별첨 1

자료추출 및 비뚤림 위험평가

1. 자료추출

1.1. NOTION 연구 자료추출

<table>
<tr><td rowspan="6">기본 정보</td><td>Trial</td><td>NOTION trial</td></tr>
<tr><td>선택문헌 1저자(연도)</td><td>Sondergaard (2016), Thyregod (2015), Sondergaard (2019), Thyregod (2019)</td></tr>
<tr><td>NCT no.</td><td>NCT01057173</td></tr>
<tr><td>연구디자인</td><td>RCT (The Nordic Aortic Valve intervention, NOTION)</td></tr>
<tr><td>연구국가</td><td>다국가(덴마크, 스웨덴)</td></tr>
<tr><td>모집기관</td><td>다기관(3)</td></tr>
<tr><td rowspan="2">연구 방법</td><td>연구목적</td><td>심폐우회술(cardiopulmonary bypass)을 이용한 SAVR과 비교하여, CoreValve System을 이용한 TAVI의 안전성 및 효과성을 평가하기 위함</td></tr>
<tr><td>연구대상자</td><td>
<table>
<tr><td>모집기간</td><td>2009.12.-2013.04.</td></tr>
<tr><td>질환</td><td>■ Severe AS (■ with symptom, ■ without symptom*)
*모두 포함 (아래 선택기준 참조)</td></tr>
<tr><td>risk</td><td>□1. High risk group
□2. Intermediate risk group
■3. Low risk group
□4. 기타 (_____)</td></tr>
<tr><td>선택기준</td><td>- 퇴행성 대동맥 판막 협착증 환자 (calcified AV, effective orifice area 〈1 cm^2 or indexed for body surface area 〈0.6 cm2/m^2, mean AV gradient 〉40 mmHg, or AV peak systolic velocity 〉4.0 m/second)
- 유증상 환자 (dyspnoea ≥NYHA class II, angina pectoris, or syncope)
- 아래 항목 중 1개 이상이면서, 무증상 환자
• 좌심실 후벽 두께 ≥17 mm
• 좌심실 박출률 (LVEF) 〈60% but ≥20%
• 심방 세동
- 70세 이상
- 다학제팀 회의에서 판단된 TAVI와 SAVR 후보군
- 시술 후 1년이상 생존이 예상(Expected to survive ≥1)되는 환자
- 동의서 작성자</td></tr>
<tr><td>배제기준</td><td>- 단독 대동맥판막기능부전 (Isolated Aortic Valve insufficiency)
- 다른 중요한 심장 판막 또는 중격 질환 (septal diseases)
- 혈관재생술(PCI 또는 CABG)을 필요로 하는 관상동맥합병증
- 심장내 병변 (혈전, 종양, 증식)</td></tr>
</table>
</td></tr>
</table>

	- 과거 개복 심장수술 - 지난해 심근경색 또는 PCI - 30일 이내 뇌졸중 또는 일과성 허혈 발작(TIA) - 혈액 투석을 요하는 신부전증 - 폐 기능 부전 (FEV1 or diffusion capacity 〈40% of expected) - 항생제가 필요한 활동성 감염병 - 응급 처치 (within 24 hours after the indication for intervention has been made) - inotropic support or mechanical cardiac assistance를 필요로 하는 불안정한 시술 전 상태 - 약물에 대한 알려진 과민증 : 니티놀, 헤파린, 클로피도그렐, 아스피린(acetyl salicylic acid) 또는 조영제 - 현재 임상 시험 (약물 또는 디바이스)에 참여하고 있는 환자
심장팀 논의	■ 유(□ 전원동의 □일부동의 ■ 불확실) □무 □ 기타 (_____)
심장팀 구성	• 심장외과전문의(cardiac surgeons), 중재심장전문의(interventioncardiologists), 심초음파전문의의 다학제 컨퍼런스
합의 기준	• 환자는 심장외과전문의(cardiac surgeons), 중재심장전문의(interventioncardiologists), 심초음파전문의의 다학제 컨퍼런스를 통한 TAVI와 SAVR 기준에 적합한 환자를 선택해야 함

연구 중재

중재명	Transcatheter aortic valve implantation (TAVI)
Device	■ Corevale (CoreValve self-expanding bioprosthesis (Medtronic) □ Sapien (상세 제품 :) □ lotus (상세 제품 :) □ 기타 _____ (상세 제품 :)
세대구분	□ 1세대(CoreValve)
접근 경로	■ TF ■ TA(transaxillary) □ 기타 □ NR - 대퇴동맥접근법(femoral artery access) 96%, 좌측 겨드랑이접근법(left transaxillary access) 4%
상세 중재설명	- 심장도관검사실(cardiac catheterisation laboratory)에서 국소마취 또는 전신마취하에 수행됨 - 밸브 크기는 CT 혈관조영술에 기초하여 결정 - CoreValve sizes :23, 26, 29, or 31 mm - 모든 TAVR 및 SAVR 환자는 전립선 예방 항생제 및 수술 후 항혈소판제 및 항응고제를 받았음 : 시술 전과 시술 후 3개월까지 Dual antiplatelet therapy(매일 아스피린 최소 81mg, 매일 클로피도그렐 75mg)를 권고하였으며, 아스피린 또는 클로피도그렐 단독요법을 무기한 동일용량으로 수행함

비교중재

중재명	Surgical aortic valve replacement (SAVR)
Device	□ tissue valve (상세 제품 : NR) □ 기타 (상세 제품 :)
상세	- cardiopulmonary bypass를 이용하여 일반적인 open-heart

		중재설명	방법으로 수행 - 인공 밸브의 선택과 크기는 외과의사 재량에 맡김 - 모든 TAVR 및 SAVR 환자는 전립선 예방 항생제 및 수술 후 항혈소판제 및 항응고제를 받았음 : 시술 후, 모든 환자는(지속적으로 와파린 치료를 받고 있는 환자 포함) 매일 최소 81mg의 아스피린을 무기한으로 투여함
	결과변수 정의	결과는 Valve Academic Research Consortium 기준에 따라 정의됨. - Definitions of outcomes are adopted from the generally accepted Valve Academic Research Consortium consensus report for TAVI clinical trials. Outcomes defined according to Valve Academic Research Consortium criteria.

결과변수	정의	측정 도구	측정시기 (보고시기)
the composite rate of death from any cause, stroke, MI			1년, 2년
All-cause death			30일, 1년, 2년
Cardiovascular death			30일, 1년, 2년
Neurological events			30일, 1년, 2년
- Stroke			30일, 1년, 2년
- Transient ischemic attack			30일, 1년, 2년
Myocardial infarction			30일, 1년, 2년
New-onset or worsening atrial fibrillation			30일, 1년, 2년
Permanent pacemaker implantation			30일, 1년, 2년
주요혈관합병증 (Major vascular complications)			Index Hospitalization
심각한 출혈	Major, life threatening, or disabling bleeding		Index Hospitalization
대동맥판 역류 (Total Aortic Valve Regurgitation)			3개월, 1년, 2년
급성신장손상	Acute kidney injury stage II or III		Index Hospitalization
심내막염 (valve endocarditis)			30일, 1년
NHYH Functional Class			3개월, 1년, 2년
Aortic Valve Hemodynamics - Effective Orifice Area - Mean Gradient			3개월, 1년, 2년
Cardiogenic shock			Index Hospitalization

연구 결과

대상자수

	총 수	TAVR	SVAR
스크리닝수(enroll)	280	145	135
randomised			
수술/시술 수행자	276	142	134
분석대상자*	276	142	134
1년시점 대상자	253	133	120
2년시점 대상자	236	123	113
탈락율			

*composit outcome은 ITT분석하였음

대상자 특성

■ 연구대상 특성

Trial	중재	N	평균 연령	남자	평균 STS	평균 LES	NYHA 3/4	이전시술/수술			
								CABG	PCI	Pace maker	AVR
Thyregod (2015	TAVI	145	79.2	53.8	2.9	1.9**	48.5	NR	7.6	3.4	NR
	SAVR	135	79.0	52.6	3.1	2.0**	45.5	NR	8.9	4.4	NR
Sondergaard (2019)	TAVI	139	79.4	52.5	3.0	2.0**	46.4	NR	NR	3.6	NR
	SAVR	135	78.8	53.3	3.0	2.0	46.3	NR	NR	4.4	NR

†neurological event, §AF와 atrial flutter를 합친 대상자, **Logistics EuroSCORE II, *** Prior stroke

