureless Aortic Valve Replacement: Assessment Report Tier 3. Wellington: National Health Committee

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Additional relevant papers

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Andreas M, Wallner S et al (2016). Conventional versus rapid deployment aortic valve replacement: a single-centre comparison between the Edwards Magna valve and its rapid-deployment successor. Interactive Cardiovascular and Thoracic Surgery. 22: 799-805.	Comparative case series N=116 patients who had rapid-deployment (Edwards Intuity valve) AVR compared with 132 patients who had conventional AVR (with Edwards Magna valve) Follow-up: 3 years	The mean implanted valve size was higher in the conventional group [23.2 mm (SD: 2.0) vs 22.5 mm (SD: 2.2); P = 0.007], but postoperative transvalvular mean gradients were comparable [15 mmHg (SD: 6) vs 14 mmHg (SD: 5); P = 0.457]. A subgroup analysis of the most common valve sizes (21 and 23 mm; implanted in 63% of patients) revealed significantly reduced mean postoperative transvalvular gradients in the rapid-deployment group [14 mmHg (SD: 4) vs 16 mmHg (SD: 5); P = 0.025]. A significantly higher percentage received minimally invasive procedures in the rapid-deployment group (59 vs 39%; P < 0.001). The 1- and 3-year survival rate was 96 and 90% in the rapid-deployment group and 95 and 89% in the conventional group (P = 0.521), respectively. Valve-related pacemaker implantations were more common in the rapid-deployment group (9 vs 2%; P = 0.014) and postoperative stroke was more common in the conventional group (1.6 vs 0% per patient year; P = 0.044).	Similar studies included in studies added to table 2.

Aymard T, Kadner A, Walpoth N et al. (2010) Clinical experience with the second-generation 3f Enable sutureless aortic valve prosthesis. Journal of Thoracic & Cardiovascular Surgery 140: 313–6	Case series N=28 Follow-up=12 months	Mean aortic cross-clamp time was 39±15 minutes (29–103 minutes), mean cardiopulmonary bypass time was 58 ±20 minutes (41–127 minutes), mean hospital stay was 11 days (7–22 days), and 30-day mortality was 3.5%. Mean and peak intraoperative transvalvular pressure gradients were 6.1±2.6 and 1 ±5 mmHg respectively. Trivial and mild paravalvular leaks were observed in 1 patient each. One patient had preoperative aortic valve replacement 4 months after initial surgery for severe valve-unrelated paravalvular leakage. Five patients (18.5%) needed permanent pacemakers.	Included in systematic reviews added to table 2.
Balan R, Mogilansky C et al (2017). Severe aortic regurgitation after implantation of a sutureless valve prosthesis using an automatic knot fastener device. Interactive CardioVascular and Thoracic Surgery 25; 153–154	Case report N=1 severe aortic regurgitation 8 months after implantation of a 25-mm sutureless pericardial aortic valve prosthesis Intuity Elite	The patient was reoperated, a paravalvular leak was not observed. The sutureless prosthesis was explanted and a conventional biologic valve prosthesis was implanted instead. On examination of the explanted valve prosthesis, a perforation was observed in one of the leaflets. The leaflet perforation was in alignment with one of the knots produced by the automatic knot fastener. Obviously, the leaflet had hit the knot repeatedly which had caused the perforation. We conclude that knots produced by an automatic fastener device have the potential to cause leaflet perforation.	Larger studies included in table 2.

Barnhart GR, Shrestha ML (2016). Current clinical evidence on rapid deployment aortic valve replacement. Sutureless aortic bioprostheses. Innovations; 11:7-14.	Review	Recent advances in prosthetic valve technology, such as transcatheter AVR, have expanded the indication for AVR to the extreme high-risk population, and the most recent surgical innovation, rapid deployment AVR, provides an additional tool to the surgeons' armamentarium.	Review
Barnhart GR, Accola KD et al (2017). TRANSFORM (multicentre experience with rapid deployment Edwards INTUITY valve system for aortic valve replacement) US clinical trial: performance of a rapid deployment aortic valve. The Journal of Thoracic and Cardiovascular Surgery. 153(2)): 241-51.	Case series 839 patients underwent rapid deployment aortic valve replacement (RDAVR) with Edwards Intuity valve Follow-up: 1 year	Technical success rate was 95%. For isolated RDAVR, mean cross clamp and cardiopulmonary bypass times for FS were 49.3 ± 26.9 minutes and 69.2 ± 34.7 minutes, respectively, and for minimally invasive surgical 63.1 ± 25.4 minutes and 84.6 ± 33.5 minutes, respectively. At 30 days, all-cause mortality was 0.8%; valve explant, 0.1%; thromboembolism, 3.5%; and major bleeding, 1.3%. In patients with isolated aortic valve replacement, the rate of permanent pacemaker implantation was 11.9%. At 1 year, mean effective orifice area was 1.7 cm^2; mean gradient, 10.3 mm Hg; and moderate and severe paravalvular leak, 1.2% and 0.4%, respectively.	Similar studies included in table 2.
Bening C, Hamouda K et al (2017). Rapid deployment valve system shortens operative times for aortic valve replacement through right anterior minithoracotomy. J Cardiothorac Surg; 12(1):27.	N=68 had right anterior minithoracotomy aortic valve replacement (RAT-AVR) 43 had rapid deployment with Edwards Intuity valve and 25 had conventional stented valve.	Aortic cross-clamp (42.1 ± 12 min vs. 68.3 ± 20.3 min; $p < 0.001$) and bypass time (80.4 ± 39.3 min vs. 106.6 ± 23.2 min; $p = 0.001$) were shorter in the rapid deployment group (R-group). We observed no differences in clinical outcome. Postoperative gradients	Similar studies included in studies added to table 2.

		(R-group: max gradient, 14.3 ± 8 mmHg vs. 15.5 ± 5 mmHg (C-group), mean gradient, 9.2 ± 1.7 mmHg (R-group) vs. 9.1 ± 2.3 mmHg (C-group) revealed no differences. However, larger prostheses were implanted in C-group (25 mm; IQR 23-27 mm vs. 23 mm; IQR 21-25; p = 0.009).	
Berreta P and Eusanio MD (2016). Aortic valve replacement with sutureless and rapid deployment aortic valve prostheses. Journal of Geriatric Cardiology 13: 504-510.	Review	Current evidence suggests SU-AVR may be a safe and effective alternative to conventional AVR allowing for shortened CPB and cross-clamp times. Sutureless and rapid deployment prostheses seem to provide excellent haemodynamic results together with reduced surgical trauma by facilitating minimally invasive approach. However there is still a paucity of robust, evidence-based data on the role and performance of sutureless AVR on the long term. Therefore, strongest long-term data, randomized studies and registry data are required to adequately assess the durability and long-term outcomes of SU-AVR.	Review
Beckmann E, Martens A et al (2016). Aortic valve replacement with sutureless prosthesis: better than root enlargement to avoid patient-prosthesis mismatch? Interactive Cardiovascular and Thoracic Surgery. 22: 744-749.	Retrospective comparative case series N=128 patients with small aortic annulus underwent AVR. 36 had conventional AVR with aortic root enlargement (ARE) and 92 had sutureless AVR (with Perceval S).	The mean operation, cardiopulmonary bypass and cross-clamp times were significantly lower in sutureless patients (147 ± 42, 67 ± 26 and 35 ± 13 min, respectively) than in conventional ARE patients (181 ± 41, 105 ± 29 and 70 ± 19 min, respectively, P < 0.001). The mean postoperative effective orifice area (EOA) indexed to the body surface area was	Similar studies included in studies added to table 2.

		0.91 ± 0.2 cm(2)/m(2) in conventional ARE patients and 0.83 ± 0.14 cm(2)/m(2) in sutureless patients (P = 0.040). The rate of patients with severe PPM was 6% (n = 2) in conventional ARE patients and 11% (n = 8%) in sutureless patients (not significant, n.s.). The 30-day mortality rates were 2% (n = 2) in sutureless patients and 6% (n = 2) in conventional ARE patients (n.s.). The 1- and 5-year survival rates of the sutureless group were 92 and 54% years, respectively, whereas the 1- and 5-year survival rates of the conventional ARE group were 76% (n.s.).	
Belluschi I, Moriggia S et al (2017). Can Perceval sutureless valve reduce the rate of patient-prosthesis mismatch? Eur J Cardiothorac Surg; 51(6):1093-1099	Retrospective observational study N=65 SUAVR and 177 conventional AVR. 62 patients with a sutureless aortic valve replacement (with the Perceval bioprosthesis) compared with matched group of 62 patients with conventional sutured bioprosthesis.	After matching, the indexed effective orifice area was 1.50 ± 0.18 cm 2 /m 2 and 0.81 ± 0.19 cm 2 /m 2 in the sutureless and the sutured group, respectively (P < 0.001). No PPM occurred in patients who received a Perceval bioprosthesis (n = 62). In the sutured group (n = 62), 38 patients (61.3%) developed a PPM, which was moderate in 41.9% (n = 26) and severe in 19.4% (n = 12) (P < 0.001).	Similar studies included in studies added to table 2.
Biancari F, Barbanti M et al (2016). Immediate outcome after sutureless versus transcatheter aortic valve replacement. Heart Vessels.vol 31 (3), pp 427-433.	Propensity score matched study N=773 Patients undergoing transcatheter (TAVI, N=394) versus SAVR with the sutureless Perceval bioprosthesis (n=379) with or without concomitant myocardial revascularization. One-to-one propensity score-matched	In-hospital mortality was 2.6 % after SU-AVR and 5.3 % after TAVI (p = 0.057). TAVI was associated with a significantly high rate of mild (44.0 vs. 2.1 %) and moderate-severe paravalvular regurgitation (14.1 vs. 0.3 %, p < 0.0001) as well as the need for permanent pacemaker implantation (17.3 vs. 9.8 %, p = 0.003) compared with SU-	Included in Qureshi 2018, Tagaki 2016, 2017 Wang 2016, NHC 2015 report added to table 2.

	analysis done in 144 pairs (144 sutureless Perceval valve versus 144 TAVI with corevalve, sapien, lotus, portico valves 'immediate outcome'	AVR. The analysis of patients within the 25th and 75th percentiles interval of EuroSCORE II, i.e., 2.1-5.8 %, confirmed the findings of the overall series. One-to-one propensity score-matched analysis resulted in 144 pairs with similar baseline characteristics and operative risk. Among these matched pairs, in-hospital mortality (6.9 vs. 1.4 %, p = 0.035) was significantly higher after TAVI. SU-AVR with the Perceval prosthesis in intermediate-risk patients is associated with excellent immediate survival and is a valid alternative to TAVI in these patients.	
Borger MA. Minimally invasive rapid deployment Edwards Intuity aortic valve implantation. Annals of cardiothoracic surgery, 2015; 4(2):193-195.	Case report N=1	Rapid deployment aortic valve replacement (RDAVR) using the first generation of the Intuity RDAVR system (Edwards Lifesciences; Irvine, CA, USA) via a minimally invasive approach.	Larger studies included in table 2
Borger MA, Dohmen PM et al (2016). Haemodynamic benefits of rapid deployment aortic valve replacement via a minimally invasive approach: 1-year results of a prospective multicentre randomized controlled trial. European Journal of Cardio-Thoracic Surgery, 50, 4, 713–720.	Randomised controlled trial (CADENCE-MIS). N= 100 patients with aortic stenosis were randomized to undergo minimally invasive surgery-rapid deployment of AVR (MIS-RDAVR) via upper hemisternotomy (EDWARDS INTUITY) or conventional AVR via full sternotomy (FS) with a commercially available stented valve. Follow-up: 1 year	Technical success was achieved in 94% of MIS-RDAVR patients. MIS-RDAVR was associated with significantly reduced cross-clamp times compared with FS (41.3 ± 20.3 vs 54.0 ± 20.3 min, $P < 0.001$). Clinical and functional outcomes were similar at 30 days and 1 year postoperatively for both groups. While both groups received a similarly sized implanted valve (22.9 ± 2.1 mm MIS-RDAVR vs 23.0 ± 2.1 mm FS-AVR; $P = 0.91$), MIS-RDAVR patients had significantly lower peak gradients 1 year	Included in Qureshi 2018, Tagaki 2017, Paone 2015 HTA report added to table 2.

		postoperatively (16.9 ± 5.3 vs 21.9 ± 8.6 mmHg; *P* = 0.033) and a trend towards lower mean gradients (9.1 ± 2.9 vs 11.5 ± 4.3 mmHg; *P* = 0.082). In addition, MIS-RDAVR patients had a significantly larger effective orifice area 1 year postoperatively (1.9 ± 0.5 vs 1.7 ± 0.4 cm^2 ; *P* = 0.047). Paravalvular leaks, however, were significantly more common in the MIS-RDAVR group (P = 0.027).	
Bouhout I et al (2016). First case of Perceval S prosthesis early structural valve deterioration: not an easy reoperation. J Thorac Cardiovasc Surg; 152; e71-3.	Case report N=1 Perceval valve	Early dysfunction of the prosthesis. Explantation of the valve was difficult because the stent was embedded in the aortic wall. The hardest part was to free the sealing collar that was embedded in the annulus. Careful dissection was done to avoid damage to the annulus.	Larger studies included in table 2
Bouhout I, Mazine A, Rivard L, et al. Conduction disorders after sutureless aortic valve replacement. Ann Thorac Surg. 2017; 103:1254–1260.	N=102 patients who had undergone SAVR with the Perceval,	Postoperatively, new-onset AV block occurred in 52% (first-degree AV in 34%, Mobitz II AV block in 2%, and complete AV block in 16%).52 New-onset LBBB and RBBB occurred in 33% and 22% of patients, respectively. The rate of in-hospital permanent pacemaker implantation was 23%. Independent predictors of new-onset conductive disorder or permanent pacemaker implantation were preoperative RBBB (P = 0.03), small preoperative EOA (P = 0.02), and age younger than 85 years (P = 0.03).	Larger studies included in table 2