Trial	중재	기저질환									
		CAD	PVD	뇌혈관 질환	AF	MI	당뇨병	고혈압	신장질 환	간질환	COPD
Thyregod (2015	TAVI	NR	4.1	16.6†	27.8§	5.5	17.9	71.0	1.4	NR	11.7
	SAVR	NR	6.7	16.3†	25.6§	4.4	20.7	76.3	0.7	NR	11.9
Sondergaard (2019)	TAVI	NR	4.3	5.8 ***	29.0§	NR	17.9	NR	1.4	NR	12.2
	SAVR	NR	6.7	9.6	24.8§	NR	20.7	NR	0.7	NR	11.9

추적관찰 기간

평균추적관찰 기간 : 5년

결과

1) 이분형 변수

결과변수	1저자 (연도)	시점	TAVR			SAVR			P value
			N	event	%	N	event	%	
Aortic valve reintervention	Thyregod(2019)	5년	145	55	38	135	49	36.3	0.86
All-cause mortality*	Thyregod(2019)	5년	145	40	27.6	135	39	28.9	0.75
Cardiovascular mortality	Thyregod(2019)	5년	145	30	20.8	135	31	23	0.62
Stroke	Thyregod(2019)	5년	145	13	9	135	10	7.4	0.65
TIA	Thyregod(2019)	5년	145	9	6.2	135	5	3.7	0.33
MI	Thyregod(2019)	5년	145	11	7.7	135	10	7.4	0.96
Atrial fibrillation	Thyregod(2019)	5년	145	34	23.4	135	82	60.8	<0.0001
Pacemaker†	Thyregod(2019)	5년	145	58	41.7	135	10	7.8	<0.0001
Aortic valve reintervention	Thyregod(2019)	5년	145	3	2.1	135	1	0.7	0.35
Valve endocarditis†	Thyregod(2019)	5년	145	9	6.2	135	6	4.4	0.51
composite rate [1)]	Thyregod(2015)	1년	145	19	13.1	135	22	16.3	0.43
composite rate [1)]	Sondergaard(2016)	2년	145	23	15.8	135	25	18.8	0.43
전체사망	Thyregod(2015)	30일	142	3	2.1	134	5	3.7	0.43
전체사망	Thyregod(2015)	1년	142	7	4.9	134	10	7.5	0.38
전체사망	Sondergaard(2016)	2년	142	11	8.0	134	13	9.8	0.54
CVD death	Thyregod(2015)	30일	142	3	2.1	134	5	3.7	0.43
CVD death	Thyregod(2015)	1년	142	6	4.3	134	10	7.5	0.25

결과변수	1저자 (연도)	시점	TAVR			SAVR			P value
			N	event	%	N	event	%	
CVD death	Sondergaard(2016)	2년	142	9	6.5	134	12	9.1	0.40
Neurological events	Thyregod(2015)	30일	142	4	2.8	134	4	3.0	0.94
Neurological events	Thyregod(2015)	1년	142	7	5.0	134	8	6.2	0.68
Neurological events	Sondergaard(2016)	2년	142	13	9.7	134	10	7.8	0.67
뇌졸중	Thyregod(2015)	30일	142	2	1.4	134	4	3.0	0.37
뇌졸중	Thyregod(2015)	1년	142	4	2.9	134	6	4.6	0.44
뇌졸중	Sondergaard(2016)	2년	142	5	3.6	134	7	5.4	0.46
일과성허혈발작	Thyregod(2015)	30일	142	2	1.4	134	0	0	0.17
일과성허혈발작	Thyregod(2015)	1년	142	3	2.1	134	2	1.6	0.71
일과성허혈발작	Sondergaard(2016)	2년	142	8	6.0	134	4	3.3	0.30
주요혈관합병증	Thyregod(2015)	입원	142	8	5.6	134	2	1.5	0.10
심각한 출혈	Thyregod(2015)	입원	142	16	11.3	134	28	20.9	0.03
급성신장손상 II or III	Thyregod(2015)	입원	142	1	0.7	134	9	6.7	0.01
심근경색	Thyregod(2015)	30일	142	4	2.8	134	8	6.0	0.20
심근경색	Thyregod(2015)	1년	142	5	3.5	134	8	6.0	0.33
심근경색	Sondergaard(2016)	2년	142	7	5.1	134	8	6.0	0.69
심방세동	Thyregod(2015)	30일	142	24	16.9	134	77	57.8	<.0001
심방세동	Thyregod(2015)	1년	142	30	21.2	134	79	59.4	<.0001
심방세동	Sondergaard(2016)	2년	142	32	22.7	134	80	60.2	<.0001
영구심박동기	Thyregod(2015)	30일	142	46	34.1	134	2	1.6	<.0001
영구심박동기	Thyregod(2015)	1년	142	51	38.0	134	3	2.4	<.0001
영구심박동기	Sondergaard(2016)	2년	142	55	41.3	134	5	4.2	<.0001
심내막염	Thyregod(2015)	30일	142	1	0.7	134	0	0	0.33
심내막염	Thyregod(2015)	1년	142	4	2.9	134	2	1.6	0.47
심인성쇼크	Thyregod(2015)	입원	142	6	4.2	134	14	10.4	0.05
reintervention	Thyregod(2015)	30일	142	0	0	134	0	0	
reintervention	Sondergaard(2016)	1년	142	0	0	134	0	0	
reintervention	Sondergaard(2016)	2년	142	0	0	134	0	0	
Bioprosthetic valve dysfunction	Søndergaard(2019)	6년	139	78	56.1	135	90	66.7	0.073

※빨간색 숫자는 계산값임

*Percentages are Kaplan-Meier rates. P values were calculated from log-rank tests.

†Baseline pacemakers are not included.
‡Confirmed definite cases according to modified Duke criteria.
1) composite rate of death from any cause, stroke, or myocardial infarction

3) 그림 2에서 NYHA class I 의 % 만 추출하였으며, 나머지는 아래 그림 캡쳐하였음

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P value	RR (HR	95% CI	N
				N	event	%	N	event	%				
Total aortic valve regurgitation	Thyegod (2019)	12	Moderate or severe	121	19	15.7	113	1	0.9	<0001			
		24	Moderate or severe	123	17	13.8	112	1	0.9	<0001			
		36	Moderate or severe	109	9	8.3	107	1	0.9	<0001			

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P value	RR (HR	95% CI	
				N	event	%	N	event	%				
		48	Moderate or severe	100	6	6	99	1	1	<0.001			
		60	Moderate or severe	85	7	8.2	84	0	0	<0.001			
Total aortic valve regurgitation	Thyregod (2016)	3	Moderate or severe	124	19	15.3	111	2	1.8				
Total aortic valve regurgitation	Thyregod (2016)	12	Moderate or severe	121	19	15.7	113	1	0.9	<0.001			
Total aortic valve regurgitation	Thyregod (2016)	48	Moderate or severe	123	19	15.4	112	1	0.9	<0.001			
NYHA class	Thyregod (2016)	3	3 or 4	135	7	5.2	115	4	3.5	0.23			
NYHA class	Thyregod (2016)	12	3 or 4	132	4	3	120	4	3.3	0.01			
NYHA class	Thyregod (2016)	24	3 or 4	123	4	3.3	114	4	3.5	0.44			

* %로 event 수 추출

저자의 결론	- 저위험군 환자에서 TAVR와 SAVR의 5년 임상적 결과는 유의한 차이가 없음
기타(funding 등)	This work was supported by the Danish Heart Foundation (grant numbers: 09-10-AR76-A2733-25400, 12-04-R90-A3879-22733, and 13-04-R94-A4473-22762). Statistical analyses for this report were conducted by a Medtronic statistician.
기타 참고사항	※프로토콜 논문 Thyregod HG, et al. The Nordic Aortic Valve Intervention (NOTION) trial comparing transcatheter versus surgical valve implantation: study protocol for a randomised controlled trial. Trials. 2013 Jan 9;14:11.