Breitenbach I, Wimmer-Greinecker G, Bockeria LA et al. (884) Sutureless aortic valve replacement with the Trilogy Aortic Valve System: multicenter experience. Journal of Thoracic & Cardiovascular Surgery 140:878–84	Case series (prospective) N=32 Trilogy Aortic Valve System implanted Follow-up= up to 2 years	Mean bypass time was 111±42 minutes, and cross-clamp time was 70±23 minutes. The transvalvular gradients at discharge were 10±3 mmHg (mean) and 20±7 mmHg (peak), and the effective orifice area was 1.9±0.4 cm^2. At 2-year follow-up, gradients were 7±3 mmHg (mean) and 14±4 mmHg (peak), and the effective orifice area was 1.9±0.3 cm^2. There was no intraoperative mortality: Two patients died of causes unrelated to the valve during follow-up. One redo aortic valve replacement was performed at 22 months for prosthetic valve endocarditis.	Included in Phan 2015 added to table 2.
Bruno P, Cesare AD et al (2017). Rapid-deployment or transcatheter aortic valves in intermediate-risk patients? Asian cardiovascular & thoracic annals. 25 (4):264-270.	propensity-matched study n=60 patients with intermediate surgical risk 30 patients who had rapid-deployment AVR compared with 30 patients who underwent transcatheter AVR	Freedom from paravalvular regurgitation was higher in the rapid-deployment valve group ($p<0.001$), while postoperative mean transprosthetic gradient was lower in the transcatheter valve group ($p=0.03$). Permanent pacemaker implantation was required more frequently in transcatheter valve patients ($p=0.01$). Postoperative atrial fibrillation was more common in the rapid-deployment valve group ($p=0.03$). Hospital mortality was similarly low in both groups ($p=0.33$). At midterm follow-up, mortality was comparable ($p=0.42$) but the rapid-deployment valve group still had a lower degree of paravalvular regurgitation.	Similar studies included in studies added to table 2.
CADTH 2015. Perceval S sutureless valve for aortic	Rapid Response Summary.	Pooled data on all valves reports that	Included in CADTH report 2015 added to

valve replacement: a review of the clinical effectiveness, safety and cost-effectiveness (Rapid response report: summary with critical appraisal).	Includes 1 systematic review, 3 rapid reviews, 5 non-randomised comparative studies. Focuses on the Perceval S valve, but includes reviews on all sutureless valves (3f Enable, Edwards Intuity, Triology aortic valve system). Systematic reviews: SU AVR versus SAVR 693 patients, SUAVR versus TAVR 570 patients; Case series: 550 patients. Follow-up range not reported.	SU AVR the mean aortic cross clamp time was 33 minutes, CPB time 57 minutes, 30 day mortality rate 2%, 1 year mortality 4.9%, rate of reoperation for bleeding 1%, rate of paravalvular leakage 3%. SU AVR versus SAVR No difference in overall survival rate, reoperation for bleeding heart attack or stroke between the groups. Rate of paravalvular leak was high in SUAVR. SUAVR versus TAVR No difference in stroke, heart attack or renal failure rates., lower mortality, paravalvular leaks and pacemaker implantations for SUAVR and higher perioperative bleeding for SUAVR.	existing assessments section in this report.
Cerillo AG, Bevilacqua S, Farneti PA et al. (2012) Sutureless aortic valve replacement through a right minithoracotomy. Journal of Heart Valve Disease 21: 168–71	Case series N=3 Follow-up=unclear	Mean cross-clamp time was 89 minutes. Mean gradient at last echocardiography was 8, 6, and 16 mmHg. There was no aortic regurgitation.	
Concistre G, Farneti P, Miceli A et al. (2012) Surtureless aortic bioprosthesis in severe aortic root calcification: an innovative approach Interactive Cardiovascular and Thoracic Surgery 14: 670–2	Case report N=1 Follow up = 12 months	Good position and normal function without paravalvular leakage of the valve was assessed immediately after weaning from cardiopulmonary bypass. Patient was asymptomatic without aortic sutureless prosthesis malfunction and without paravalvular leakage. At 12 month follow-up, the mean pressure gradient (9 mmHg) remained stable relative to discharge (10 mmHg).	
Concistre G, Miceli A, Chiaramonti F et al. (2012)	Case report n=1	Sutureless aortic bioprosthesis	

Delayed dislocation of a sutureless aortic bioprosthesis: the first case. Interactive Cardiovascular & Thoracic Surgery 14: 892-3	follow-up 3 months	implantation is an alternative technique in high-risk patients undergoing aortic valve replacement with a possible reduction in the extracorporeal circuit time and reliable haemodynamic features. A 3F Enable (ATS Medical-Medtronic, Inc., Minneapolis, MN, USA) has shown very good results. We report the first upward displacement of 3F Enable three months post implantation.	
Concistre G, Santarpino G et al (2013). Two alternative sutureless strategies for aortic valve replacement: a two-center experience. Innovations Technology and Techniques in Cardiothoracic and Vascular Surgery 8(4):253-7.	Perceval S (P group, n=97) and 3f Enable (E group, n=32) sutureless aortic bioprostheses compared.	The mean ± SD prosthesis diameter was 23.5 ± 1.4 mm (P group) compared with 22.1 ± 2 mm (E group) (P < 0.001). In isolated AVR, aortic cross-clamp time was 36 ± 12.7 minutes in the P group and 66 ± 18 minutes in the E group (P < 0.001). At a mean ± SD follow-up of 8.3 ± 4.5 months, survival was 97% (one death in the P group). In 5 patients (P group = 1, E group = 4), a moderate paravalvular leak was present (P = 0.013). The mean ± SD transvalvular gradient was 9.1 ± 3.3 mm Hg with the Perceval S and 11.2 ± 5.2 mm Hg with the 3f Enable (P = 0.017). The Perceval S showed lower operative times and moderate paravalvular leaks and lower mean transvalvular gradients than did the 3f Enable, related to the larger diameter of the Perceval S implanted. Both prostheses showed an excellent hemodynamic performance.	Included in Phan 2015 added to table 2. Both comparisons received sutureless valve replacement.

Concistre G, Chiaramonti F et al (2018). Aortic Valve Replacement With Perceval Bioprosthesis: Single-Center Experience With 617 Implants. The Annals of Thoracic Surgery. 105 (1): 40-6.	Case series N=617 patients underwent AVR with a Perceval bioprosthesis. Mean follow-up 16.3 months	The 30-day mortality rate was 1.9% (12 of 617). Cardiopulmonary bypass and aortic cross-clamp times were 81.7 ± 29.1 minutes and 50.5 ± 19.8 minutes for isolated AVR and 139.7 ± 51.5 minutes and 91.5 ± 29.5 minutes for combined procedures, respectively. The survival rate was 91.3%, the rate of freedom from reoperation was 99%, and the mean transvalvular pressure gradient was 11.9 ± 5.4 mm Hg. Left ventricular ejection fraction increased from 53.6% ± 8.4% to 54.5% ± 4.8% (p = 0.40), left ventricular mass decreased from 146.5 to 112.6 g/m^2 (p < 0.001), and moderate paravalvular leakage occurred in 3 patients without hemolysis who did not require any treatment.	Similar studies included in studies added to table 2.
Dalen M, Binacari F et al (2015).Ministernotomy Versus Full Sternotomy Aortic Valve Replacement With a Sutureless Bioprosthesis: A Multicenter Study. The Annals of Thoracic Surgery. 99 (2):524-530.	Retrospective non-randomised comparative study with mixed historical and concurrent controls (matched pairs 56). N=189 patients who had SU AVR through ministernotomy with Perceval S compared with 78 patients who had SAVR through full sternotomy with a stented valve. Follow-up: 2 years.	In the overall cohort of ministernotomy and full sternotomy patients, in-hospital mortality was 1.1% and 2.6% and 2-year survival was 92% and 91%, respectively. Propensity score matching resulted in 56 pairs with similar characteristics and operative risk. Aortic cross-clamp (44 minutes in both groups, p = 0.931) and cardiopulmonary bypass time (69 vs 74 minutes, p = 0.363) did not differ between the groups. Apart from higher values in the ministernotomy group for postoperative peak gradients (28.1 vs 23.3 mm Hg, p = 0.026) and mean aortic valve gradients (15.2 vs 11.7	Similar studies included in studies added to table 2.

		mm Hg, p = 0.011), early postoperative outcomes did not differ in the propensity-matched cohort. There were no differences in the in-hospital mortality rate or 2-year survival between the groups.	
Dalen M, Binacari F et al (2016). Aortic valve replacement through full sternotomy with a stented bioprosthesis versus minimally invasive sternotomy with a sutureless bioprosthesis. European Journal of Cardio-Thoracic Surgery, 49(1): 220–227.	Retrospective non-randomised comparative study with mixed historical and concurrent controls (matched pairs). N=171 patients who had SU AVR through ministernotomy with Perceval S compared with 171 patients who had SAVR through full sternotomy with a stented valve. Follow-up: mean 2.7 years.	In the overall cohort, 30-day mortality was 1.6 and 2.1%, and 2-year survival was 92 and 92% in the ministernotomy sutureless group and in the full sternotomy stented group, respectively. Propensity score matching resulted in 171 pairs with similar characteristics and operative risk. Aortic cross-clamp (40 vs 65 min, P < 0.001) and cardiopulmonary bypass time (69 vs 87 min, P < 0.001) were shorter in the ministernotomy sutureless group. Patients undergoing ministernotomy received less packed red blood cells but the risk for postoperative permanent pacemaker implantation was higher. There were no differences regarding 30-day mortality or 2-year survival between the two groups.	Included in Qureshi 2018, Tagaki 2017, CADTH 2015 added to table 2.
Davies RA, Bandara TD et al (2016). Do rapid deployment aortic valves improve outcomes compared with surgical aortic valve replacement? Interactive CardioVascular and Thoracic Surgery 23 (2016) 814–820.	Evidence review of rapid deployment valves (RDVs) implanted in these studies include balloon expandable [Intuity (Edwards Lifesciences, CA, USA) and 3F Enable (Medtronic, MN, USA)] and self-expanding [Perceval (Sorin, Saluggia, Italy)] stented bioprostheses	Data from 11 studies demonstrate that rapid deployment valves are invariably associated with shorter aortic cross-clamp times (30–56 vs 49–88 min). Despite this, postoperative mortality (0–5.8 vs 0–6%), ICU (1–3 vs 0.9–2.8 days) and hospital length of stay (6–14.1 vs 6–15.9 days) are similar compared with conventional aortic	Similar studies added to table 2.

		valve replacement (AVR). However, reduced postoperative bleeding (328 vs 564 ml), blood transfusion requirements (1.4 vs 2.4 units), ventilation time (4.9–9.5 vs 7–16.6 h) and renal injury (5.3 vs 14.7%) have been demonstrated with RDVs indicating possible clinical benefit to shorter procedural time. transvalvular gradients were frequently lower with rapid deployment valves compared with conventional AVR, indicating an improved haemodynamic profile. However, in some studies using the Perceval RDV, the transvalvular gradients were higher than with conventional AVR. Also, mean valve sizes were often larger in those receiving RDVs. Rates of paravalvular regurgitation were similar between RDVs and conventional AVR in most studies, although pacemaker implantation occurred more often with RDV in some studies (2–28.5 vs 0–8.5%).	
Dedeilias P, Baikoussis NG, Prappa E, et al. Aortic valve replacement in elderly with small aortic root and low body surface area; the perceval S valve and its impact in effective orifice area. J Cardiothorac Surg. 2016; 11:54.	Prospective randomised study 25 patients who underwent aortic valve replacement with sutureless Perceval S valve compared with 25 patients with conventional stented biological prosthesis (soprano LivaNova group).	The Perceval S valve reported shorter ischemia time (40 ± 5.50 min vs 86 ± 15.86 min; $p < 0.001$), shorter extracorporeal circulation time (73.75 ± 8.12 min vs 120.36 ± 28.31 min $p < 0.001$), less operation time (149.38 ± 15.22 min vs 206.64 ± 42.85 min; $p < 0.001$) and better postoperative recovery. The postoperative gradients were 23.5 ± 19.20 mmHg vs 24.5 ± 19.90 mmHg respectively. The	Included in Powell systematic review added to table 2.

		postoperative effective orifice area in these two groups were respectively 1.5 =/-0.19 cm2 vs 1.1=/-0.5 cm2 (p 0.002).	
Dionne PO, Poulin F et al (2017). Early Hemodynamic Results in Patients With Small Aortic Annulus After Aortic Valve Replacement. Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery. 12(2):254-58.	Retrospective comparative case series 50 TAVI with Edwards system (SAPIEN) compared with 113 sutureless AVR with Perceval prostheses.	There were no significant difference in predischarge effective orifice area (SAPIEN: 1.5 ± 0.5 cm^2 and Perceval: 1.48 ± 0.34 cm^2, *P* = 0.58) and indexed effective orifice areas (SAPIEN: 0.93 ± 0.32 cm^2/m^2 and Perceval: 0.88 ± 0.22 cm^2/m^2, *P* = 0.42). Predischarge mean ± SD transaortic gradient was lower with the SAPIEN than with Perceval valves (12 ± 6 and 17 ± 6 mm Hg, respectively, *P* < 0.001). Rates of moderate and severe prosthesis-patient mismatch were similar (SAPIEN: 44% and 10% and Perceval: 50% and 14%, *P* = 0.53 and 0.75, respectively). There were no moderate-severe paravalvular leaks.	Similar studies added to studies included in table 2.
Doss M, Martens S et al (2005). Aortic leaflet replacement with the new 3F stentless aortic bioprosthesis. Ann Thorac Surg; 79:682-5.	Prospective case series N=24 3F aortic bioprostheses were implanted 12-month follow-up.	At 12-month follow-ups, the 3F bioprosthesis showed a good hemodynamic performance with a significant drop of mean gradients to 10.3 mm Hg, a mean effective orifice area of 1.7 cm^2, and a mean ejection fraction of 61.5%.	Included in Phan 2015 added to table 2.
Doss M, Buhr E, Moritz A et al (2012). Sutureless aortic valve replacement: Catheter-based transapical versus direct transaortic implantation. Journal of Heart Valve Disease.21 (6): 758-63	Case series N=56 (sutureless – Enable valve 27, 29 TAVI sapien valve) FU= unclear	The 30-day mortality was 17% in the transapical group and 11% in the transaortic group. Two conversions were performed in each group. One valve migration, one complete heart block and two cases of coronary obstruction occurred in the transapical group. The implantation times	Included in Tagaki 2016, NHC 2015 report added to table 2.