1.2. PARTNER 3 연구 자료추출

<table>
<tr><td rowspan="6">기본
정보</td><td>Trial</td><td>PARTNER3</td></tr>
<tr><td>1저자(연도)</td><td>Mack 2019, Baron 2019, Pibarot 2020</td></tr>
<tr><td>NCT no.</td><td>NCT02675114</td></tr>
<tr><td>연구디자인</td><td>RCT</td></tr>
<tr><td>연구국가</td><td>다국가 (미국, 캐나다, 호주, 뉴질랜드, 일본)</td></tr>
<tr><td>모집기관</td><td>71개의 기관</td></tr>
<tr><td rowspan="2">연구
방법</td><td>연구목적</td><td>수술저위험군 환자에서 풍선 확장형 밸브를 사용하여 수행된 TAVR과 SAVR의 안전성과 효능을 비교하기 위함</td></tr>
<tr><td>연구대상자</td><td>
<table>
<tr><td>모집기간</td><td>2016.03. - 2017.10.</td></tr>
<tr><td>질환</td><td>■ Severe AS (■ with symptom, □ without symptom)
baseline health status was mildly impaired with a mean KCCQ-OS score of 70 (corresponds to NYHA functional class II symptoms)</td></tr>
<tr><td>risk</td><td>□ Intermediate risk group
■ Low risk group (기준: STS score 4% 이하)
□ 기타 (_____)</td></tr>
<tr><td>선택기준</td><td>1. 다음 기준에 해당하는 중증의 석회성 대동맥 협착증 (*심초음파 결과는 무작위화 90일 이전에 시행된 것이어야 함);
- AVA ≤1.0㎠ 혹은 AVA index 〈0.6㎠/㎡
- Jet velocity ≥ 4.0 m/s 혹은 평균 gradient ≥ 40mmHg

위 기준을 충족하면서 아래 중 1개 이상에 해당하는 경우
- NYHA Functional Class II 이상
- 제한된 운동 능력, 비정상적 혈압, 부정맥을 증명하는 운동부하검사
- 무증상의 LVEF가 50% 미만

2. Heart Team이 수술 사망률이 낮고 STS-PROM에 따른 30일 수술 사망률이 4% 미만이라고 동의한 경우
3. 대상 환자가 연구에 대한 정보를 제공받은 후 해당 조항에 동의하였고, 각 연구 시행 지역에 위치한 IRB/윤리위원회 승인에 따른 동의서에 서면으로 동의를 시행한 경우</td></tr>
<tr><td>배제기준</td><td>1. 3D 영상분석 결과에 근거하여 대동맥 환형 크기가 THV 20, 23, 26, 29 ㎜에 적합하지 않은 경우
2. introducer sheath의 안전한 통과를 불가능하게 하는 장대퇴골혈관 특성
3. 무작위배정 1개월(30일) 전 급성 심근경색의 증거
4. 대동맥판막이 단첨판, 이첨판 또는 석회화되지 않은 경우
5. 중증의 대동맥 역류(〉3+)
6. 중증의 승모판 역류(〉3+) 혹은 중등도 이상의 협착
7. 모든 위치에 해당하는 기존의 기계적 또는 생체인공판막 (승모판 고리 제외)
8. 복합적인 관상동맥 질환:
a. 보호되지 않은 좌주관상동맥
b. Syntax 점수가 32점 이상(이전의 혈관재건이 없는 경우)
c. Heart team이 최적의 혈관재건이 수행되지 않았다고 판단한 경우
9. 무작위배정 30일 이내에 증상이 있는 경동맥, 척추동맥 질환 또는 경동맥 협착증의 성공적인 치료 경험
10. 백혈구 감소증(WBC 〈3000 cell/mL), 빈혈(Hgb〈9g/dL), 혈소판 감소증 (platelet count 〈50,000 cells/mL), 출혈 체질 또는 응고장애 또는 응</td></tr>
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	고항진상태 11. 무작위배정 30일 이내 기계적 환기 또는 기계적 심장 보조 등 심장수축기능의 지원이 요구되는 혈역학적 또는 호흡성 불안정의 경우 12. 폐색이 있는 비대성 심근병증 13. LVEF 30% 미만의 심실기능장애 14. 심초음파,CT,MRI 등의 심장 영상에서 심내 종양, 혈전 또는 증식 15. 시술/수술 중 또는 후에 항혈전/항응고제를 이용한 치료를 견딜 수 없거나 불가능한 상태 16. 무작위배정 90일 이내에 뇌졸중 또는 일과성허혈성발작 17. screening 시에 신기능부전(eGFR 30ml/min 미만) 그리고/또는 신장대체요법 환자의 경우 18. 무작위배정 180일 이내에 활동적 세균성 심내막염] 19. 중증의 폐질환(FEV1 50% 미만) 또는 가정에서 산소요법 사용하는 경우 20. 중증의 폐고혈압(PA systolic pressure ≥ 2/3 systemic pressure) 21. 간경변 또는 모든 활동성 간질환 병력 22. Heart team에 의해 결정되는 중요한 취약성(취약점 매개변수의 객관적인 평가 후) 23. porcelain 대동맥, 동맥류, 심한 석회화, 대동맥 협착 등의 복부 또는 흉부 대동맥 질환이 SAVR을 위한 대동맥절개술 또는 캐뉼라삽입, 전달체계의 안전한 통과를 방해하는 경우 24. 안전한 재수술을 방해하는 이전 수술로부터 발생한 합병증 또는 적성 흉부 상태(예. 종격동염, 방사선손상, 비정상적 흉벽, 대동맥 또는 내흉동맥 유착 등) 25. 대상자의 혈액제제 거부 26. BMI 50kg/㎡ 이상 27. 기대수명 24개월 미만 28. 적절한 사전 약물처치를 할 수 없는 절대적 금기증 또는 요오드 조영제 알레르기 대상자 29. 연구 수행 완료를 방해하는 부동성(예. 6분 보행 테스트 등) 30. 대상자는 연구의 두 군 모두에 지원할 수 없음 (단일군 등록은 해당하지 않음) 31. 현재 타 약물 및 의료기기 임상시험에 참여하고 있는 자
심장팀 논의	■ 유(□전원동의 □일부동의 ■ 불확실) □무 □ 기타 (_____)
심장팀 구성	the site heart team
합의 기준	심장 팀과 임상시험검토위원회가 확인하여 동의함에 따라 진행함

연구 중재	**중재명**	**TAVR**
	Device	□ Corevale (상세 제품 :) ■ Sapien (Edwards SAPIEN 3 THV system Model 9600 TFX(20,23,26 and 29mm) □ lotus (상세 제품 :) □기타 Evolut R (상세 제품 :)
	세대구분	■ 3세대
	접근 경로	■ TF □ TA □ 기타( ) □ NR
	상세 중재설명	모두 TF를 통해 시행하였고 밸브의 크기는 CT 및 심초음파 결과를 통해 결정함. TAVR 전후에 풍선대동맥 판막 성형술은 시술자의 재량에 따라 시행함. A. 다음 중 하나에 추가하여 시술 전 aspirin 81-100mg QD 복용 a. 한 달 이내 bare metal stent (BMS) 또는 12개월 이내 drug eluting

		stent (DES) 시술을 받는 환자는 시술 이전에 clopidogrel/prasugrel을 계속 사용해야 함 b. 와파린 복용 중인 심방세동 환자는 시술 전 LMW or UF 헤파린과 연결되어야 함 c. TAVR중 심초음파상 혈전이 나타나면, 시술 중단 후 warfarin 또는 dabigatran 30일동안 사용하며 이 동안은 시술이 지연됨 d. TAVR/PCI 수반하는 환자의 경우, aspirin에 추가하여 시술 전 clopidogreal 300mg or 600mg loading이 권장됨

비교중재

중재명	Surgery
Device	■ tissue valve (상세 제품 :) □ 기타 (상세 제품 :)
상세 중재설명	Heart team에 의해 대상자의 상태가 생체인공판막으로 대체하기 위해 좋은 상태임이 판단됨에 따라 수술을 시행하였다. 부위에 따른 표준화된 수술 절차를 의무화하는 것은 환자에게 최선의 이익이 아닌 것으로 간주하였는데, 이는 표준 기술을 벗어난 어떤 것을 의무화 할 경우, 숙련된 외과의사 조차도 "편안함"에서 벗어날 수 있기 때문이다. 따라서 SAVR 절차의 대부분은 운영자의 재량권이 허용되었다. (예. 최소 흉골절개술 또는 우측 앞 개흉술 절개가 허용되었고 환자의 24.3%에서 시행되었다.)