		were 8 min in the transapical group and 10 min in the transaortic group. Four paravalvular leaks occurred in the transapical group, but none occurred in the transaortic group.	
D'Onofrio A, Messina A, Lorusso R et al. (2012) Sutureless aortic valve replacement as an alternative treatment for patients belonging to the "gray zone" between transcatheter aortic valve implantation and conventional surgery: A propensity-matched, multicenter analysis. The Journal of Thoracic and Cardiovascular Surgery 144(5): 1010-8. doi: 10.1016/j.jtcvs.2012.07.040. Epub 2012 Sep 10	Non-randomised comparative study (propensity score matched multicentre study) Retrospective analysis of data registry n=76 (38 perceval versus 38 Sapien/Sapien XT) Hospital outcomes	Preoperative characteristics of the 2 groups were comparable. Hospital mortality was 5.3% and 0% in the TA-TAVI and SU-AVR groups, respectively (*P* = .49). We did not observe stroke or acute myocardial infarction in the 2 groups. Permanent pacemaker implantation was needed in 2 patients of each group (5.3%, *P* = 1.0). Dialysis was required in 2 patients (5.3%) in the SU-AVR group and in 1 patient (2.7%) in the TA-TAVI group (*P* = 1.0). Predischarge echocardiographic data showed that the incidence of paravalvular leak (at least mild) was greater in the TA-TAVI group (44.7% vs 15.8%, *P* = .001), but there were no differences in terms of mean transprosthetic gradient (10.3 ± 5 mm Hg vs 11 ± 3.7 mm Hg, *P* = .59).	Included in Tagaki 2016, 2017, Phan 2015 added to table 2.
D'Onofrio A, Rizzoli G et al (2013). Conventional surgery, sutureless valves, and transapical aortic valve replacement: What is the best option for patients with aortic valve stenosis? A multicenter, propensity-matched analysis. J Thorac Cardiovasc Surg 146(5),:1065-70.	Propensity- matched retrospective analysis Used a propensity-matching strategy to compare on-pump (SAVR, SU-AVR) and off-pump (TA-TAVR) surgical techniques. Analysed data from 566 TA-TAVR, 349 SAVR, and 38 SU-AVR patients.	In the matched cohorts, the 30-day overall mortality was significantly lower after SAVR than TA-TAVR (7% vs 1.8%, P = .026), with no differences in mortality between SU-AVR and TA-TAVR. Multivariate analysis showed SU-AVR to have a protective effect, although not statistically significant, against	Included in Qureshi 2018, Paone S 2015 HTA report.

		aortic regurgitation, pacemaker implantation, and renal replacement therapy compared with TA-TAVR. Compared with TA-TAVR, SAVR demonstrated significant protection against aortic regurgitation (odds ratio, 0.04; P<.001) and a trend toward protection against death, pacemaker implantation, and myocardial infarction. The mean transaortic gradient was 10.3 ±4.4 mm Hg, 11 ± 3.4 mm Hg, and 16.5±5.8 mm Hg in the TA-TAVR, SU-AVR, and SAVR patients, respectively.	
D'Onofrio A, Salizzoni S, Rubino AS, et al. The rise of new technologies for aortic valve stenosis: A comparison of sutureless and transcatheter aortic valve implantation. J Thorac Cardiovasc Surg 2016; 152:99-109.e2.	Propensity score matching study Patients who underwent TAVI and SU-AVR. n=2177 patients were included in the analysis: 1885 (86.6%) treated with TAVI; 292 (13.4%) treated with SU-AVR. follow-up 1 year	Mortality in unmatched TAVI and SU-AVR patients was 7.1% and 2.1%, respectively, at 30 days, and 12.9% and 4.6%, respectively, at 1 year. No differences were found in 30-day mortality in the 214 matched patient pairs (3.7% vs 2.3%; *P* = .4), but patients treated with TAVI showed a lower incidence of device success (85.9% vs 98.6%; *P* < .001) and pacemaker implantation (2.8% vs 9.4%; *P* = .005), and a higher incidence of any paravalvular leakage (PVL).	Included in Wang 2016, Tagaki 2017 added to table 2.
D'Onofrio A, Fabozzo A, Gerosa G. Comparison of hemodynamic and clinical outcomes of transcatheter and sutureless aortic bioprostheses: how to make the right choice in intermediate risk patients. Ann Cardiothorac Surg 2017; 6(5):510-515. doi: 10.21037/acs.2017.09.04	Review This paper shares perspective on therapeutic approaches for patients with severe aortic stenosis by reviewing hemodynamic data and clinical evidence for SUAVR versus TAVI.	SUAVR and TAVI are both valid surgical alternatives to conventional valve replacement in patients with AS. Lower transvalvular gradients, but higher PVL, are commonly found after TAVI. Accurate preoperative screening and prosthesis selection are mandatory to	Review

		properly select case-specific best treatment options, based on anatomical and surgical characteristics.	
Eichstaedt HC, Easo J, Härle T, et al (2014). Early single-center experience in sutureless aortic valve implantation in 120 patients. J Thorac Cardiovasc Surg; 147:370-5.	Retrospective case series N=120 patients who underwent isolated AVR or in combination with other cardiovascular procedures (71 of 120 patients underwent isolated sutureless aortic valve -**3F Enable** replacement). 18 months follow-up (mean 313 days)	(Mean aortic crossclamp time, 37 ± 11 minutes; mean bypass time, 62 ± 18 minutes). Coronary bypass grafting was performed in 30 patients. Overall mean Society of Thoracic Surgeons score was 14.8% ± 10%. Thirty-day mortality rate was 6.7% overall and 1.4% in stand-alone procedures. During a mean follow-up of 313 days, 3 more deaths occurred. The reoperation rate was 4.2%. Mean and peak transvalvular pressure gradients were 9 mm Hg (4-13 mm Hg) and 14 mm Hg (8-22 mm Hg) at discharge, respectively. In 8 patients (6.7%), permanent pacemaker implantation was necessary. No thromboembolic events or bleedings related to the bioprosthesis were observed.	Included in Phan 2015, CADTH 2015, NHC 2015 reports.
Englberger L, Carrel TP et al (2014). Clinical performance if a sutureless aortic bioprosthesis: 5 year results of the 3f Enable long-term follow-up study. J Thorac Cardiovascular Surgery. 148 (4): 1681-7.	Case series (prospective) 141 patients undergoing SU AVR with 3f Enable mean follow-up was 2.76 years (range: 2 days to 5.1 years; total: 388.7 patient-years	The mean systolic gradient was 10.4±4.4 mmHg at discharge and 7.7±4.1 mmHg at 5 years. Mean effective orifice area was 1.7±0.5 cm2 at discharge and 1.6±0.2 cm2 at 5 years. Freedom from all-cause and valve-related mortality was 87.6±2.9% and 96.8±1.6% at 1 year (113 patients at risk) and 77.0±7.5% and 93.8±4.8% at 5 years (24 patients at risk), respectively. Six patients underwent reoperation; four due to	Included in CADTH 2015 added to table 2.

		major paravalvular leakage and two for endocarditis. Freedom from reoperation was 95.4±1.9% at 1 year and 95.4±6.1% at 5 years. No structural valve deterioration occurred during the follow-up period.	
Eusanio MD & Phan K (2015). Sutureless aortic valve replacement: keynote lecture series. Annals of Cardiothoracic Surgery. 4 (2), 123-130.	Review	This keynote lecture will overview the use, potential advantages, the caveats and current evidence of sutureless and rapid deployment aortic valve replacement.	Review
Ferrari E, Roduit C et al (2017). Rapid-deployment aortic valve replacement versus standard bioprosthesis implantation. Acquired Cardiovascular Disease. Journal of Cardiac Surgery. 3(2), 322-327.	Comparative study N=32 patients underwent aortic valve replacement with the Intuity valve compared to a matched population of Perimount Magna bioprosthesis implanted during the same period of time. 1-year follow-up.	Implants were 100% successful. Mean cross-clamp (50.3 ± 25 vs 53 ± 22 min, p = 0.004), cardiopulmonary bypass (68 ± 27 vs 72 ± 31.8 min; p = 0.006), and surgical times (156.8 ± 54 vs 165 ± 40 min; p = 0.018) were shorter with the Intuity despite more concomitant procedures. Mean valve size was 23.7 mm (Intuity-group) and 24.1 mm (Perimount-group); hospital mortality was zero (Intuity-group) and 3% (Perimount-group); new pacemaker implants were 6% (Intuity) and 3% (Perimount) (p = 0.55) and hospital stay was equivalent. Mean gradients were: 9.9 ± 3.4 (Intuity) versus 12.5 ± 3.8 mmHg (Perimount) (p = 0.022) at discharge and 9 ± 4 mmHg (Intuity) versus 14 ± 4 mmHg (Perimount) (p = 0.02) at follow-up. At discharge, one Intuity valve had 3+ aortic insufficiency (AI) which was unchanged at 1 year and will require an intervention. Another patient had	Larger studies included in table 2.

		1 + AI which progressed to 2+ at 1 year. There were no paravalvular leaks in the Perimount valves at discharge and follow-up.	
Fleissner F, Molitoris U et al (2015). Stent distortion after sutureless aortic valve implantation: a new complication seen with a novel surgical technique. Interactive Cardiovascular and Thoracic Surgery. 20:436-8	Case report N=2	2 cases of delayed distortion of a sutureless aortic valve stent resulting in paravalvular leakage and increased transvalvular gradients. One patient underwent a reoperation with an aortic valve replacement using a standard biological aortic valve, the other patient was treated with balloon dilatation of the aortic valve stent.	Larger studies included in table 2.
Flameng W, Herregods MC, Hermans H et al. (2011) Effect of sutureless implantation of the Perceval S aortic valve bioprosthesis on intraoperative and early postoperative outcomes. Journal of Thoracic & Cardiovascular Surgery 142: 1453-7	Case series n=32 follow-up=median 16 months	Aortic crossclamp time needed for aortic valve replacement was 18 ± 6 minutes. Hemodynamics at discharge showed good function of all Perceval S valves with low transvalvular pressure gradients (mean, 12 ± 5 mm Hg and peak, 23 ± 9 mm Hg) and low incidence of paravalvular or valvular leakage. Operative mortality was 0%. Follow-up at 1 year showed 3 non–valve-related deaths. Survivors showed good clinical outcome and stable hemodynamic function of the valve prosthesis, except for 1 patient in whom endocarditis developed. Despite a moderate decrease in platelet counts persisting up to 12 months, freedom of bleeding and thromboembolic events was 100%.	Included in Sian 2017, Phan 2015 added to table 2.
Fischlein T, Pfeiffer S, Pollari F, et al (2015). Sutureless Valve Implantation via Mini J-	Prospective case series N= 262 patients affected by aortic	Mean logistic EuroSCORE (I) was 9.9 ± 5.9%, and mean aortic cross-clamp time	Included in Sian 2017 added to table 2.

Sternotomy: A Single Center Experience with 2 Years Mean Follow-up. Thorac Cardiovasc Surg; 63:467-71.	valve stenosis underwent AVR with a sutureless bioprosthesis (Perceval), of these, 145 patients underwent surgical AVR through a mini J-sternotomy. Mean follow-up (23.5 ± 14.4 months	was 38 ± 12 minutes (35 ± 11 minutes in isolated procedures). Two conversions to full sternotomy were necessary because of bleeding. Thirty-day mortality was 2.1% (all noncardiac deaths); mean hospital stay was 11.6 ± 4.9 days. We recorded 11 pacemaker implantations (7.6%). At follow-up (23.5 ± 14.4 months), five patients were dead (three noncardiac and two cardiac deaths). At echocardiographic control, mean transprosthetic gradients were as follows: 12.8 ± 4.9, 12.5 ± 4.5, 11.8 ± 4.7 mm Hg, postoperatively at 6 months, 1 year, and 2 years, respectively. No paravalvular leaks were recorded.	
Fischlein T, Meuris B et al (2016). The sutureless aortic valve at 1 year: A large multicenter cohort study. The Journal of Thoracic and Cardiovascular Surgery. 151(6):1617-1626.	Case series N= 658 patients underwent sutureless AVR with Perceval valve. Follow-up: 1 year	One-year site-reported event rates were 8.1% for all-cause mortality, 4.5% for cardiac mortality, 3.0% for stroke, 1.9% for valve-related reoperation, 1.4% for endocarditis, and 0.6% for major paravalvular leak. No valve thrombosis, migration, or structural valve deterioration occurred. NYHA class improved at least 1 level in 77.5% and remained stable (70.4% NYHA I or II at 1 year). Mean effective orifice area was 1.5 ± 0.4 cm^2; pressure gradient was 9.2 ± 5.0 mm Hg. Left ventricular mass decreased from 138.5 g/m^2 before surgery to 115.3 g/m^2 at 1 year ($P < .001$). Echocardiographic core laboratory findings confirmed that	Similar studies included in studies added to table 2.

		paravalvular leak was rare and remained stable during follow-up.	
Folliguet TA, Laborde F, Zannis K et al. (2012) Sutureless perceval aortic valve replacement: results of two European centers. Annals of Thoracic Surgery 93: 1483-8	Prospective case series (Part of Cavalier trial) n= 208 high-risk patients (mean European system for cardiac operative risk evaluation: 8.7 _ 5.3 years) received a Perceval bioprosthesis in 2 European centers. Follow-up median 10 months, maximum 4 years	Valve implantation resulted in significant improvement of patients' symptoms. Mean preoperative and postoperative gradients were 48.6 ± 18.6 mm Hg and 10.4 ± 4.3 mm Hg, respectively, and preoperative and postoperative mean effective orifice areas were 0.7 ± 0.2 and 1.4 ± 0.4 cm^2. Survival at 12 months was 87.1%, success of implantation was 95%, and freedom from reoperation was 96%. In hospital mortality was 2.4%. During follow-up, 9 patients (4%) required reoperation for paravalvular regurgitation; 7 early and 2 late reoperations. Mean cross-clamp time (CCT) and extracorporeal circulation time (ECT) were, respectively, 33 ± 14 minutes and 54 ± 24 minutes, including 45 patients who underwent surgery through ministernotomy. Concomitant coronary bypass was done in 48 patients with mean CCT 43 ± 13 and ECT 68 ± 25 minutes.	Included in Sian 2017, Phan 2015, NHC 2015 report added to table 2.
Forcillo J, Bouchard D et al (2016). Perioperative outcomes with sutureless versus stented biological aortic valves in elderly persons. The Journal of Thoracic and Cardiovascular Surgery. 151 (6): 1629-36.	Propensity score matched study 76 patients underwent SU AVR with the Perceval prosthesis and was compared with 319 c patients who received conventional AVR with the stented valve	Median cardiopulmonary bypass and cross clamp times were lower in the Perceval group than in the stented valve group ($P < .001$). Mortality was 5% in the Perceval group and 6% in the stented valve group ($P = .8$). There were more pacemaker implantations in the Perceval group than in the stented valve group	Included in Tagaki 2017 added to table 2.

		(17% vs 8%; *P* = .02). A subgroup analysis of patients who underwent aortic valve replacement and concomitant procedures showed the same results as the entire cohort.	
Fuzellier JF, Campisis S et al (2016). Two Hundred Consecutive Implantations of the Sutureless 3f Enable Aortic Valve: What We Have Learned. The Annals of Thoracic Surgery. 101(5):1716-23.	Retrospective case series N=200 patients who had sutureless AVR with 3f Enable valve. Follow-up: mean 12.6 months.	Mean cross-clamp and cardiopulmonary bypass (CPB) times were 65 ± 31 and 91 ± 39 minutes, respectively. Sixteen (8%) patients required early implantation of a pacemaker (PM). At a mean follow-up of 12.6 ± 8.1 months, mean transvalvular gradient and effective orifice area (EOA) were 9.8 ± 4.4 mm Hg and 1.87 ± 0.6 cm^2, respectively. Mild PVL was present in 7 (3.5%) patients and moderate PVL was present in 5 (2.5%) patients. No device migration was registered, and no moderate PVL was detected in the last 100 patients of the cohort. Overall, 3-year survival was 78%.	Similar studies were included in studies added to table 2.
Ghoneim A, Bouhout I et al (2016)> Management of small aortic annulus in the era of sutureless valves: A comparative study among different biological options. The Journal of Thoracic and Cardiovascular Surgery. 152(4): 1019-28.	Retrospective comparative study. N=351 patients with small aortic annulus who had AVR. Standard AVR =259, aortic root enlargement n=20, stentless bioprosthesis n=23, sutureless Perceval bioprosthesis n=49.	Patients in the stentless group had the lowest aortic valve mean gradients on predischarge transthoracic echocardiography (10.9 ± 6.2 mm Hg; *P* < .001). In the stented group, the Trifecta prosthesis displayed the lowest postoperative mean transaortic gradient (10.3 ± 3.6; *P* < .001) with no severe prosthesis-patient mismatch. Postoperative gradients of the sutureless group were comparable with stented prostheses.	Similar studies were included in studies added to table 2.

Gilmanov D, Miceli A, Bevilacqua S, et al (2013). Sutureless implantation of the perceval s aortic valve prosthesis through right anterior minithoracotomy. Ann Thorac Surg; 96:2101-8.	Retrospective case series N= 137 patients undergoing aortic valve replacement (sutureless Perceval valve) through a right anterior minithoracotomy	The mean aortic cross-clamp and cardiopulmonary bypass times were 59.3 ± 19 min and 92.3 ± 27 min, respectively. No operative mortality occurred. Median stay in the intensive care unit was 1 day, with assisted ventilation necessary for a median of 6 hours. Three cases of postoperative ischemic stroke were observed (1 patient with a previous history of an ischemic cerebral event). Median hospital length of stay was 6 days.	Included in Sian 2017, Phan 2015, NHC report 2015 added to table 2.
Gilmanov D, Bevilacqua S, Murzi M, et al (2013). Minimally invasive and conventional aortic valve replacement: a propensity score analysis. Ann Thorac Surg; 96:837-43.	Retrospective observational study 709 patients undergoing isolated primary aortic valve replacement, of these 338 were done either through right anterior minithoracotomy or upper mini sternotomy. Propensity score matched analysis 182 patients (minimally invasive group with Perceval valve) were compared with 182 patients in conventional sternotomy (control group). Postoperative outcomes	After propensity matching, the 2 groups were comparable in terms of preoperative characteristics. Cardiopulmonary bypass time (117.5 vs 104.1 min, $p < 0.0001$) and aortic cross-clamping time (83.8 vs 71.3 min, $p < 0.0001$) were longer in the minimally invasive group, with no difference in length of stay (median 6 vs 5 days, $p = 0.43$), but shorter assisted ventilation time (median 8 vs 7 hours, $p = 0.022$). Overall in-hospital mortality was identical between the groups (1.64 vs 1.64%, $p = 1.0$). No difference in the incidence of major and minor postoperative complications and related morbidity was observed. Minimally invasive aortic valve replacement was associated with a lower incidence of new onset postoperative atrial fibrillation (21% vs 31%, $p = 0.04$). Reduction of the complication rate was observed. Median transfusion pack per	

		patient was higher in the control group (2 vs 1 units, *p* = 0.04).	
Gilmanov D, Miceli A et al (2014). Aortic valve replacement through right anterior minithoracotomy: can sutureless technology improve clinical outcomes? The Annals of Thoracic Surgery. 98 (5), 1585-92.	Retrospective propensity matched study. N=515 patients undergoing primary aortic valve replacement through a right anterior minithoracotomy (269 conventional versus 246 sutureless prostheses) 133 pairs were retrospectively analysed. 133 patients SU AVR with **Perceval** by right anterior minithoracotomy compared with 133 patients with standard AVR (Medtronic, perimount valves). Follow-up: overall median, 21 months	Cardiopulmonary bypass (p<0.0001) and cross-clamping (p<0.0001) times were shorter in the sutureless group (S group). Same in-hospital mortality (1 versus 2; p=0.62) and incidence of postoperative stroke and pacemaker implant between the groups, but shorter duration of mechanical ventilation (6 versus 7 hours; p=0.001) in the S group. Generally, larger prostheses were implanted in the S group (p<0.0001). Follow-up was longer (p<0.0001) for sutured valves: 52 versus 15 months Overall Kaplan-Meier survival rate was 87.2% versus 97.0% (p=0.33) and 50% versus 100% (p=0.02) in elderly patients for sutured versus sutureless prostheses, respectively. Freedom from reoperation at follow-up (p=0.64) and transaortic gradients (12 versus 11 mm Hg; p=0.78) did not differ in the two groups.	Included in Qureshi 2018, Tagaki 2017, NHC report 2015 added to table 2.
Gilmanov D, Solinas M et al (2015) Minimally invasive aortic valve replacement: 12-year single center Experience. *Ann Cardiothorac Surg* 2015;4(2):160-169.	Retrospective review minimally invasive aortic valve replacement (MIAVR), performed through a right anterior minithoracotomy or ministernotomy (MS). N=853	443 (51.9%) and 368 (43.1%) patients received biological and sutureless prostheses, respectively. Median cardiopulmonary bypass time and aortic cross-clamping time were 108 and 75 minutes, respectively. Nineteen (2.2%) cases required conversion to full median sternotomy. Thirty seven	Mix of biological and sutureless valves. Outcomes not reported separately.

		(4.3%) patients required re-exploration for bleeding. Perioperative stroke occurred in 15 (1.8%) patients, while transient ischemic attack occurred postoperative in 11 (1.3%). New onset atrial fibrillation was reported for 243 (28.5%) patients. After a median follow-up of 29.1 months (2,676.0 patient-years), survival rates at 1 and 5 years were 96%±1% and 80%±3%, respectively. Cox multivariable analysis showed that advanced age, history of cardiac arrhythmia, preoperative chronic renal failure, MS approach, prolonged mechanical ventilation and hospital stay as well as wound revision were associated with higher mortality.	
Gilmanov D, Farneti PA et al (2015). Full sternotomy versus right anterior minithoracotomy for isolated aortic valve replacement in octogenarians: a propensity-matched study. Interactive CardioVascular and Thoracic Surgery 20, 732–742.	283 elderly patients >80 years underwent isolated AVR With propensity score matching (1: 1), minimally invasive surgery (RAMT) compared with FS approach (100 vs 100 patients). TAVRs and partial sternotomy cases were excluded from the analysis.	Minimally invasive AVR through right anterior minithoracotomy can be safely performed in patients aged ≥80 years with acceptable morbidity and mortality rates. It is an expeditious and effective alternative to full sternotomy AVR and might be associated with lower postoperative stroke incidence, earlier extubation and shorter hospital stay.	Mix of different types of prosthesis. Outcomes not reported separately.
Glauber M, Gilmanov D et al (2015). Right anterior minithoracotomy for aortic valve replacement: 10-year experience of a single center. The Journal of Thoracic and Cardiovascular Surgery Volume 150 (3) 548-556.e2	Retrospective review 10-year experience with right anterior minithoracotomy (RAMT) for AVR. N=593 patients	In 302 (50.9%) patients, a sutureless or rapidly implantable biological prosthesis was used; in 23 (3.9%), a mechanical prosthesis; and in the remainder, a conventional biological prosthesis. A total of 113 (19.1%) patients had a small aortic annulus (≤21 mm). Operative times	Mix of different types of prosthesis. Outcomes not reported separately.

		averaged 80 (median: 74) minutes of cross clamping time, and 117 (107) minutes of perfusion time; these were significantly shorter with a sutureless prostheses, compared with a sutured prostheses: perfusion 99 versus 134 minutes, *P* < .0005; aortic cross clamping time: 64 versus 97 minutes, *P* < .0005. The mean (median) assisted ventilation time was 9.8 (6) hours; intensive care unit stay was 1.5 (1) days; hospital length of stay was 6.6 (6) days. Overall in-hospital mortality was 9 deaths (1.5%). At 31.5 months mean follow-up time (1531 cumulative patient-years), 94.8% survival was observed.	
Haverich A, Wahlers TC et al (2014). Three-year hemodynamic performance, left ventricular mass regression, and prosthetic-patient mismatch after rapid deployment aortic valve replacement in 287 patients. J Thorac Cardiovasc Surg 2014; 148:2854-61.	Prospective case series 287 patients with aortic stenosis underwent rapid deployment aortic valve replacement using Edwards Intuity Valve. Follow-up: 3 years	The mean aortic valve gradient significantly decreased from discharge to 3 years of follow-up. The mean effective orifice area remained stable from discharge to 3 years. At 1 year, the left ventricular mass index had decreased by 14% (p<0.0001) and at 3 years by 16 %(p<0.0001) compared with discharge. The prevalence of severe patient-prosthesis mismatch was 3% at discharge and remained stable during the follow-up period.	Similar studies included in table studies.
Hoffman TC, Heiner JA et al (2017). Review of minimal access versus transcatheter aortic valve replacement for patients with severe aortic stenosis. Annals of cardiothoracic surgery. 6, 5: 498-503.	Review	There is a compelling role for miniAVR in low- and intermediate-risk patients, but due to the paucity of data, neither TAVR nor miniAVR should be discounted before a randomized, risk-stratified trial is	Review

		performed. More studies are needed to compare TAVR and miniAVR in low- and intermediate-risk patients.	
Hurley ET, O'Sullivan KE et al (2015). A Meta-Analysis Examining Differences in Short-Term Outcomes Between Sutureless and Conventional Aortic Valve Prostheses. Innovations; 10:375Y382.	systematic review Examined the incidence of PPM insertion associated with sutureless compared with conventional surgical aortic valve replacement.	A total of 832 patients were included in the sutureless group and 3,740 in the conventional group. Aortic cross-clamp (39.8 vs 62.4 minutes; p=0.001) and cardiopulmonary bypass (64.9 vs 86.7 minutes; p=0.002) times were shorter in the sutureless group. Permanent pacemaker implantation rate was higher in the sutureless cohort (9.1% vs 2.4%; p=0.025).	Similar studies included in table 2.
Jiritano F, Cristodoro L, Malta E, et al (2016). Thrombocytopenia after sutureless aortic valve implantation: comparison between intuity and Perceval bioprostheses. J Thorac Cardiovasc Surg; 152:1631–1633.	Retrospective comparative study Comparing rates of thrombocytopenia after SAVR between the Intuity (n = 27) and Perceval (n = 16) sutureless bioprostheses	More red blood cell transfusions were given to the Perceval group as compared with the Intuity (10 vs 7 U, p=0.012) as well as platelets (4 vs 0 U, p<0.01). Platelet counts at postoperative days 3 and 5 as well as at discharge were significantly lower in the Perceval group (p=0.004, p<0.001, p=0.001). Platelet count at discharge for Perceval was 102.18 ± 29.34.56 In addition, mean platelet volume was significantly larger in the Perceval group on postoperative days 1, 3, and 5 (p=0.04, p=0.001, p=0.015), whereas platelet distribution width was significantly larger in the Perceval group on postoperative days 3 and 5 (p=0.018, p=0.026). clinical outcomes were similar.	Included in studies added to table 2.
Kamperidis V, van Rosendael PJ, de Weger A, Katsanos S, Regeer M, van	Observational comparative study	Compared with the 3f Enable valve, TAVR prostheses CoreValve	Included in Qureshi 2018, Tagaki 2016,

der Kley F, Mertens B, Sianos G, Ajmone Marsan N, Bax JJ, Delgado V. Surgical sutureless and transcatheter aortic valves: hemodynamic performance and clinical outcomes in propensity score-matched high-risk populations with severe aortic stenosis. JACC Cardiovasc Interv 2015; 8:670e677.	(propensity score matched study) 80patients with severe aortic stenosis treated with SAVR with the 3f Enable sutureless prosthesis (n=40) or transcatheter aortic valve replacement (corevalve TAVR, n=40). Follow-up: 1.5 years	had larger effective orifice area index (1.00 ± 0.30 cm^2/m^2 vs. 0.76 ± 0.22 cm^2/m^2; p < 0.001), lower pressure gradient (8.14 ± 4.21 mm Hg vs. 10.72 ± 4.01 mm Hg; p = 0.006), less frequent prosthesis-patient mismatch (30.0% vs. 67.5%; p = 0.001), and low flow (46.2% vs. 72.5%; p = 0.02), but more frequent aortic regurgitation (87.5% vs. 20.0%; p < 0.001). The presence of prosthesis-patient mismatch was independently associated with a low-flow state at discharge (odds ratio: 4.70; p = 0.004) and independently associated with the use of the sutureless prosthesis (odds ratio: 3.90; p = 0.02). However, the survival of the 2 groups was comparable after 1.5-year (interquartile range: 0.79 to 2.01 years) follow-up (log-rank test, p = 0.95). TAVR prostheses demonstrated better hemodynamics than the 3f Enable valve but a higher incidence of aortic regurgitation. However, these differences did not influence mid-term survival of patients.	Wang 2016 added to table 2.
Karangelis D, Mazine A et al (2017). What is the role of sutureless aortic valves in today's armamentarium? Expert review of Cardiovascular Therapy. 15, 2: 83-91.	Review	This review summarises the current literature on sutureless and rapid-deployment aortic bioprostheses, focusing on their hemodynamic and clinical performance. Moreover, we highlight clinical caveats associated with these devices and report the current recommendations for	Review

		their use, as advocated by experts in the field.	
Kocher, AA, Laufer G, Haverich A. et al. (2013). One-year outcomes of the Surgical Treatment of Aortic Stenosis with a Next Generation Surgical Aortic Valve (TRITON) trial: A prospective multicenter study of rapid-deployment aortic valve replacement with the EDWARDS INTUITY Valve System. Journal of Thoracic and Cardiovascular Surgery.145 (1): 110-6	Case series (prospective, part of TRITON trial) n=152 Edwards Intuity valve follow-up mean 9 months	Implantation success was 96.1% (146/152), early valve-related mortality was 1.4% (2/146), and cumulative survival was 92.5% at a mean follow-up of 9.8 ± 5.1 months. Crossclamp time for isolated aortic valve replacement was 41.1 ± 10.6 minutes. Independent core laboratory-adjudicated mean effective orifice area and aortic valve pressure gradient were 1.7 ± 0.2 cm(2) and 8.8 ± 3.0 mm Hg at 3 months, and 1.7 ± 0.2 cm(2) and 8.4 ± 3.4 mm Hg at 1 year, respectively.	Included in Phan 2015, NHC 2015 report added to table 2.
Laborde F, Fisclein T et al (2016).Clinical and haemodynamic outcomes in 658 patients receiving the Perceval sutureless aortic valve: early results from a prospective European multicentre study (the Cavalier Trial). European Journal of Cardio-Thoracic Surgery 49 (2016) 978–986	Cohort study (25 European centres) N=685 patients with Perceval sutureless aortic valve 40.0% were octogenarians. Follow-up: 30 days	Implantation was successful in 628 patients (95.4%). In isolated AVR through sternotomy, the mean cross-clamp time and the cardiopulmonary bypass (CPB) time were 32.6 and 53.7 min, and with the less invasive approach 38.8 and 64.5 min, respectively. The 30-day overall and valve-related mortality rates were 3.7 and 0.5%, respectively. Valve explants, stroke and endocarditis occurred in 0.6, 2.1 and in 0.1% of cases, respectively. Preoperative mean and peak pressure gradients decreased from 44.8 and 73.24 mmHg to 10.24 and 19.27 mmHg at discharge, respectively. The mean effective orifice area improved from 0.72 to 1.46 cm^2	Similar studies included in table 2 systematic reviews
Linneweber J, Heinbokel T et al (2010). Clinical experience with ATS 3F stentless aortic	Case series	The overall survival was 86%, and none of the deaths was valve-related. No severe	Larger studies included in table 2.