결과변수 정의

지표명	정의기준	기타
Access siterelated complication	Site of access complication for TAVR will be classified as: • Femoral access site • Axillary access site • Subclavian access site • Transaortic access site Site of access complication for Surgery will be classified as: • Sternotomy • Minimally invasive/Port Access Types of access injury for TAVR: • Nerve Injury • Seroma • Infection (Access Site) • Lymphocoele/Lymphatic injury Types of access injury for Surgery: • Nerve Injury • Infection (Access Site) • Wound dehiscence/non-union • Effusion • Lymphocoele/Lymphatic injury	
Acute kidney injury	An abrupt loss of kidney function, resulting in the retention of urea and other nitrogenous waste products The increase in creatinine meeting at least Stage 1 must occur within 48 hours. Staging will be based on the worst stage that occurs within 7 days of the index procedure. Stage 1 • Increase in serum creatinine to 150–199% (1.5–1.99 × increase compared with baseline) OR increase of ≥0.3 mg/dL (≥26.4 mmol/L) OR • Urine output 〈0.5 ml/kg per hour for 〉6 but 〈12 hours Stage 2 • Increase in serum creatinine to 200–299% (2.0–2.99 × increase compared with baseline) OR	

지표명	정의기준	기타
	• Urine output 〈0.5 ml/kg per hour for 〉12 but 〈24 hours Stage 3 • Increase in serum creatinine to ≥300% (〉3 × increase compared with baseline) OR serum creatinine of ≥4.0 mg/dL (≥354 mmol/L) with an acute increase of at least 0.5 mg/dL (44 mmol/L) OR • Urine output 〈0.3 ml/kg per hour for ≥24 hours OR • Anuria for ≥12 hours Patients receiving renal replacement therapy (dialysis, hemodialysis, peritoneal dialysis, hemofiltration, transplant) are considered to meet Stage 3 criteria irrespective of other criteria	
Annular dissection	Disruption or tear of the valve annulus extending to the aorta caused by mechanical injury from over sizing a balloon or the valve device itself.	
Aortic dissection	Aortic dissection is a separation of an intimal layer of wall that may or may not require intervention.	
Aortic stenosis, native	Aortic stenosis is classified as “severe” when the following are present: Jet velocity 〉 4.0 m/s Mean gradient 〉 40mmHg Valve area 〈 1.0 cm2 Valve area index 〈 0.6cm2/m2	
Arrhythmia / Conduction System Injury	Any reported Arrhythmia: an irregular heart rate or abnormal rhythm resulting in symptoms or requiring medical intervention. This includes (but is not limited to) sinus bradycardia, premature atrial contractions, atrial tachycardia, supraventricular tachycardia, atrial fibrillation†, atrial flutter†, AV nodal reentrant tachycardia, junctional rhythm, premature ventricular contractions, ventricular fibrillation, ventricular tachycardia, and torsade de pointes. Conduction system defect: an impairment of the electrical pathways and specialized muscular fibers that conduct impulses through the heart. This includes (but is not limited to) 1st degree AV block, 2nd degree AV block (Mobitz I, Mobitz II), 3rd degree (complete) AV block, incomplete RBBB, RBBB, intraventricular conduction delay, LBBBB, incomplete LBBB, left anterior fascicular block, left posterior fascicular block, bifascicular block, and trifascicular block. Interventions that may be required include (but are not limited to) permanent pacemaker, temporary pacemaker, CID, electrical cardioversion, electrical cautery/ablation, medical cardioversion, and new mediation (oral anticoagulation, rhythm or rate controlling therapy). † New-onset atrial fibrillation (or flutter)* is diagnosed as any arrhythmia within hospitalization that has the ECG characteristics of atrial fibrillation (or flutter) and lasts sufficiently long to be recorded on a 12-lead ECG, or at least 30 seconds on a rhythm strip	
Bicuspid aortic valve	Congenital malformation resulting in 2 functioning leaflets as defined by Sievers and Schmidtke	

지표명	정의기준	기타
Bioprosthetic valve dysfunctiom	Bioprosthetic valve dysfunction includes all failure modes, including structural (ex. leaflet tears, leaflet mobility restriction, etc.) or non-structural (ex. paravalvular leak or endocarditis) or hemodynamic (aortic regurgitation or aortic stenosis) or a combination of these dysfunctions. Patients with BVD may be asymptomatic or symptomatic requiring medical therapy (ex. addition of anticoagulation), hospitalization, or require intervention and/or valve explant.	
Bleeding	Bleeding is defined as overt and actionable. Overt bleeding is defined as any clinically obvious source of bleeding or bleeding source identified after appropriate investigation and diagnostic testing, including procedural blood loss. Actionable bleeding is more bleeding than expected for the clinical circumstance and needing increased level of care, such as increased observation, hospitalization, medical/surgical intervention or transfusion of whole blood or PRBCs etc. Procedural bleeding has to be clinically obvious and actionable bleeding from vascular system either at, or remote from, the access/surgical site occurring during Index procedure or soon after Index and related to Index procedure. • TAVR procedural bleeding: The Site thresholds for reporting non-transfusion, non-Hgb based procedural bleeding for TAVR is 〉100 ml total EBL (Estimated Blood Loss) from access site • Surgery procedural bleeding: It is difficult to differentiate intra-procedural blood loss from immediate post-procedure blood loss. Therefore, the Site threshold for reporting nontransfusion, non- Hgb based surgical bleeding is considered to be 〉 600 mL bloody chest tube output (as captured on Intake and Output Chart, I/O) within 24 hours of leaving the OR/cath lab and should have a correlative drop in Hgb and/or transfusion of RBCs BARC Bleeding Criteria Type 1: bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a healthcare professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional BARC1 is non-actionable overt bleeding. It would be the criteria for all procedural bleeds that do not meet Type 2 or above as this requires only overt bleed to occur. Post procedural bleeds can fall into BARC1 like untreated minor nasal bleed or minor bruises in a patient on Coumadin that resolve with self-reduction of Coumadin dose without seeking medical advice Type 2: any overt, actionable sign of hemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for type 3, 4, or 5 but does meet at least one of the following criteria: • Requiring nonsurgical, medical intervention by a healthcare professional OR • Leading to hospitalization or increased level of care OR	

지표명	정의기준	기타
	• Prompting evaluation Type 3: Type 3a • Overt bleeding plus hemoglobin drop of 3 to 〈 5 g/dL* (provided hemoglobin drop is related to bleed) • Any transfusion with overt bleeding Type 3b • Overt bleeding plus hemoglobin drop ≥ 5 g/dL* (provided hemoglobin drop is related to bleed) • Cardiac tamponade • Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/hemorrhoid) • Bleeding requiring intravenous vasoactive agents	
	Type 3b • Overt bleeding plus hemoglobin drop ≥ 5 g/dL* (provided hemoglobin drop is related to bleed) • Cardiac tamponade • Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/hemorrhoid) • Bleeding requiring intravenous vasoactive agents Type 3c • Intracranial hemorrhage (does not include microbleeds or hemorrhagic transformation, does include intraspinal) • Subcategories confirmed by autopsy or imaging or lumbar puncture • Intraocular bleed compromising vision Type 4: Overt bleeding that occurs at any time during or after the index procedure hospitalization and fulfills one of the following criteria: • Perioperative intracranial bleeding within 48 h • Reoperation after closure of sternotomy for the purpose of controlling bleeding AND Hgb drop 〉 3 g/dL • Transfusion of ≥ 5 U whole blood or packed red blood cells within a 48-h period • Chest tube output ≥ 2L within a 24-h period AND Hgb drop 〉 3g/dL Type 5: Fatal bleeding Type 5a Probable fatal bleeding; no autopsy or imaging confirmation but clinically suspicious Type 5b Definite fatal bleeding; overt bleeding or autopsy or imaging confirmation * Given one unit of packed RBC typically will raise blood hemoglobin concentration by 1 g/dL, an estimated decrease in hemoglobin will be calculated. ** Overt: actionable sign of hemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone). Should be observable and visible, not hidden or occult, and overt bleeding should be in proportion to the blood loss and should not include minor bruising, microscopic hematuria. Severity:	

지표명	정의기준	기타
	Life-threatening or disabling bleeding • Fatal bleeding OR • Bleeding in a critical organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome) OR • Bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery OR • Overt source of bleeding with drop in hemoglobin ≥5 g/dL or whole blood or packed red blood cells transfusion ≥ 4 units	
	Major bleeding: • Overt bleeding either associated with a drop in the hemoglobin level of at least 3.0 g/dL or requiring transfusion of two or three units of whole blood/RBC, or causing hospitalization or permanent injury, or requiring surgery AND • Does not meet criteria of life-threatening or disabling bleeding Minor bleeding: • Any bleeding worthy of clinical mention (e.g. access site hematoma) that does not qualify as life-threatening, disabling, or major.	
Cerebro vascular disease	Cerebrovascular disease includes all disorders in which an area of the brain is temporarily or permanently affected by ischemia or bleeding and one or more of the cerebral blood vessels are involved in the pathological process It includes: • Stroke • TIA • Noninvasive or invasive arterial imaging test demonstrating 〉=50% stenosis of any of the major extracranial or intracranial vessels to the brain • Previous cervical or cerebral artery revascularization surgery or percutaneous intervention This does not include chronic (nonvascular) neurological diseases or other acute neurological insults such as metabolic and anoxic ischemic encephalopathy	
Congestive Heart Failure (CHF)	Diagnosis requires physician documentation or report of any of the following: • Unusual dyspnea on light exertion • Recurrent dyspnea occurring in the supine position • Fluid retention; or the description of rales, jugular venous distension • Pulmonary edema on physical exam, or pulmonary edema on chest x-ray presumed to be cardiac dysfunction A low ejection fraction alone, without clinical evidence of heart failure does not qualify as heart failure. An elevated BNP without other supporting documentation should not be reported as CHF	
Conversion to open surgery	Any conversion to open sternotomy during the TAVR procedure secondary to any procedure-related complications	
Coronary obstruction	Angiographic or echocardiographic evidence of a new, partial or complete, obstruction of a coronary ostium, either by the	