bioprosthesis: five years follow-up. 19(6), 772-777.	N=35 AVR with the ATS 3F valve implanted total patient follow up was 123 patient-years	structural or non-structural valve dysfunction was identified. Freedom from severe adverse events (SAE) was 89%; the SAE included one permanent and three transient neuroembolic events. Freedom from endocarditis was 100%. Minimal paravalvular regurgitation was detected in four patients. The mean transvalvular pressure gradients were 12.9 +/- 6.3, 11.2 +/- 4.2, and 15.2 +/- 5.3 mmHg at one, three, and five years, respectively. The left ventricular mass and NHYA class were each improved significantly. The left ventricular geometries showed also a trend towards improvement.	
Liakopoulos O, Gerfer S et al (2018). Direct Comparison of the Edwards Intuity Elite and Sorin Perceval S Rapid Deployment Aortic Valves. The Annals of Thoracic Surgery. 105(1): 108-114.	Retrospective analysis N=156 patients underwent RDAVR with the Intuity Elite [Intuity group, n = 117] or the Perceval S [Perceval group, n = 39]).	Implanted RDAVR size (23.3 ± 1.8 mm versus 23.4 ± 1.5 mm), concomitant coronary artery bypass graft surgery (48% versus 33%), number of grafts, cardiopulmonary bypass, and aortic clamp time were comparable between the Intuity group and the Perceval group. Thirty-day mortality (Intuity 2.6% versus Perceval 5.1%) and valve-related complications (Intuity 12.0% versus Perceval 20.5%), including postoperative pacemaker implantation (Intuity 8.5% versus Perceval 12.8%), did not differ between groups. At discharge echocardiography, indexed effective orifice area was higher in the Intuity group, but peak or mean pressure gradients were	Comparison between 2 SU valves.

		comparable between groups.	
Lorusso R, Gelsomino S et al (2013). Sutureless aortic valve replacement: an alternative to transcatheter aortic valve implantation? Curr Opin Cardiol 28 (2):158-163.	Review	A two-centre experience in 208 patients has shown safety, ease of implantation, excellent haemodynamic performance and limited aortic cross-clamp (ACC) and cardiopulmonary (cardiopulmonary bypass, CPB) times, also in the case of associated coronary artery bypass grafting. Another multicentre experience with a third sutureless, albeit stented, valve implanted in 146 patients has been also presented with early favourable results. The sutureless aortic valve has been reported to be competitive also in relation to the transcatheter aortic valve implantation (TAVI) procedure in high-risk patients, as demonstrated by a propensity score based comparative analysis in a multicentre study, with reduced paravalvular leak rate but with increased atrial fibrillation occurrence in SU-AVR cases. Other single-centre series have been published with satisfactory results in terms of excellent haemodynamic performances or of enhanced implantability in high-risk patients or during minimally invasive procedures.	Review
Margaryan R, Kallushi E et al (2015). Sutureless aortic valve prosthesis sizing: estimation and prediction using multidetector-row	235 patients underwent sutureless aortic valve implantation through a	We identified 54 patients who had preoperative contrast-enhanced MDCT. Seven patients received	Valve size determination study.

computer tomography. Innovations, 10(4), 230-5.	right anterior minithoracotomy.	a size S, 21 received a size M, and 26 received a size L prosthesis. The mean age of the patients at the time of intervention was 76.3 ± 6.8 years, and the mean logistic EuroSCORE was 10.4% ± 8.7%. Echocardiographic measurements showed lower accuracy compared to MDCT measurements. Echocardiographic LVOT measurement was 61.11% to predict the valve size, whereas annulus measurement was 53.7%. The aLVOT from MDCT had an accuracy of approximately 62.96%, and cLVOT had 64.81% predictive accuracy. Aortic annulus perimeter cD had the highest accuracy to predict the valve size [62.96%, under the curve, 0.61] followed by aortic annular surface aD having an accuracy of approximately 70.37% (under the curve, 0.75). Classification tree models, after pruning with 4 nodes, increased their accuracy (83.33%), and it was easy to interpret and possibly to implement for clinical use.	
Martens S, Zierer A, Ploss A et al. (2009) Sutureless aortic valve replacement via partial sternotomy. Innovations: Technology & Techniques in Cardiothoracic & Vascular Surgery 5(1):12-5	Case series N=22 Follow up=12 months	Cardiopulmonary bypass and aortic cross-clamp time were 87±16 and 55 ± 11 minutes, respectively. The mean transvalvular gradients were 9 ± 6 mm Hg at discharge and 8 ±2 mm Hg at 1-year follow-up Early mortality (<90 days) was 9% (2 patients). No paravalvular leakage was detected intraoperatively or in	Larger studies included in table 2.

		follow-up echocardiography.	
Martens S, Ploss A, Sirat S et al. (2009) Sutureless aortic valve replacement with the 3f Enable aortic bioprosthesis. Annals of Thoracic Surgery 87: 1914–7	Case series N=32 Follow-up=12 months	Cardiopulmonary bypass and aortic cross-clamp time were 87 minutes and 55 minutes respectively for stand-alone procedures. Because of misalignment of the valve 2 patients were converted to standard procedure.	
Martens S, Sadowski J, Eckstein FS et al (2011). Clinical experience with the ATS 3f Enable Sutureless Bioprosthesis. European Journal of Cardio-thoracic Surgery 40(3): 749-55	Case series (prospective) n=140 3f Enable valve follow-up:1 year	Valve implantation resulted in significant improvement of patients' symptoms. Mean systolic gradient was 9.04 ± 3.56 and 8.62 ± 3.16 mmHg with mean effective orifice area of 1.69 ± 0.52 and 1.67 ± 0.44 at 6 months and 1 year, respectively. No significant transvalvular aortic regurgitation was observed. Early complications included three major paravalvular leaks (PVL; 2.1%) resulting in valve explantation and one thrombo-embolic (0.7%) event. All, but one, of the early PVLs were evident intra-operatively with the medical decision made not to reposition or resolve immediately. Late adverse events included three explantations (2.5% per patient-year): one due to PVL and two due to endocarditis. There was an additional case of late endocarditis (0.8% per patient-year) that resolved by medical management. No structural deterioration, valve-related thrombosis or hemolysis was documented.	Included in Phan 2015, NHC report 2015 added to table 2.
Martinez-Comendador, Castano M et al (2017). Sutureless aortic bioprosthesis. Interactive	Review	In this article, we review the latest evidence on these new sutureless bioprosthesis, including	Review

Cardiovascular and Thoracic Surgery. 25, 114-21.		their advantages and possible disadvantages.	
Mazine A, Teoh K, Bouhout I, et al (2015). Sutureless aortic valve replacement: a Canadian multicentre study. Can J Cardiol; 31:63-8.	Retrospective case series N= 215 patients who underwent sutureless AVR with Perceval S bioprosthesis	For isolated AVR, mean aortic cross-clamp time was 41±12 minutes. In-hospital mortality occurred in 9 patients (4%). No postoperative valve migration was reported. A total of 37 patients (17%) underwent postoperative implantation of a permanent pacemaker, including 20 patients (9%) who had complete atrioventricular block. Postoperative stroke occurred in 7 patients (3%). Echocardiographic evaluation demonstrated well-seated valves with no significant (2+) valvular or paravalvular aortic insufficiency and a mean aortic gradient of 13 ± 6 mm Hg.	Included in Sian 2017 added to table 2.
Mazine A, Christopher B et al (2017). Sutureless aortic valves: who is the right patient? Curr Opin Cardiol 32 (2): 132-136.	Review	Reduction in operative times represents the main advantage of sutureless valves over conventional surgical prostheses, and the possibility of complete annular decalcification and hence a reduced incidence of paravalvular leak is the primary advantage over TAVI. There is limited data regarding long-term outcomes, durability or reoperation.	Review
Meco M et al (2018). Sutureless aortic valve replacement versus transcatheter aortic valve implantation: a meta-analysis of comparative matched studies using propensity score matching. Interactive Cardiovascular and Thoracic Surgery 26:202-209.	A systematic review and meta-analysis compares outcomes of patients undergoing transcatheter aortic valve implantation (TAVI) with those undergoing surgical aortic valve replacement using sutureless valves	Six comparative studies using propensity score matching. meta-analysis identified 1462 patients in that 731 patients underwent surgical aortic valve replacement using sutureless valves (SU) and 731 patients underwent a TAVI.	Similar systematic reviews added to table 2.

		30-day or in-hospital mortality was lower in the SU group [odds ratio (OR) 0.54, 95% confidence interval (CI) 0.36–0.80; p=0.003]. In the TAVI group, the incidence of postoperative stroke was higher (OR 0.36, 95% CI 0.17–0.79; p=0.01). The incidence of moderate or severe paravalvular regurgitation was higher in the TAVI group (OR 0.22, 95% CI 0.14–0.35; p=0.001). There were neither differences in the postoperative renal failure (OR 1.44, 95% CI 0.46–4.58; p=0.53) nor in the number of patients requiring postoperative pacemaker implantation (OR 1.06, 95% CI 0.54–2.08; p=0.86). Patients in the SU group required more transfusions (OR 4.47, 95% CI 2.77–7.21; p=0.0001), whereas those in the TAVI group had higher major vascular complications (OR 0.06, 95% CI 0.01–0.25; p=0.0001). Intensive care unit stay was not different (mean difference 0.99, 95% CI - 1.22 to 1.40; p=0.53). One-year survival was better in the SU group (Peto OR 0.35, 95% CI 0.18–0.67; p=0.001), as was the 2-year survival (Peto OR 0.38, 95% CI 0.17–0.86; p=0.001).	
Meuris B, Flameng WJ, Laborde F, et al (2015). Five-year results of the pilot trial of a sutureless valve. J Thorac Cardiovasc Surg. 150:84-8.	Prospective case series N=30 patients with aortic stenosis Perceval sutureless valve	Procedural success was 100%. Cardiopulmonary bypass time and cross-clamp time in isolated aortic valve replacement were 46.4 ± 6.7 minutes and 29.3 ± 8.0 minutes, respectively. One	Included in Sian 2017 added to table 2.

	Cumulative follow-up was 92.67 patient-years, with a median of 4.2 years	patient died during the hospital stay. Postoperative complications included 1 patient with mediastinal bleeding, and 1 with atrioventricular block that led to pacemaker implantation. No stroke occurred in either the early or late period. At the last available follow-up, 22 patients were alive. The mean gradient was 9.3 mm Hg, with an effective orifice area of 1.7 cm^2 at 5 years. No dislodgement, structural valve deterioration, hemolysis, or valve thrombosis was reported.	
Miceli A, Santarpino G, Pfeiffer S, et al. Minimally invasive aortic valve replacement with Perceval S sutureless valve: early outcomes and one-year survival from two European centers. J Thorac Cardiovasc Surg 2014;148:2838-43.	Retrospective observational study 281 high-risk patients underwent minimally invasive aortic valve replacement with the Perceval S sutureless valve through either right anterior minithoracotomy (n =164) or upper ministernotomy (n =117) at 2 cardiac centers. Follow-up 1 year	The overall in-hospital mortality was 0.7% (2 patients). The overall median cardiopulmonary bypass and crossclamp time was 81 minutes (interquartile range, 68-98) and 48 minutes (interquartile range, 37-60), respectively. Postoperative stroke occurred in 5 patients (1.8%). The incidence of paravalvular leak greater than 1 of 4 and atrioventricular block requiring pacemaker implantation was 1.8% (5 patients) and 4.2% (12 patients), respectively. No migration occurred, and the mean postoperative gradient was 13 ± 4 mm Hg. At a median follow-up of 8 months (interquartile range, 4-14), the overall survival was 90%.	Included in Sian 2017 added to table 2.
Miceli A, Gilmanov D et al (2016). Minimally invasive aortic valve replacement with a sutureless valve through a right anterior	Propensity score matched study N=269 patients with severe aortic stenosis underwent either RT	Baseline characteristics were similar in both groups (mean age 79 ± 6 years) and the median logistic EuroSCORE	Included in Qureshi 2018, Tagaki 2016, Wang 2016 added to table 2.

mini-thoracotomy versus transcatheter aortic valve implantation in high-risk patients. European Journal of Cardio-Thoracic Surgery 49, 960–965.	with perceval S sutureless valves (n = 178 patients, 66.2%) or TAVI (n = 91, 33.8%: 44 transapical and 47 trans-femoral). Of these, 37 patients undergoing RT with the perceval S valve were matched to 37 patients with TAVI Sapien valve by the propensity score. Follow-up 1-2 years.	was 14% (range 9–20%). In the matched group, the in-hospital mortality rate was 8.1% (n = 3) in the TAVI group and 0% in the RT group (P = 0.25). The incidence rate of stroke was 5.4% (n = 2) versus 0% in the TAVI and RT groups (P = 0.3). In the TAVI group, 37.8% (n = 14) had mild paravalvular leakage (PVL) and 27% (n = 10) had moderate PVL, whereas 2.7% (n = 1) had mild PVL in the RT group (P < 0.001). One- and 2-year survival rates were 91.6 vs 78.6% and 91.6 vs 66.2% in patients undergoing RT with the perceval S sutureless valve compared with those undergoing TAVI, respectively (P = 0.1).	
Miceli A (2017). Sutureless valve associated a minimally invasive approach covers the gap between transcatheter aortic valve implantation and conventional aortic valve replacement. Cardiology 137 (supplement 1): 112	Review	Based on current literature, TAVI is recommended for inoperable and very high risk patients whereas sutureless and rapid deployment valve in combination with minimally invasive approach are advised for medium risk operable patients. The low risk patients may benefit from a minimal invasive approach but still with a conventional sutured valve.	Review
Minami T, Sainte S et al (2017). Hospital cost savings and other advantages of sutureless vs stented aortic valves for intermediate-risk elderly patients. Surg Today. 47: 1268-73.	Comparative study 52 patients with sutureless valves were matched to 180 patients who had a stented valve inserted during the same period.	The sutureless group had a higher Euroscore (logistic Euroscore I) risk (12.8 vs 9.7; $p = 0.02$), with significantly shorter aortic cross-clamp (ACC) time ($p < 0.01$), cardiopulmonary bypass (CPB) time ($p < 0.01$), intensive care unit stay ($p < 0.01$), intubation time ($p < 0.01$), and overall	Compared clinical outcomes and hospital costs between the two groups. Economic domain out of remit.

		hospital stay ($p = 0.05$). The sutureless group also revealed a significant hospital cost saving of approximately 8200€ ($p = 0.01$).	
Misfield M (2015). Minimally invasive aortic valve replacement using the Perceval S sutureless valve. Annals of Cardiothoracic Surgery. 4(2), 203-5.	Case report N=1 combined aortic valve disease with severe aortic stenosis and mild aortic regurgitation. Perceval valve	Valve was appropriately positioned without any paravalvular leak. The maximum/mean pressure gradients were 16/8 mmHg with a trace of central regurgitation. The patient left the operating room in sinus rhythm without the need for inotropic support and was extubated 3 hours postoperatively. The overall postoperative course was uneventful.	Larger studies included in table 2.
Morita S (2016). Aortic valve replacement and prosthesis-patient mismatch in the era of transcatheter aortic valve implantation. Gen Thorac Cardiovascular Surgery.64, 435-440.	Review	The results of the long-term survival after aortic valve replacement (AVR) have indicated that an IEOA less than 0.65 cm^2/m^2 should be avoided in all cases, whereas the indications for patients with an IEOA between 065 and 0.85 cm^2/m^2 should be determined by considering multiple factors. A large body size and younger age have a significantly negative influence on the long-term survival. In Asian population, the prevalence of PPM was low, despite the fact that the size of the aortic annulus was small. The IEOA after TAVI was larger than after surgical AVR in population-matched studies. To evaluate the role of TAVI and other modalities for a small aortic root, studies with a longer follow-up and larger volume are thus warranted.	Review
Muneretto C, Alfieri O et al (2015). A comparison of conventional surgery, transcatheter aortic valve	Propensity score matched study on the basis of the therapeutic	30 day mortality was significantly higher in the transcatheter aortic valve replacement	Included in Qureshi 2018, Wang 2016, Tagaki 2017 added to table 2.

replacement, and sutureless valves in “real-world” patients with aortic stenosis and intermediate-to high-risk profile.JThorac Cardiovasc Surg 2015;150:1570e1579.	strategy: Patients with isolated severe aortic stenosis and an intermediate-to high-risk profile surgical aortic valve replacement (n = 204), sutureless valve implantation (n =204), and transcatheter aortic valve replacement (n = 204). Mean 42.5 months follow-up	group (surgical aortic valve replacement = 3.4% vs sutureless =5.8% vs transcatheter aortic valve replacement = 9.8%; P = .005). The incidence of postprocedural was 3.9% in a surgical aortic valve replacement vs 9.8% in sutureless vs 14.7% in transcatheter aortic valve replacement (P<.001) and peripheral vascular complications occurred in 0% of surgical aortic valve replacement vs 0% of sutureless vs 9.8% transcatheter aortic valve replacement (P<.001). At 24-month follow-up, overall survival (surgical aortic valve replacement = 91.3%_ 2.4%vs sutureless = 94.9%± 2.1% vs transcatheter aortic valve replacement =79.5% ± 4.3%; P <.001) and survival free from the composite end point of major adverse cardiovascular events and periprosthetic regurgitation were significantly better in patients undergoing surgical aortic valve replacement and sutureless valve implantation than in patients undergoing transcatheter aortic valve replacement (surgical aortic valve replacement ± 92.6%±2.3% vs sutureless±96%±1.8% vs transcatheter aortic valve replacement =77.1% ± 4.2%; P <.001). Multivariate Cox regression analysis identified transcatheter aortic valve replacement as an independent risk factor for overall mortality	

		hazard ratio (hazard ratio, 2.5; confidence interval,1.1-4.2; P = .018).	
Muneretto C, Bisleri G, Moggi A, Di Bacco L, Tespili M, Repossini A, Rambaldini M. Treating the patients in the 'grey-zone' with aortic valve disease: a comparison among conventional surgery, sutureless valves and transcatheter aortic valve replacement. Interact Cardiovasc Thorac Surg 2015;20:90–5.	Observational comparative study N=163 patients with intermediate to high risk for atherosclerotic disease of the aorta/peripheral vessels underwent SAVR (G1, n = 55), sutureless valve Perceval implantation (G2, n = 53) or TAVR Corevalve implantation (G3, n = 55) 24-month follow-up	Post-procedural pacemaker implantation (G1 = 1.8% vs G2 = 2% vs G3 = 25.5%, P <0.001) and peripheral vascular complications (G1 = 0% vs G2 = 0% vs G3 = 14.5%, P <0.001) occurred more frequently in patients undergoing TAVR. Hospital mortality was similar among the groups (G1 = 0% vs G2 = 0% vs G3 = 1.8%, P = NS). At the 24-month follow-up, overall survival free from major adverse cardiac and cerebrovascular events and prosthetic regurgitation was better in patients who had undergone sAVR and sutureless valves than those who had undergone TAVR (G1 = 95.2 ± 3.3% vs G2 = 91.6 ± 3.8% vs G3 = 70.5 ± 7.6%; P = 0.015).	Included in Tagaki 2016, Sian 2017, Paone 2015 HTA, NHC 2015 report added to table 2.
Murzi M, Cerillo AG et al (2016). Exploring the learning curve for minimally invasive sutureless aortic valve replacement. The Journal of Thoracic and Cardiovascular Surgery. 152 (6): 1537-46.	Case series N=300 patients who had right minithoracotomy aortic valve replacement with a sutureless bioprosthesis. Learning curve was analyzed by dividing the study population into tertiles of 100 patients each.	The overall mortality was 0.7% (2 patients). No significant differences were noted in terms of mortality and complications between tertiles. The sutureless valve was implanted successfully in 99% of patients (298/300). Cumulative sum analysis failed to identify any significant learning effects for technical success. Nevertheless, surgeons A, B, and C had a small initial learning curve, and surgeons D, E, and F did not, reflecting a trend toward a positive effect of cumulative institutional experience on the individual learning curve. The 30-	Learning curve effect

		day complications analysis revealed a cluster of failures at the beginning of the experience.	
O' Sullivan KE, Bargenda S et al (2016). Advances in the management of severe aortic stenosis. Irish Journal of Medical Science; 185(2), 309-17.	Review	Minimally invasive operative approaches include mini-sternotomy and mini-thoracotomy. Sutureless aortic prostheses reduce aortic cross-clamp time and cardiopulmonary bypass time; however, long-term follow-up data are unavailable at this time. Mechanical prostheses are advised for those under 60.	Review
Pfeiffer S, Fischlein T et al (2016). Sutureless Sorin Perceval aortic valve implantation. Seminars in thoracic and cardiovascular surgery. 29 (1), pp 1-7.	Review on Perceval sutureless valve.	Overall, excellent performances have been demonstrated in hemodynamic outcomes, safety and of use. In this article the most important studies published until now are discussed providing a state of the art overview of current knowledge as well as future directions and indications for the use of the Perceval valve based on preliminary results of ongoing studies.	Review
Pfeiffer S, Wilbring M et al (2017). The 'entangled' stent: a preventable cause of paravalvular leak of the Perceval prosthesis. Interactive Cardiovascular and Thoracic Surgery. 25, 987-989.	Review published reports by assessing photographic and radiological images	In vitro study was also conducted with stent twisting that may occur during the collapse of the valve, termed 'stent entanglement', demonstrating consecutive successful valve collapse and implantation. This result has led us to hypothesize that infolding is due to a number of triggers, e.g. distortion of the stent overlooked during the final visual inspection of the implanted valve, rather than to excessive oversizing of the prosthesis as the sole cause, as repeatedly	Review

		suggested in previous reports.	
Pfeiffier S & Santarpino G (2016). Sutureless valves in the era of transcatheter aortic valve implantation. European Journal of Cardiothoracic Surgery. 49, 1028-30.	Review	Aortic valve surgery has recently undergone a second revolution with the introduction of sutureless aortic bioprosthetic valves into clinical practice, which has the potential to be a 'game changer': specifically in the setting of minimally invasive surgery, the use of sutureless valves can result in a significant reduction in cross-clamp and CPB times, which were reported to be 39.4% shorter than those obtained with other types of bioprosthetic valves.	Review
Pfeiffer S, Deli'aqulia AM et al (2017). Efficacy of sutureless aortic valves in minimally invasive cardiac surgery: an evolution of the surgical technique. Journal of Cardiovascular Surgery 58 (5): 731-738.	N=627 patients underwent elective isolated AVR and were divided into three groups: patients who underwent sutureless-AVR via J sternotomy (group A, N.=206) and patients who underwent stented-AVR via J sternotomy (group B, N.=247) or full-sternotomy (group C, N.=174).	Aortic cross-clamp and cardiopulmonary bypass times were shorter in group A than in groups B and C. As expected, aortic cross-clamp time was prolonged in group B as compared to groups A and C (60±18 vs. 36±10 and 54±16 min; P<0.001). After multivariate adjustment, minimally invasive AVR resulted in significantly fewer postoperative complications in terms of drainage bleeding and the need for blood transfusions (385±287 vs. 500±338 mL, P=0.006; and 1.3±2.1 vs. 1.8±2.6 IU, P=0.001, respectively). No differences in postoperative outcomes were observed among groups.	Similar studies included in table 2.
Pollari F, Santarpino G et al (2014). Better short-term outcome by using sutureless valves: a propensity matched score analysis. Ann Thoracic Surgery 98:611-616.	Propensity matched retrospective study 566 patients underwent aortic valve replacement with bioprostheses; of	There were 3 hospital deaths in the stented group and 2 in the sutureless group (p = 0.65). Aortic cross-clamp, cardiopulmonary bypass, and operation times were significantly	Included in Qureshi 2018, Tagaki 2017, NHC 2015 report added to table 2.

	these, 166 received a sutureless valve, and 400 received a stented valve Propensity matched scored analysis: 2 groups (sutureless and stented) with 82 matched pairs.	shorter in the sutureless group ($p < 0.001$). Patients in the sutureless group required blood transfusion less frequently (1.2 ± 1.3 vs 2.5 ± 3.7 units, $p = 0.005$), with a similar need for reexploration for bleeding (2 vs 5, $p = 0.221$). The sutureless group had a shorter intensive care unit stay (2.0 ± 1.2 vs 2.8 ± 1.3 days, $p < 0.001$), hospital stay (10.9 ± 2.7 vs 12.4 ± 4.4 days, $p = 0.001$) and intubation time (9.5 ± 4.6 vs 16.6 ± 6.4 hours, $p < 0.001$), and a lower incidence of postoperative atrial fibrillation ($p = 0.015$), pleura effusions ($p = 0.024$), and respiratory insufficiency ($p = 0.016$). Pacemaker implantation and occurrence of neurologic events were similar between groups ($p > 0.05$). A lower rate of postoperative complications resulted in reduced resource consumption in the sutureless group for diagnostics (€2,153 vs €1,387), operating room (€5,879 vs €5,527), and hospital stay (€9,873 vs €6,584), with a total cost saving of approximately 25% (€17,905 vs €13,498).	
Regeer M, Merkestein L et al (2017). Left bundle branch block after sutureless, transcatheter, and stented biological aortic valve replacement for aortic stenosis. EuroIntervention 12 (13): 1660-1666.	Retrospective analysis N=501 patients who had TAVI or AVR Comparing the incidence of left bundle branch block (LBBB) after su-AVR and TAVI, in comparison to conventional AVR.	Su-AVR patients and TAVI patients had a higher incidence of new-onset LBBB at hospital discharge (23% and 16%, respectively) compared to patients treated with conventional AVR (4%; p<0.001). On multivariate logistic regression analyses, the type of AVR was independently	Similar studies added to table 2.

		associated with complete LBBB, after correcting for age, preoperative QRS duration and heart rate (su-AVR and TAVI relative to the reference category conventional AVR: odds ratio [OR] 8.5, 95% confidence interval [CI]: 3.7-19.5; p<0.001, and OR 5.8, 95% CI: 2.4-14.1; p<0.001, respectively).	
Rubino AS, Santarpino G, De Praetere H, et al (2014). Early and intermediate outcome after aortic valve replacement with a sutureless bioprosthesis: Results of a multicenter study. J Thorac Cardiovasc Surg;148:865-71.	Retrospective observational study analysis of 314 patients who underwent aortic valve replacement with the Perceval S valve with (94 patients) or without (220 patients) concomitant coronary artery bypass surgery.	The Perceval S valve was successfully implanted in all but 1 patient (99.7%). The mean aortic cross clamping time was 43 ±20 minutes (isolated procedure, 39±15 minutes; concomitant coronary surgery, 52±26 minutes). Severe paravalvular leak occurred in 2 patients (0.6%). In-hospital mortality was 3.2% (1.4% after isolated procedure and 7.4%after concomitant coronary surgery). In-hospital mortality was 2.8% and 4.0% among patients with a European System for Cardiac Operative Risk Evaluation II less than 10% and 10% or greater, respectively (P =.558). Octogenarians had slightly higher in-hospital mortality (5.2% vs 2.0%, P = .125; after isolated procedure: 2.7% vs 0.7%, P= .223; after concomitant coronary surgery: 9.5% vs 5.8%, P = .491) compared with younger patients. Full sternotomy did not increase the in-hospital mortality risk compared with ministernotomy or minithoracotomy access (1.3% vs 1.4%, when	Included in Sian 2017 added to table 2.

		adjusted for baseline covariates: P = .921; odds ratio, 0.886; 95% confidence interval, 0.064-12.346). One-year survival was 90.5%. Freedom from valve related mortality, stroke, endocarditis, and reoperation was 99.0%, 98.1%, 99.2%, and 98.3%, respectively.	
Rubino A, Biancari F et al (2018). Hemodynamic assessment of Perceval sutureless bioprosthesis by dobutamine stress echocardiography. Echocardiography. 35: 65-70.	Case series N=32 patients with AVR with Perceval sutureless bioprosthesis. Follow-up: median 19.5 months	Dobutamine stress echocardiography (DSE) significantly increased heart rate, stroke volume, ejection fraction, and transvalvular gradients (peak gradient, 24.0 ± 7.6 vs 38.7 ± 13.6 mm Hg, *P* < .001; mean gradient, 12.6 ± 4.2 vs 19.8 ± 8.3, *P* < .001). When compared to baseline, estimated valve areas significantly increased at follow-up (EOA, 1.48 ± 0.46 vs 2.06 ± 0.67, *P* < .001; EOAi, 0.84 ± 0.26 vs 1.17 ± 0.37, *P* < .001). Mean percentage increase in EOAi was 40.3% ± 28.0%. S size prostheses had the highest increase in EOA1, but the difference was not significant (S 46.0% ± 27.5% vs M 45.4% ± 34.5% vs L 32.7% ± 26.4% vs XL 32.1% ± 20.5%, *P* = .66). Severe patient-prosthesis mismatch (EOAi ≤ 0.65 cm^2/m^2) was present at rest in 8 patients (25%), but only in one patient (3.1%) during DSE.	Larger studies included in table 2.
Sadowski J, Kapelak B, Pfitzner R et al. (2009) Sutureless aortic valve bioprothesis '3F/ATS	Case series N=27	There was no mortality in the perioperative period and during follow-up. Clinical	Larger studies included in table 2.