지표명	정의기준	기타
	valve prosthesis itself, the native leaflets, calcifications, or dissection, occurring during or after the TAVR or Surgery procedure.	
Device	For the determination of device relationship, the study device consists of: • The Edwards SAPIEN 3 valve • The Edwards Valve Delivery System • The Edwards Expandable Sheath • Any surgical valve implanted during index procedure	
Device (Valve) migration	After initial correct positioning, the valve prosthesis moves upward or downward by 5 mm, within the aortic annulus from its initial position, with or without consequences.	
Device (Valve) embolization	The valve prosthesis moves during or after deployment such that it loses contact with the aortic annulus.	
Device (Valve) fracture	The separation of any portion of the frame into two or more parts; as may be determined by radiography, computed tomography, magnetic resonance imaging or by direct examination.	
Device (Valve) thrombosis	Any thrombus attached to or near an implanted valve that occludes part of the blood flow path, interferes with valve function, or is sufficiently large to warrant treatment. Note that valve-associated thrombus identified at autopsy in a patient whose cause of death was not valve-related should not be reported as valve thrombosis.	
Ectopic valve deployment	Permanent deployment of the valve prosthesis in a location other than the aortic root.	
Endocarditis	Any one of the following affecting study valve: • Fulfillment of the Duke endocarditis criteria • Evidence of abscess, paravalvular leak, pus, or vegetation confirmed as secondary to infection by histological or bacteriological studies during a re-operation • Findings of abscess, pus, or vegetation involving a repaired or replaced valve during an autopsy	
Frailty	Slowness, weakness, exhaustion, wasting and malnutrition, poor endurance and inactivity, loss of independence Criteria: • 5 meter walking time • Grip strength • BMI 〈 20 kg/m2 and/or weight loss 5 kg/yr • Serum albumin 〈 3.5 g/dL • Cognitive impairment or dementia	
Hemolysis	Evidence of RBC destruction best explained by hemolysis (LDH 〉350 u/L and decreased haptoglobin based on site lab normals) and no other explanation for the findings. Microscopic evidence may be considered supportive.	
Hospitalization	Any admission to the hospital for either a diagnostic or therapeutic	

지표명	정의기준	기타
(repeat)	purpose (e.g. diuretics, inotropes, chronotropes, oral or intravenous therapy) following discharge from the index hospitalization. It includes either: • Admission to an inpatient unit (treated by a physician in a hospital for at least a 24 hour period) OR • Visit to an Emergency Room/Observation unit greater than 24 hours Valve-related rehospitalization: Repeat hospitalization for symptoms of prosthetic valve related decompensation due to an acute, subacute, or late valve prosthesis dysfunction such as valve thrombosis, endocarditis, prosthesis degeneration, patient prosthesis mismatch, delayed coronary obstruction, coronary embolization, aortic valve-related heart failure*, or bleeding complications related to oral anticoagulation or antiplatelet therapy for valve-related thromboembolic event prevention. Procedure-related rehospitalization: Include complications related to the index valve procedure such as bleeding and vascular complications, stroke/TIA, arrhythmias, and AKI. This does not include complications indirectly related to the procedure or related to the hospitalization such as UTI, dehydration, other hospital acquired infections, etc. Onset of the complication is generally within 30 days of the procedure. Heart failure related hospitalization: Defined as hospitalization with clinical symptoms and objective signs of heart failure including pulmonary edema, hypoperfusion or documented volume overload AND necessitating a medical intervention i.e. administration of IV diuresis or inotropic therapy, performance of aortic valvuloplasty, institution of mechanical support (IABP or ventilation for pulmonary edema) or hemodialysis for volume overload. Administration of IV therapies in clinic without admission will not qualify as hospitalization events.	
Hypertension	Systolic pressure 〉 140 or a diastolic pressure 〉 90 mmHg	
Hypotension	Systolic pressure 〈 90 or a diastolic pressure 〈 60 mmHg	
Index hospitalization	The beginning of the Index Hospitalization is defined as the day the patient is admitted for valve implant procedure and continues until the patient is discharged from the hospital.	
Lung disease, severe	FEV1 〈 50% predicted or currently on home oxygen	
Liver disease, chronic	MELD Score ≥ 10 or Child-Pugh Class B or C	

지표명	정의기준	기타
Modified Rankin Scale (mRS)	A commonly used scale for measuring the degree of disability or dependence in the daily activities of people who have suffered a stroke, as follows: 0 No symptoms at all 1 No significant disability despite symptoms; able to carry out all usual duties and activities 2 Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance 3 Moderate disability; requiring some help, but able to walk without assistance 4 Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance 5 Severe disability; bedridden, incontinent and requiring constant nursing care and attention 6 Dead	
Mortality, all cause	Cardiovascular mortality Any of the following criteria: • Death due to proximate cardiac cause (e.g. myocardial infarction, cardiac tamponade, worsening heart failure) • Death caused by non-coronary vascular conditions such as neurological events, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular disease • All procedure-related deaths, including those related to a complication of the procedure or treatment for a complication of the procedure • All device-related deaths including structural or nonstructural valve dysfunction or other valve-related adverse events • Sudden death • unwitnessed death • Death of unknown cause Non-cardiovascular mortality Any death which is due primarily to an identifiable noncardiovascular cause or etiology. Specific diagnoses may include respiratory failure, pneumonia, trauma, suicide, or any other non-cardiovascular defined causes (e.g., liver disease, malignancies etc.) not included in the previous categories.	
Myocardial infarction	An acute ischemic event that is associated with documented and clinically significant myocardial necrosis MI can be either peri-procedural (≤72h after the valve implant procedure) or spontaneous (〉72 after the valve implant procedure) or a prior MI (before study initiation). Peri-procedural MI is defined as: • New ischemic symptoms (e.g., chest pain or shortness of breath), or new ischemic signs (e.g., ventricular arrhythmias, new or worsening heart failure, new ST-segment changes, hemodynamic instability, new pathological Q waves in at least two contiguous leads, imaging evidence of new loss of viable myocardium or new wall motion abnormality) AND • Elevated cardiac biomarkers (preferable CK-MB) within 72 h after the valve implant procedure, consisting of at least one sample post-procedure with a peak value exceeding 15x upper reference limit (troponin) or 5x for CK-MB.* If cardiac biomarkers are increased at baseline (〉99th percentile), a	

지표명	정의기준	기타
	further increase of at least 50% post-procedure is required AND the peak value must exceed the previously stated limit. Spontaneous MI is defined as any one of the following criteria: • Detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile URL, together with evidence of myocardial ischemia with at least one of the following: • Symptoms of ischemia • ECG changes indicative of new ischemia [new ST-T changes or new left bundle branch block (LBBB)] • New pathological Q waves in at least two contiguous leads • Imaging evidence of new loss of viable myocardium or new wall motion abnormality • Sudden, unexpected cardiac death, involving cardiac arrest, often with symptoms suggestive of myocardial ischemia, and accompanied by presumably new ST elevation, or new LBBB, and/or evidence of fresh thrombus by coronary angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood. • Pathological findings of an acute myocardial infarction. Prior MI is defined as the presence of any of the following: • Pathological Q waves with or without symptoms in the absence of non-ischemic causes • Imaging evidence of a region of loss of viable myocardium that is thinned and/or fails to contact, in the absence of a nonischemic cause • Pathological findings of a prior MI.	
National Institutes of Health Stroke Scale (NIHSS)	The NIHSS can help physicians determine the severity of a stroke, predict clinical outcomes and can help guide management.	
New York Heart Association Classification (NYHA)	Class I: Patients with cardiac disease but without resulting limitations of physical activity. Class II: Patients with cardiac disease resulting in slight limitation of physical activity. Patients are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain. Class III: Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain. Class IV: Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.	
Peripheral vascular disease (PVD)	Includes peripheral arterial disease of upper and lower extremity, renal, mesenteric, and abdominal aortic systems, as follows: • Claudication, either with exertion or at rest • Amputation for arterial vascular insufficiency	

<table>
<tr><th>지표명</th><th>정의기준</th><th>기타</th></tr>
<tr><td></td><td>• Vascular reconstruction, bypass surgery, or percutaneous intervention to the extremities (excluding dialysis fistulas and vein stripping)
• Documented abdominal aortic aneurysm with or without repair
• Positive noninvasive test (e.g., ankle brachial index =〈0.9, ultrasound, magnetic resonance or computed tomography imaging of 〉 50% diameter stenosis in any peripheral artery, i.e., renal, subclavian, femoral, iliac) or angiographic imaging