Enable'--4.5 years of a single-centre experience. Kardiologia Polska 67: 956-63	Follow-up= 3 months to 4.5 years	improvement of 1 to 3 NYHA classes was observed.	
Santarpino G, Pfeiffer S, Fischlein T. (2012) Perceval sutureless approach in a patient with porcelain aorta unsuitable for transcatheter aortic valve implantation. International Journal of Cardiology 155: 168–70	Case report N=1 Follow-up=12 months	Implantation, aortic cross-clamp and cardiopulmonary bypass times were 9, 112, and 167 minutes. No paravalvular leakage intraoperatively, mean gradient of 9 mmHg and peak gradient of 15 mmHg.	Larger studies included in table 2.
Santarpino G, Pfeiffer S, Concistre G et al. (2012) A supra-annular malposition of the Perceval S sutureless aortic valve: the 'chi-movement' removal technique and subsequent reimplantation. Interactive Cardiovascular & Thoracic Surgery 15: 280–1	Case report N=1 Follow-up= during the procedure	Removal and subsequent re-implantation of an undamaged prosthesis after incorrect placement in the supra-annular position.	Larger studies included in table 2.
Santarpino G, Pfeiffer S, Schmidt J et al. (2012) Sutureless aortic valve replacement: first-year single-center experience. Annals of Thoracic Surgery 94: 504-8	Case series n=83 follow-up=mean 8 months	The patients received a size S (4), M (38), or L (41) prosthesis, either as isolated (57) or combined procedures (26). Fifty-one patients (61.5%) received a “J” sternotomy. Mean logistic European system for cardiac operative risk evaluation was 10. ± 7.5%, mean aortic cross-clamp time was 43.8 ± 20.8 minutes (36 ± 12.7 minutes for isolated procedures). Mean implantation time was 8 ± 3.8 minutes (range 4 to 28 minutes). In-hospital mortality was 2.4% (1 patient for multiorgan failure and 1 for liver insufficiency); mean hospital stay was 11.5 ± 4.4 days (range 2 to 28 days). We recorded 5 pacemaker implantations (6%). At follow-up, we had 2 deaths (1 patient for congestive heart failure and 1 for gastrointestinal bleeding). At 1 year, mean New York Heart	Included in NHC 2015 report added to table 2.

		Association functional class was 1.0 ± 0.6. Mean transprosthetic gradients were 13.4 ± 2.8, 12.6 ± 2.3, and 10.8 ± 1.3 mm Hg postoperatively, at 6 months, and at 1 year, respectively.	
Santarpino G, Pfeiffer S, Fischlein T. (2012) Sutureless valve implantation in a patient with bicuspid aortic valve. International Journal of Cardiology 157(2) e21–e22	Case report N=1 Follow-up= 5 days	Postoperative course was uneventful.	Larger studies included in table 2.
Santarpino, Pfeiffer S et al (2013). The Perceval S aortic valve has the potential of shortening surgical time: Does it also result in improved outcome?. Ann Thorac Surg 96:77-81.	Comparative case series N=100 patients underwent minimally invasive isolated aortic valve replacement. 50 patients received a Perceval bioprosthesis (group P) and 50 patients received a conventional non-Perceval valve (group NP).	One implant failure occurred in group P (p = 0.5), and conversion to full sternotomy was necessary in 1 patient from each group. Aortic cross-clamp and cardiopulmonary bypass times were 39.4% and 34% shorter in group P (both p < 0.001). Within 30 days, a total of 5 patients died (2 in group P and 3 in group NP, p = 0.5). No significant differences were observed between groups in postoperative arrhythmias and need for pacemaker implantation (p = 0.3 and p = 0.5, respectively). Despite the higher surgical risk, group P patients less frequently required blood transfusion (1.1 ± 1.1 units versus 2.3 ± 2.8 units, p = 0.007), and had a shorter intensive care unit stay (1.9 ± 0.7 versus 2.8 ± 1.9 days, p = 0.002) and a shorter intubation time (9.2 ± 3.6 hours versus 15 ± 13.8 hours, p = 0.01). Group NP patients had a mean prosthesis size significantly smaller than for group P (23 ± 2 mm versus 23.9 ± 1.1 mm, p = 0.01). The	Included in Paone 2015 HTA, NHC 2015 report added to table 2.

		Perceval valve provided comparable hemodynamic performance to that of non-Perceval valves (mean gradient 8.4 ± 6 mm Hg versus 10 ± 4.9 mm Hg, *p* = 0.24).	
Santarpino G, Pfeiffer S et al (2015). Clinical outcome and cost analysis of sutureless versus transcatheter aortic valve implantation with propensity score matching analysis. Am J Cardiol; 116:1737e1743.	Propensity score matched study N= 102 perceval sutureless valve versus 102 TAVI Sapien valve	In-hospital death occurred in 5 patients in sutureless group and 3 patients in TAVI group (p = 0.36). Blood transfusions were higher in sutureless group (2.1±2.3 vs 0.4 ± 1.0 U). TAVI group had a shorter intensive care unit and hospital stay (2.2 ±2.7 vs 3.2 ± 3.5 days, p = 0.037; 12 ± 6 vs 14 ± 6 days, p = 0.017). No differences in postoperative neurologic (p = 0.361), renal (p =0.106), or respiratory (p =0.391) complications were observed between groups. At follow-up (24.5 ±13.8 months), 1 patient in sutureless group and 7 patients in TAVI group died (p =0.032). Paravalvular leakage occurred more frequently in patients in TAVI group (35 [34%] vs 7 [6.9%]; p <0.001) with an impact on follow-up survival rate. The costs associated to the 2 procedures are similar when the cost of the device was excluded (p = 0.217). When included, the sutureless approach resulted a cost saving (V22,451 vs V33,877, p <0.001).	Included in Qureshi 2018, Wang 2016, Tagaki 2017 added to table 2.
Santarpino G, Pfeiffer S, Jessl J, Dell'Aquila AM, Pollari F, Pauschinger M, Fischlein T (2014). Sutureless replacement versus transcatheter valve implantation in aortic valve stenosis: a propensity-	Propensity score matched retrospective study N= 122 patients underwent sutureless aortic valve replacement, and 122 underwent TAVI. After	Preoperative characteristics and risk scores of matched groups were comparable. In-hospital mortalities were 0% in the sutureless group and 8.1% (n = 3) in the	Included in Tagaki 2016, Phan 2015, NHC report 2015 added to table 2.

matched analysis of 2 strategies in high risk patients. J Thorac Cardiovasc Surg;147:561–7.	propensity matching 37 pairs were analysed. 37perceval sutureless valve versus 37 TAVI Sapien valve. Mean follow-up of 18.9 ±10.1 months	TAVI group (P = .24). Permanent pacemaker implantation was required in 4 patients in the sutureless group and 1 patient in the TAVI group (10.8% vs 2.7%; P =.18). A neurologic event was recorded in 2 patients of each group. Predischarge echocardiographic data showed higher paravalvular leak rate in the TAVI group (13.5% vs 0%; P= .027). At mean follow-up of 18.9 ±10.1 months, overall cumulative survival was 91.9% and significantly differed between groups (sutureless 97.3% vs TAVI 86.5%; P = .015). In the TAVI group, a significant difference in mortality was observed between patients with (n = 20) and without (n =17) paravalvular leak (25% vs 0%; P = .036).	
Santarpino G, Pfeiffer S, Pollari F, et al (2014). Left ventricular mass regression after sutureless implantation of the Perceval S aortic valve bioprosthesis: preliminary results. Interact Cardiovasc Thorac Surg;18:38-42.	Retrospective observational study 78 patients with symptomatic AS underwent isolated aortic valve replacement (AVR) with the Perceval bioprosthesis. follow-up (mean 13.5 ± 7.3 months	There was 1 in-hospital non-cardiac death and 3 late deaths. LV mass index decreased from 148.4 ± 46 g/m(2) at baseline to 119.7 ± 38.5 g/m(2) at follow-up (P = 0.002). No significant changes were observed in LV hypertrophy and/or relative wall thickness >0.42 as well as in LV ejection fraction. Mean aortic gradient decreased from 49.5 ± 15.8 mmHg at baseline to 11.6 ± 5.1 mmHg at discharge and 8.3 ± 4.4 mmHg at follow-up (P < 0.001), resulting in significant clinical improvement. No moderate or severe paravalvular leakage was observed at discharge and at follow-up. n AS patients, isolated AVR with the Perceval sutureless	Included in Sian 2017 added to table 2.

		bioprosthesis is associated with significant LV mass regression at 1-year follow-up.	
Santarpino G, Kalisnik G et al (2016). What's up on sutureless valves. Minerva Cardioangiologica. 64(5): 552-9.	Review	Studies published to date evaluating the sutureless bioprosthesis are reviewed along with future directions and indications for the target patient population.	Review
Shrestha M, Khaladj N, Bara C et al. (2008) A staged approach towards interventional aortic valve implantation with a sutureless valve: initial human implants. Thoracic & Cardiovascular Surgeon 56: 398–400	Case series N=30 Follow-up=12 months	One patient died during hospital stay for unknown reasons. Autopsy revealed no valve related pathologies. Cardiopulmonary bypass time was 60 minutes (41–130), cross-clamping time was 36 (22–79) min. Intraoperative as well as postoperative echocardiography revealed neither aortic insufficiency nor paravalvular leakage in any of the patients.	Larger studies included in table 2.
Shrestha M, Folliguet T, Meuris B et al. (2009) Sutureless Perceval S aortic valve replacement: a multicenter, prospective pilot trial. Journal of Heart Valve Disease 18(6): 698-702	Case series n=30 follow-up=12 months	The mean aortic cross-clamp and ECC times were 34 +/- 15 min and 59 +/- 21 min, respectively. There was one in-hospital death (3.3%), and three deaths occurred within 12 months of follow up (one death was valve-related, and two deaths were independent of the valve implantation). A total of 28 patients was assessed at one month post-implantation, and 23 after 12 months. No migration or dislodgement of the valve had occurred, but there were two mild paravalvular leakages and two mild intravalvular insufficiencies.	Larger studies included in table 2.
Shrestha M, Folliguet TA, Pfeiffer S, et al (2014). Aortic valve replacement and concomitant	Retrospective case series	Mean aortic cross-clamp and extracorporeal circulation (ECC) times	Included in Sian 2017 added to table 2.

procedures with the Perceval valve: results of European trials. Ann Thorac Surg; 98:1294-300.	243 patients underwent SAVR (Perceval) with concomitant procedures Follow up 1 year	were 50.7 ± 22.8 minutes and 78.9 ± 32.3 minutes, respectively. Thirty-day mortality was 2.1%. Mean postoperative gradient and effective orifice area were 10.1 ± 4.7 mm Hg and 1.5 ± 0.4 cm^2 and 8.9 ± 5.6 mm Hg and 1.6 ± 0.4 cm^2, respectively, at 1 year. There were early explantations, 4 of which resulted from paravalvular leaks. One additional valve explantation resulted from aortic root bleeding, probably caused by excessively extensive decalcification. In the late period, there was 1 mild paravalvular leak and no intravalvular insufficiency. No migration, dislodgement, or degeneration of the valve occurred during follow-up. Median follow-up was 444 days.	
Shrestha M, Maeding I, Höffler K, et al (2013). Aortic valve replacement in geriatric patients with small aortic roots: are sutureless valves the future? Interact Cardiovasc Thorac Surg;17:778-82; discussion 782.	Prospective case series N=120 isolated SAVRs in patients with a small annulus (conventional valves (n=70, C group) and sutureless valves (n=50, P group) Follow-up up to 5 years	The cardiopulmonary bypass (CPB) and cross-clamp times of the C group were 75.3 ± 23 and 50.3 ± 14.2 min vs 58.7 ± 20.9 and 30.1 ± 9 min in the P group, ($P < 0.001$). In the C group, two annulus enlargements were performed. Thirty-day mortality was 4.3% (n = 3) in the C group and 0 in the P group, (n.s.). At follow-up (up to 5 years), mortalities were 17.4% (n = 12) in the C group and 14% (n = 7) in the P group (n.s).	Included in Qureshi 2018, Sian 2017, Phan 2015, Paone 2015, NHC 2015 report added to table 2.
Shrestha M, Fischlein T (2016). European multicentre experience with the sutureless Perceval valve: Clinical and haemodynamic outcomes up to 5 years in over 700	Prospective case series N=731 patients who had SU-AVR with Perceval S 5 years follow-up.	Isolated AVR, mean cross-clamp and cardiopulmonary bypass times were 30.8 and 50.8 min in full sternotomy, and 37.6 and 64.4 min in the	Included in table 2.