Peripheral arterial disease excludes disease in the carotid, cerebrovascular arteries or thoracic aorta.
PVD does not include DVT.</td><td></td></tr>
<tr><td>Porcelain aorta or severely atherosclerotic aorta</td><td>Heavy circumferential calcification or severe atheromatous plaques of the entire ascending aorta extending to the arch such that aortic cross-clamping is not feasible.</td><td></td></tr>
<tr><td>Prosthesis patient mismatch</td><td>
<table>
<tr><th></th><th>Insignificant</th><th>Moderate</th><th>Severe</th></tr>
<tr><td>Indexed effective orifice area a</td><td>>0.85 c m2/m2</td><td>0.85–0.65 cm2 /m2</td><td><0.65 cm2 /m2</td></tr>
<tr><td>Indexed effective orifice area b</td><td>> 0 . 7 0 cm2/m2</td><td>0.70–0.55 cm2/m2</td><td><0.55 cm2/m2</td></tr>
</table>
a Use in setting of BMI ,30 kg/m2
b Use in setting of BMI ≥ 30 kg/m2
</td><td></td></tr>
<tr><td>Prosthetic aortic valve stenosis criteria a</td><td>
<table>
<tr><th></th><th>Normal</th><th>Possible (Mild) Stenosis</th><th>Significant (Moderate/Severe) Stenosis</th></tr>
<tr><td colspan="4">Quantitative Parameters (flow-dependent) b</td></tr>
<tr><td>Peak velocity (m/s)</td><td><3 m/s</td><td>3-4 m/s</td><td>>4m/s</td></tr>
<tr><td>Mean gradient (mmHg)</td><td><20 mmHg</td><td>20-40 mmHg</td><td>>40 mmHg</td></tr>
<tr><td>Increase in mean gradient during follow-up</td><td><10 mmHg</td><td>10-19 mmHg</td><td>≥20 mmHg</td></tr>
<tr><td colspan="4">Quantitative parameters (flow-independent)</td></tr>
<tr><td>Doppler velocity index c</td><td>>0.35</td><td>0.35-0.25</td><td><0.25</td></tr>
<tr><td>Effective orifice area d</td><td>>1.1 cm2</td><td>> 1 . 1 - 0 . 8 cm2</td><td><0.8 cm2</td></tr>
<tr><td>Decrease in effective orifice area during follow-up</td><td>< 0.3 cm2</td><td>0 . 3 - 0 . 5 9 cm2</td><td>≥0.6 cm2</td></tr>
</table>
a In conditions of normal or near normal stroke volume (50–70mL).
b These parameters are more affected by flow, including concomitant aortic regurgitation.
c For LVOT 〉2.5 cm, significant stenosis criteria is 〈0.20.
d Use in setting of BSA ≥1.6 cm2 (note: dependent on the size of the valve and the size of the native annulus).
</td><td></td></tr>
</table>

<table>
<tr><th>지표명</th><th>정의기준</th><th>기타</th></tr>
<tr><td>Prosthetic aortic valve stenosis criteria</td><td>
<table>
<tr><th></th><th>None/ Trace</th><th>Mild</th><th>Mo sev</th></tr>
<tr><td colspan="4">Qualitative Parameters</td></tr>
<tr><td>Extensive/wide jet origin– Color Doppler</td><td>Absent</td><td>Absent</td><td>Pre</td></tr>
<tr><td>Multiple jets</td><td>Possible</td><td>Possible</td><td>Oft</td></tr>
<tr><td>Jet path visible along the stent– Color Doppler</td><td>Absent</td><td>Absent</td><td>Oft</td></tr>
<tr><td>Proximal flow convergence visible– Color Doppler</td><td>Absent</td><td>Absent</td><td>Pos</td></tr>
<tr><td colspan="4">Semi-quantitative Parameters</td></tr>
<tr><td>Jet width at its origin (% LVOT diameter) – Color Doppler</td><td>Narrow (<5%)</td><td>Intermediate (5-29%)</td><td>Lar</td></tr>
<tr><td>Vena contracta width – Color Doppler</td><td>< 2mm</td><td>2-3.9 mm</td><td>≥ 4</td></tr>
<tr><td>Circumferential extent of prosthetic valveparavalvular regurgitation (%) – Color Doppler</td><td><5%</td><td>1-19%</td><td>≥20</td></tr>
<tr><td>Jet deceleration rate (PHT, ms) - CW Doppler</td><td>Slow (>500 ms)</td><td>Slow (>500 ms)</td><td>Var ms)</td></tr>
<tr><td>Diastolic flow reversal in the descending aorta—PW Doppler</td><td>Absent or brief early diastolic</td><td>Intermediate</td><td>Pro hol</td></tr>
<tr><td colspan="4">Quantitative parameters</td></tr>
<tr><td>Regurgitant volume (mL/beat)</td><td><15 mL</td><td>15-29 mL</td><td>≥30</td></tr>
<tr><td>Regurgitant fraction (%)</td><td><15%</td><td>15-29 %</td><td>≥30</td></tr>
<tr><td>EROA (cm2)</td><td>< 5 mm2</td><td>5-9 mm2</td><td>≥ 1</td></tr>
</table>
</td><td></td></tr>
<tr><td>Re intervention</td><td>Any operation that repairs, alters, or replaces a previously operated valve and refers to events occurring for any reason after the index procedure. These interventions include:
• Balloon aortic valvuloplasty
• Surgical aortic valve replacement
• Valve in valve
• Percutaneous paravalvular leak closure</td><td></td></tr>
<tr><td>Sternal wound dehiscence</td><td>Opening of sternal with negative cultures and no signs of infection requiring a procedure or operation for treatment</td><td></td></tr>
<tr><td>Valve implant procedure</td><td>Placement of study device and/or additional procedures occurring in the cath lab and/or operating room which are completed prior to subject transfer to a post-procedure recovery unit (e.g. Recovery Room, ICU/CCU, etc.)

The valve implant procedure will be considered to have</td><td></td></tr>
</table>

지표명	정의기준	기타
	started when: • The first interventional access related puncture (venous or arterial) is established for TAVR. • The first skin incision is performed for Surgery. Performance of TEE does not by itself constitute start of procedure	
Valve thrombosis	Valve thrombosis is any thrombus not caused by infection attached to or near an operated valve that occludes part of the blood flow path, interferes with valve function, or is sufficiently large to warrant treatment.	
Stroke /transient ischemic attack (TIA)	**Stroke Diagnostic Criteria** • Acute episode of a focal or global neurological deficit with at least one of the following: • change in level of consciousness • hemiplegia • hemiparesis • numbness or sensory loss affecting one side of the body • dysphasia or aphasia • hemianopia • amaurosis fugax • or other neurological signs or symptoms consistent with stroke • Duration of a focal or global neurological deficit ≥ 24 h; **OR** 〈 24 h, if available neuroimaging documents a new hemorrhage or infarct; **OR** the neurological deficit results in death • No other readily identifiable nonstroke cause for the clinical presentation (e.g., brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences) to be determined by or in conjunction with designated neurologist* • Confirmation of the diagnosis by at least one of the following#: 1. Neurology or neurosurgical specialist 2. Non-neurologist physician (if neurologist is not available) 3. Neuroimaging procedure (MR or CT scan) 4. Clinical presentation alone **Stroke severity†:** • Non-disabling: mRS score of 〈 2 at 90 days (or the last available clinical visit with evaluable data) or one that does not result in an increase of at least one mRS category from prestroke baseline • Disabling: a mRS score of 2 or more at 90 days (or the last available clinical visit with evaluable data) and an increase of at least one mRS category from an individual's pre-stroke baseline **Stroke types:** • Hemorrhagic: an acute episode of focal or global cerebral or spinal dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage.	

지표명	정의기준	기타
	• Ischemic: an acute symptomatic episode of focal cerebral, spinal, or retinal dysfunction caused by an infarction of the central nervous system tissue • Undetermined: stroke with insufficient information to allow categorization as ischemic or hemorrhagic. Transient Ischemic Attack (TIA) Acute episode of a focal or global neurological deficit fulfilling the following criteria: 1. Resulting in at least one of the following 5. _Change in level of consciousness 6. _Hemiplegia 7. _Hemiparesis 8. _Numbness 9. _Sensory loss affecting one side of the body 10. _Dysphasia or aphasia 11. _Hemianopia 12. _Amaurosis fugax 13. _Other neurological signs or symptoms consistent with stroke 2. Duration of deficit could be one of the following: 14. _A focal or global neurological deficit 〈 24 hours 15. _Any available neuroimaging does not demonstrate a new hemorrhage or infarct 3. No other readily identifiable non-stroke cause for the clinical presentation (e.g. brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences) to be determined by or in conjunction with designated neurologist.*	
Structural valve deterioration (SVD)	Dysfunction or deterioration resulting from changes intrinsic to the valve, such as wear, fracture, calcification, leaflet tear, leaflet retraction and stenosis as determined by reoperation, autopsy or clinical investigation. SVD excludes failures due to external causes to the valve such as endocarditis, valve thrombosis, and trauma. Must fulfill both criteria: • Structural and hemodynamic valve deterioration (moderate or severe prosthetic valve stenosis, AND/ OR moderate or severe transprosthetic valve regurgitation) AND • Requiring repeat procedure such as: o Surgical aortic valve replacement (Surgery) o Transcatheter aortic valve replacement (Valve-in-Valve) o Balloon aortic valvuloplasty (BAV) o Percutaneous paravalvular leak closure / plug	
STS Adult Cardiac Surgery Risk Calculator	The Society of Thoracic Surgeons' risk models predict the risk of operative mortality and morbidity after adult cardiac surgery on the basis of patient demographic and clinical variables.	
6-minute Walk Test	A performance-based measure of functional exercise capacity. The test measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface.	

지표명	정의기준	기타
THV-in-THV	An additional valve prosthesis is implanted within a previously implanted prosthesis because of suboptimal device position and/or function, during or after the valve implant procedure	
Transient ischemic attack (TIA)	See “Stroke / Transient Ischemic Attack (TIA)”	
Vascular access site and accessrelated complications	Major vascular complications: • Any aortic dissection, aortic rupture, annulus rupture, left ventricle perforation, or new apical aneurysm/pseudoaneurysm OR • Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia or neurological impairment OR • Distal embolization (non-cerebral) from a vascular source requiring surgery or resulting in amputation or irreversible endorgan damage OR • The use of unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischemia or neurological impairment OR • Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram OR • Surgery for access site-related nerve injury OR • Permanent access site-related injury • Percutaneous closure device failure* resulting in death, BARC Type 3 or 4 bleeding, visceral ischemia or irreversible neurologic impairment Minor vascular complications: • Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysms, hematomas, percutaneous closure device failure) not leading to death, life-threatening or major bleeding*, visceral ischemia or neurological impairment OR • Distal embolization treated with embolectomy and/or thrombectomy and not resulting in amputation or irreversible end-organ damage OR • Any unplanned endovascular stenting or unplanned surgical intervention not meeting the criteria for a major vascular complication OR • Vascular repair or the need for vascular repair (via surgery,	

지표명	정의기준	기타
	ultrasound-guided compression, transcatheter embolization, or stent-graft) • Percutaneous closure device failure not leading to death, BARC Type 3 or 4, visceral ischemia or irreversible neurologic impairment *Percutaneous closure device failure Failure of a closure device to achieve hemostasis at the arteriotomy site leading to alternative treatment (other than manual compression or adjunctive endovascular ballooning) *Refers to VARC bleeding definitions	

대상자수

	총 수	TAVR	SVAR
스크리닝수(enroll)	1,520		
randomised	1,000	503	497
수술/시술 수행자	950	496	454
분석대상자	950	496	454
탈락율	5%	1.39%	8.65%

연구 결과

대상자 특성

■ 연구대상 특성

문헌	중재	N	평균 연령 (SD)	남자 (%)	평균 STS (SD)	평균 euro SCORE II (SD)	NYHA III or IV (%)	Pace maker(%)	Cr >2 (%)	기저질환										
										DM (%)	carotid disease (%)	stroke (%)	pul. HTN (%)	말초혈관질환 (%)	CAD (%)	MI (%)	COPD (%)	Lt. BBB (%)	Rt. BBB (%)	AF (%)
Mack 2019	TAVR	496	73.3 (5.8)	335 (67.5)	1.9 (0.7)	1.5 (1.2)	155 (31.2)	12 (2.4)	1 (0.2	155 /496 (31.2)	61 /481 (12.7)	17 /496 (3.4)	23 /495 (4.6)	34 /494 (6.9)	137 /494 (27.7)	28 /495 (5.7)	25 /495 (5.1)	15 /495 (3.0)	51 /495 (10.3	78 /496 (15.7
	대조 SAVR	454	73.6 (6.1)	323 (71.1)	1.9 (0.6)	1.5 (0.9)	108 (23.8)	13 (2.9)	1 (0.2	137 /453 (30.2)	50 /442 (11.3)	23 /453 (5.1)	24 /454 (5.3)	33 /453 (7.3)	127 /454 (28.0)	26 /452 (5.8)	28 /454 (6.2)	15 /453 (3.3)	62 /453 (13.7	85 /453 (18.8
Baron 2019	TAVR	494	73.3 (5.8)	333 (67.4)	1.9 (0.7)				1 (0.2	155 (31.4)		17 (3.4)		34 (6.9)	136 (27.6)	28 (5.7)	25 (5.1)			77 (15.6
	대조 SAVR	449	73.6 (6.1)	320 (71.3)	1.9 (0.6)				1 (0.2	135 (30.1)		23 (5.1)		33 (7.4)	124 (27.6)	26 (5.8)	27 (6.0)			84 (18.8

STS, Society of Thoracic Surgeons score; LES, Logistic EuroScore I; NYHA, New York Heart; CABG, coronary-artery bypas grafting; PCI, percutaneous coronary intervention; AVR, aortic-valve; CAD, coronary artery disease; PVD, peripheral vascula disease; AF, atrial fibrillation; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease.

문헌	중재	N	LV ejection fraction (%)	Aortic valve area (㎠)	Mean aortic valve gradient (㎜Hg)	Baseline health status							
						KCCQ overall summary (SD)	KCCQ physical limitations (SD)	KCCQ total symptoms (SD)	KCCQ quality of life (SD)	KCCQ social limitation (SD)	SF-36 physical summary (SD)	SF-36 mental summary (SD)	EQ-5D utilities (SD)
Mack 2019	TAVR	496	65.7 (9.0)	0.8 (0.2)	49.4 (12.8)								
	대조 SAVR	454	66.2 (8.6)	0.8 (0.2)	48.3 (11.8)								
Baron 2019	TAVR	494	65.7 (9.0)	0.8 (0.2)	49.4 (12.7)	70.4 (19.4)	76.6 (19.8)	74.2 (18.9)	58.1 (24.4)	72.0 (25.9)	44.1 (9.2)	52.5 (9.1)	0.83 (0.11)
	대조 SAVR	449	66.2 (8.6)	0.8 (0.2)	48.4 (11.8)	70.1 (20.9)	76.9 (20.6)	73.0 (21.3)	58.2 (25.8)	71.7 (27.2)	44.1 (9.0)	51.3 (10.0)	0.83 (0.13)