patients. European journal of cardio-thoracic surgery. 49 (1), 234-41.		minimally invasive approach, respectively. Early cardiac-related deaths occurred in 1.9%. Overall survival rates at 1 and 5 years were 92.1 and 74.7%, respectively. Major paravalvular leak occurred in 1.4% and 1% at early and late follow-up, respectively. Significant improvement in clinical status was observed postoperatively in the majority of patients. Mean and peak gradients decreased from 42.9 and 74.0 mmHg preoperatively, to 7.8 and 16 mmHg at the 3-year follow-up. LV mass decreased from 254.5 to 177.4 g at 3 years.	
Stanger O, Grabherr M, et al (2017). Thrombocytopaenia after aortic valve replacement with stented, stentless and sutureless bioprostheses. Eur J Cardiothorac Surg. 2017; 51:340–346.	Retrospective review Comparing the maximum postoperative decrease in platelet count between the Perimount Magna (n = 199), sutureless 3 F Enable (n = 3), Freedom SOLO (n = 366), mechanical ATS (n = 199), and Perceval (n = 48).	Mechanical, Perimount, and 3 F enable valves resulted in significantly smaller decreases in postoperative platelet counts (44 ± 12%, 50 ± 11%, 53 ± 12%, respectively) compared with the Pericarbon Freedom, Perceval, and SOLO (61 ± 14%, 60 ± 10%, 64 ± 12%, respectively). Overall, Sorin valves resulted in a 13% drop in platelet counts compared with non-Sorin valves; these were associated with a lower red blood cell ($P < 0.001$) or platelet ($P = 0.001$) transfusions.	Included in studies added to table 2.
Toledano B, Bisbal F, Camara ML, et al. Incidence and predictors of new-onset atrioventricular block requiring pacemaker implantation after sutureless aortic valve replacement. Interact Cardiovasc Thorac Surg. 2016;23:861–868.	Retrospective review Predictors of permanent pacemaker implantation and effect of modifying surgical technique in 140 patients.	The modification in surgical technique involved a more thorough, symmetrical decalcification and higher positioning guiding sutures to the intra-annular level. Overall incidence of permanent pacemaker implantation was 12%, whereas incidence in	Included in studies added to table 2.

		each of the standard technique and modified technique were 21% and 8%, respectively. Independent predictors of permanent pacemaker implantation were baseline first-degree atrioventricular block (P < 0.01), left QRS axis deviation (P = 0.03), and standard surgical technique. (P = 0.02)	
Theron A, Ravis E et al (2017). Rapid-deployment aortic valve replacement for severe aortic stenosis: 1-year outcomes in 150 patients. Interactive CardioVascular and Thoracic Surgery 25: 68–74.	Prospective case series N=150 patients with severe AS who underwent RDAVR with the EDWARDS INTUITY bioprosthesis. Follow-up: 1 year	Implantation was successful in all: 103 (68.7%) had isolated aortic valve replacement (AVR) and 47 (31.3%) had concomitant procedures. For isolated AVR, mean cross-clamp and cardiopulmonary bypass times were 37.6 ± 13.3 and 59.9 ± 20.4 min, respectively. Overall, the 1-year Kaplan–Meier survival rate was 97.1% (95% confidence interval 92.4–98.9%). At 1 year, stroke occurred in 5 patients (3.34%), myocardial infarction in 1 (0.69%), endocarditis in 1 (0.69%), early explantation in 1 (0.67%), pacemaker implantation in 8 (5.6%) and Grade 2 periprosthetic regurgitation in 4 (3.2%; no grade 3 of 4). There were significant decreases from baseline (P < 0.001) in the proportion at New York Heart Association Class III/V (35.3–4.1%), mean gradient (54.9 ± 17.3mmHg to 11.3 ± 4.8 mmHg) and mean left ventricular mass index (160.3 ± 44.8 g/m2 to 118.5 ± 39.4 g/m2). Mean indexed effective orifice area at 1 year was 1.02 ± 0.37	Similar studies included in table 2.

		cm2/m2. Ten patients (6.6%) had severe patient–prosthesis mismatch.	
Vale NC, Abecasis J et al (2017). Late postoperative sutureless valve distortion. European Journal of Cardio-thoracic Surgery. 51, 1018-19.	Images	Transthoracic echocardiogram with an unusual prosthetic profile with concomitant significant leak and obstruction.	Images only.
Votsch A; Weihs W et al (2016). Perceval Sutureless Valve Dysfunction Caused by Valvular Thrombosis. Annals of Thoracic Surgery. VOL 102 (4) PP e309-e311	Case report N=1 with severe aortic stenosis SAVR with a Perceval S valve	Valve dysfunction resulting from thrombosis 12 months after implantation with possible link to postoperative cortisole therapy. SAVR redo was done.	Larger studies included in table 2.
Vola M, Campisi S et al (2015). Sutureless prosthesis and less invasive aortic valve replacement: just an issue of clamping time? The Annals of Thoracic Surgery. 99 (5), 1518-23.	Retrospective non-randomised comparative study with historical controls. N=41 patients who had SU AVR with 3f Enable valve compared with 42 patients who had SAVR with conventional valve. Follow-up (average 25.5 ± 12.9 months),	In-hospital mortality was 1% (a single nonvalve-related death). Average aortic clamping times in group A and group B were, respectively, 85 ± 17 and 47 ± 11 minutes ($p < 0.0001$); the cardiopulmonary bypass time was 108 ± 21 and 69 ± 15 minutes, respectively ($p < 0.0001$). There were three paravalvular leakages in group A (grade I) and four in group B (two grade I, and two grade II); three pacemaker implantations occurred in group B ($p = 0.07$); mean transvalvular gradient at discharge was 16.9 ± 9.1 mm Hg in group A and 11.4 ± 4.3 mm Hg in group B ($p = 0.0007$). One structural valve deterioration was registered in group A, and was treated with a valve-in-valve procedure.	Included in Qureshi 2018, CADTH report added to overview.
Villa E, Alberto C et al (2016). Risk factors for permanent pacemaker after implantation of surgical or percutaneous self-expanding aortic prosthesis.	Retrospective analysis N=336 patients (56.6% CoreValve - Medtronic; 43.4% Perceval - Sorin) compared PPM group and control patients	PPM was required in 12.8% of patients (TAVI 17.5% versus AVR 6.8%, p = 0.007). PPM patients had a higher logistical EuroSCORE (median 20.77% versus	Similar studies included in table 2.

The Journal of Heart Valve Disease. 25(6), 663-671.	who had not received a PPM	15.59%, p = 0.015), a lower use of statins (18.6% versus 34.2%, p = 0.04), a pre-procedural longer QRS interval (median 117 ms versus 98 ms, p = 0.002), and a higher incidence of conduction disturbances (29.3% versus 16.8%, p = 0.034), with a prevalence of right bundle branch block. Prevalent intra-ventricular conduction disorders in both groups included left bundle branch block. AVR patients received a PPM later than the TAVI group (median 6 days versus 3 days, p = 0.01).	
Villa E, Messina A, Laborde F, et al (2015). Challenge for perceval: aortic valve replacement with small sutureless valves--a multicenter study. Ann Thorac Surg;99:1248-54.	Retrospective observational study 276 patients were reviewed to compare data on the smallest model of the Sorin-Perceval sutureless compared with larger models. The small valve (“S” size) was inserted (S group) in 47 patients, while 229 patients had a larger one (labeled “M” and “L” by manufacturer, herein L group).	Median sternotomy was the most frequent approach (S group 87.2% vs L group 79.5%, p = 0.31). The associated procedures were similar for both groups (31.9% vs 34.5%, p = 0.87). For isolated AVR, cardiopulmonary bypass and cross-clamp times were, respectively, 49.1 ± 16.0 and 30.7 ± 9.2 minutes (S group) versus 52.6 ± 23.1 and 32.3 ± 13.6 minutes (L group) (p = 0.33 and 0.45). Hospital mortality was nil (S group) versus 2.6% (L group) (p = 0.62). At discharge, the peak-pressure-gradients were 22.7 ± 7.9 and 20.9 ± 8.4 mm Hg (p = 0.24) while indexed effective orifice areas were 0.84 ± 0.16 and 0.86 ± 0.25 cm2/m2 (p = 0.76). At follow-up (1.5 ± 1.3 years), echo data and survival did not differ (p = 0.17).	Included in Sian 2017 added to table 2.

Vgot F, Pfeiffer S et al (2016). Sutureless aortic valve replacement with Perceval bioprosthesis: are there predicting factors for postoperative pacemaker implantation? Interactive CardioVascular and Thoracic Surgery 22 (2016) 253–258	Retrospective analysis N=258 patients who underwent AVR with the Perceval prosthesis.(169 isolated SU-AVR; 89 COMBINED SURGERY). Preoperative risk factors, intraoperative procedures and complications (61 variables) were compared between patients with permanent pacemaker (PPM group) and without (no-PPM group) need for postoperative PPM implantation.	Baseline, 8 patients had already an implanted pacemaker. Postoperatively, 27 patients (10.5%) required new PPM implantation due to complete atrioventricular block. On univariate analysis, age (PPM vs no-PPM group: 80±5 vs 77±5 years, P = 0.009) and preoperative presence of right bundle branch block (RBBB) [overall n = 20 (7.8%); PPM vs no-PPM group: 9 vs 11 (33 vs 4.8%); P < 0.001] were identified as independent predictors of postoperative conduction disorders, but only pre-existing RBBB persisted on multivariate analysis (odds ratio 11.3—C-statistic 0.74, error estimate 0.064, confidence interval 0.672–0.801; P = 0.0002). Among patients undergoing sutureless AVR, the rate of PPM implantation was high.	Similar studies included in table 2.
Wahlers TCW, Haverich A et al (2016). Early outcomes after isolated aortic valve replacement with rapid deployment aortic valve. The Journal of Thoracic and Cardiovascular Surgery. 151 (6), 1639-1647.	Prospective case series N=287 patients with aortic valve stenosis who underwent rapid deployment aortic valve replacement using the EDWARDS INTUITY Valve System. 158 patients underwent isolated aortic valve replacement through a full sternotomy (n = 71), upper hemisternotomy (n = 77), or right anterior thoracotomy (n = 10).	Mean aortic crossclamp and cardiopulmonary bypass times (minutes) were similar for full sternotomy and upper hemisternotomy, 43.5 ± 32.5/71.6 ± 41.8 and 43.1 ± 13.1/69.6 ± 19.1, respectively, and significantly longer for right anterior thoracotomy, 88.3 ± 18.6/122.2 ± 22.1 (*P* < .000). Early adverse event rates were similar, and in-hospital mortality rates were low regardless of surgical approach.	Similar studies included in table 2.
Wang N, Tsai YC et al (2016). Transcatheter aortic	Systematic review and meta-analysis	Six studies met our inclusion criteria giving	Similar studies included in table 2.

valve implantation (TAVI) versus sutureless aortic valve replacement (SUAVR) for aortic stenosis: a systematic review and meta-analysis of matched studies. J Thorac Dis; 8(11):3283-3293.	Included all matched or propensity score matched studies comparing SUAVR versus TAVI for severe aortic stenosis.	a total of 741 patients in both the SUAVR and TAVI arm of the study. Compared to TAVI, SUAVR had a lower incidence of paravalvular leak (OR =0.06; 95% CI: 0.03–0.12, P<0.01). There was no difference in perioperative mortality, however SUAVR patients had significantly better survival rates at 1 (OR =2.40; 95% CI: 1.40–4.11, P<0.01) and 2 years (OR =4.62; 95% CI: 2.62–8.12, P<0.01).	
Wendt D, Thielmann M, Buck T et al. (2008) First clinical experience and 1-year follow-up with the sutureless 3F-Enable aortic valve prosthesis. European Journal of Cardio-Thoracic Surgery 33: 542–7	Case series N=6 Follow-up=12 months	Extra corporeal circulation time was 87±32 minutes; aortic clamp time was 56±24 minutes. There were no intraoperative deaths or complications. At 12-months' follow-up, mean pressure gradients were 6.8±3.5 mmHg and aortic valve area was 2.2± 0.5 cm^2. One patient had successful redo aortic valve replacement after 8 months because of severe paravalvular leakage, and 1 patient died because of lung cancer 10 months after surgery. At 12 months' follow-up 4 out of 6 patients were alive and asymptotic (New York Heart Association I) however, 1 patient showed mild paravalvular leakage.	
Zannis K, Joffre J et al (2014). Aortic valve replacement with the Perceval S bioprosthesis: single centre experience in 143 patients. J Heart Valve Dis; 23:795-802.	Prospective case series N=143 patients with aortic stenosis SAVR with Perceval S bioprosthesis Follow-up mean 13.4 +/- 11.6 months	The procedural success rate was 99.3%. The mean cross-clamp and cardiopulmonary bypass times were 32.0 +/- 14.9 min and 44.7 +/- 18.6 min, respectively. In-hospital mortality was 4.9% (n=7). Pacemaker implantation was	Included in Sian 2017 added to table 2.

		required in seven patients (4.9%). Survival at five years was 85.5%. Reoperation was necessary in seven patients (4.9%); early reoperations were due to paravalvular leak (n = 3; 2.0%) and intra-prosthetic regurgitation (n=3; 2.0%). One late reoperation (at 29 months) was required, due to fibrous pannus overgrowth. One late endocarditis (0.7%) occurred at 26 months and was medically treated. No structural valve deterioration occurred during the follow up. At 12 months, 94.4% of survivors were in NYHA class I-II, and the mean pressure gradient and EOA were 9.0 +/- 3.4 mmHg and 1.60 +/- 0.3 cm2, respectively.	

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	30/10/2017	Issue 10 of 12, October 2017
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	30/10/2017	Issue 9 of 12, September 2017
HTA database (Cochrane Library)	30/10/2017	Issue 4 of 4, October 2016
MEDLINE (Ovid)	30/10/2017	1946 to October Week 3 2017
MEDLINE In-Process (Ovid)	30/10/2017	October 27, 2017
EMBASE (Ovid)	30/10/2017	1974 to 2017 Week 44
PubMed	30/10/2017	n/a
JournalTOCS	30/10/2017	n/a

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 exp Aortic Valve Stenosis/
2 Aortic Valve Insufficiency/
3 (aort* adj4 (stenos* or insufficien* or incompeten* or regurgitat*)).tw.
4 Aortic Valve/
5 (aort* adj4 valve*).tw.
6 or/1-5
7 Heart Valve Prosthesis Implantation/
8 Heart Valve Prosthesis/
9 ((heart* or aort* or cardiac*) adj4 (valv* or bioprosthe* or prosthe*)).tw.
10 Bioprosthesis/
11 or/7-10
12 (sutureless or stitchless).tw
13 11 and 12
14 6 and 13
15 (3f enable or 3f aortic bioprosthesis).tw.
16 (3f adj4 (sutureless or device or valv*)).tw.
17 perceval.tw.
18 INTUITY.tw.
19 (Trilogy adj4 valv*).tw.
20 or/15-18
21 14 or 20

22 animals/ not humans/
23 21 not 22
24 (2017013* or 201702* or 201703* or 201704* or 201705* or 201706* or 201707* or 201708* or 201709* or 20171*).ed.
25 23 and 24