추적관찰 기간

평균추적관찰 기간 : 1년

결과

1) 이분형 변수

(1) ATT 대상자

결과변수	1저자 (연도)	시점	TAVR			SAVR			P value	RR ((HR)	95% CI	S/NS
			N	event	%	N	event	%				
Death, stroke, or rehospitalization †	Mack (2019)	30일	496	21	4.2	454	42	9.3		0.45	0.27, 0.76	
		1년	496	42	8.5	454	68	15.1	0.001	0.54	0.37, 0.79	
Death from any cause	Mack (2019)	30일	496	2	0.4	454	5	1.1		0.37	0.07, 1.88	
		1년	496	5	1.0	454	11	2.5		0.41	0.14, 1.17	
Cardiac death	Mack (2019)	30일	496	2	0.4	454	4	0.9		0.46	0.08, 2.49	
		1년	496	4	0.8	454	9	2.0		0.40	0.12, 1.30	
Non-cardiac death	Mack (2019)	30일	496	0	0	454	1	0.2		0.00	NA	
		1년	496	1	0.2	454	2	0.5		0.44	0.04, 4.88	
Any stroke	Mack (2019)	30일	496	3	0.6	454	11	2.4	0.02	0.25	0.07, 0.88	
		1년	496	6	1.2	454	14	3.1		0.38	0.15, 1.00	
Disabling stroke	Mack (2019)	30일	496	0	0	454	2	0.4		0.00	NA	
		1년	496	1	0.2	454	4	0.9		0.22	0.03, 2.00	
Non-disabling stroke	Mack (2019)	30일	496	3	0.6	454	9	2.0		0.30	0.08, 1.12	
		1년	496	5	1.0	454	10	2.2		0.45	0.15, 1.32	
TIA	Mack (2019)	30일	496	0	0	454	3	0.7		0.00	NA	
		1년	496	5	1.0	454	5	1.1		0.89	0.26, 3.06	
Death or stroke	Mack (2019)	30일	496	5	1.0	454	15	3.3	0.01	0.30	0.11, 0.83	
		1년	496	9	1.8	454	22	4.9		0.36	0.17, 0.79	
Death or disabling stroke	Mack (2019)	30일	496	2	0.4	454	6	1.3		0.30	0.06, 1.51	
		1년	496	5	1.0	454	13	2.9		0.34	0.12, 0.97	
Rehospitalization †	Mack (2019)	30일	496	17	3.4	454	29	6.5		0.53	0.29, 0.97	
		1년	496	36	7.3	454	49	11.0		0.65	0.42, 1.00	
Major vascular complications	Mack (2019)	30일	496	11	2.2	454	7	1.5		1.44	0.56, 3.73	
		1년	496	14	2.8	454	7	1.5		1.83	0.74, 4.55	
Life-threatening / disabling, or major bleeding	Mack (2019)	30일	496	18	3.6	454	111	24.5		0.12	0.07, 0.21	
		1년	496	38	7.7	454	117	25.9		0.25	0.17, 0.37	
Life-threating/ disabling bleeding	Mack (2019)	30일	496	6	1.2	454	54	11.9		0.09	0.04, 0.22	
		1년	496	14	2.8	454	58	12.8		0.20	0.11, 0.36	
Myocardial infarction	Mack (2019)	30일	496	5	1.0	454	6	1.3		0.76	0.23, 2.50	
		1년	496	6	1.2	454	10	2.2		0.54	0.20, 1.49	
Acute kidney injury stage II or III ‡	Mack (2019)	30일	496	2	0.4	454	8	1.8		NA	NA	
		1년	496	NA	NA	454	NA	NA		NA	NA	
Acute kidney injury stage I or II or III	Mack (2019)	30일	496	7	1.4	454	39	8.6		-7.2	-9.96, -4.40	
Requiremnet for renal replacement ‡	Mack (2019)	30일	496	1	0.2	454	3	0.7		0.30	0.03, 2.93	
		1년	496	1	0.2	454	3	0.7		0.30	0.03, 2.93	
new permanent pacemaker	Mack (2019)	30일	496	32	6.5	454	18	4.0		1.66	0.93, 2.96	
		1년	496	36	7.3	454	24	5.4		1.39	0.83, 2.33	
new permanent pacemaker (baseline pacemaker excluded)	Mack (2019)	30일	496	32	6.6	454	18	4.1		1.65	0.92, 2.95	
		1년	496	36	7.5	454	24	5.5		1.38	0.82, 2.32	
New LBBB	Mack (2019)	30일	496	106	22.0	454	35	8.0		3.17	2.13, 4.72	
		1년	496	114	23.7	454	35	8.0		3.43	2.32, 5.08	

결과변수	1저자 (연도)	시점	TAVR			SAVR			P value	RR ((HR)	95% CI	S/NS
			N	event	%	N	event	%				
New onset atrial fibrillation	Mack (2019)	30일	417	21	5.0	369	145	39.5	<0.001	0.10	0.06, 0.16	
		1년	496	29	7.0	454	150	40.9		0.13	0.09, 0.20	
Coronary obstruction requiring intervention	Mack (2019)	30일	496	1	0.2	454	3	0.7		0.30	0.03, 2.93	
		1년	496	1	0.2	454	3	0.7		0.30	0.03, 2.93	
Aortic Valve Re-intervention	Mack (2019)	30일	496	0	0	454	0	0		NA	NA	
		1년	496	3	0.6	454	2	0.5		1.33	0.22, 7.95	
Endocarditis	Mack (2019)	30일	496	0	0	454	1	0.2		0.00	NA	
		1년	496	1	0.2	454	2	0.5		0.44	0.04, 4.89	
Asymptomatic Valve thrombosis	Mack (2019)	30일	496	1	0.2	454	0	0		NA	NA	
		1년	496	5	1.0	454	1	0.2		4.47	0.52, 38.24	
Discharged to home/ self-cares ∮	Mack (2019)	30일	495	475	96.0	453	331	73.1		22.9	18.45, 27.33	
		1년	496	NA	NA	454	NA	NA		NA	NA	
NYHA Class Ⅱ/Ⅲ/Ⅳ ∮	Mack (2019)	30일	493	97	19.7	433	144	33.3		-13.6	-19.24, -7.92	
		1년	480	85	17.7	407	68	16.7		1.0	-3.98, 5.98	
Six-minute walk test distance(m) change from baseline	Mack (2019)	30일	496	17.2 ±4.63	NA	454	-15.2 ±6.27	NA		33.7	19.9, 47.4	
		1년	496	15.4 ±5.30	NA	454	15.1 ±5.85	NA		-1.4	-15.2, 12.5	
KCCQ-OS score change from baseline	Mack (2019)	30일	496	18.5 ±0.83	NA	454	2.5 ±1.05	NA		16.1	14.2, 18.0	
		1년	496	19.4 ±0.87	NA	454	17.4 ±0.99	NA		1.8	0.2, 3.4	
Death, KCCQ score of <45, or decrease from baseline in KCCQ score of ≥10 points	Mack (2019)	30일	492	19	3.9	435	133	30.6	<0.001	-26.7	-31.4,-22.1	
Patients requiring transfusion (≥ 1 unit)	Mack (2019)	3days	496	10	2.0	454	121	26.7		-24.6	-28.9, -20.4	
		hospital	496	10	2.0	454	126	27.8		-25.7	-30.0, -21.4	
Patients requiring transfusion (≥ 4 unit)	Mack (2019)	3days	496	4	0.8	454	33	7.3		-6.5	-9.0, -4.0	
		hospital	496	4	0.8	454	33	7.3		-6.5	-9.0, -4.0	
Transfusion 1 unit	Mack (2019)	3days	10	3	30.0	121	32	26.4				
		hospital	10	3	30.0	126	37	29.4				
Transfusion 2 units	Mack (2019)	3days	10	3	30.0	121	41	33.9				
		hospital	10	3	30.0	126	41	32.5				
Transfusion 3 units	Mack (2019)	3days	10	0	0	121	15	12.4				
		hospital	10	0	0	126	15	11.9				
Transfusion ≥4 units	Mack (2019)	3days	10	4	40.0	121	33	27.3				
		hospital	10	4	40.0	126	33	26.2				

Except where otherwise specified, data are kaplan-Meier estimates % (number of patients with event) of Mean ± SE

† valve-related or procedure-related, and including heart failure

‡ AKI is derived from lab values and need for renal replacement therapy is site-reported. All other clinical outcomes are CEC-adjudicated

∮ Summary statistics are no./total observations, treatment effect [95%CI] is difference of proportions (TAVR-Surgery) in normal approximation

Note: 95% confidence intervals presented in this report have not been adjusted for multiplicity.

Therefore, inferences drawn from these intervals may not be reproducible.

(2) Subgroup Analyses – concomitant procedures

결과변수	1저자 (연도)	시점	TAVR			SAVR			P value	RR (HR)	95% CI	S/NS
			N	event	%	N	event	%				
TAVR with no PCI vs. Surgery with no CABG												
Death from any cause, stroke, or rehospitalization	Mack (2019)	30일	464	19	4.1	396	35	8.9		0.45	0.26,0.79	
		1년	457	39	8.4	334	61	15.6		0.52	0.35,0.77	
Death from any cause	Mack (2019)	30일	464	2	0.4	396	4	1.0		0.43	0.08,2.33	
		1년	457	5	1.1	334	10	2.6		0.42	0.14,1.22	
Stroke	Mack (2019)	30일	464	3	0.6	396	9	2.3		0.28	0.08,1.04	
		1년	457	6	1.3	334	12	3.1		0.42	0.16,1.11	
Rehospitalization	Mack (2019)	30일	464	15	3.2	396	25	6.4		0.51	0.27,0.96	
		1년	457	33	7.2	334	45	11.6		0.60	0.38,0.94	
TAVR with PCI vs. Surgery with CABG												
Death from any cause, stroke, or rehospitalization	Mack (2019)	30일	32	2	6.3	58	7	12.1		0.52	0.11,2.49	
		1년	32	3	9.4	58	7	12.1		0.77	0.20,2.98	
Death from any cause	Mack (2019)	30일	32	0	0	58	1	1.7		0.00	NA	
		1년	32	0	0	58	1	1.7		0.00	NA	
Stroke	Mack (2019)	30일	32	0	0	58	2	3.4		0.00	NA	
		1년	32	0	0	58	2	3.4		0.00	NA	
Rehospitalization	Mack (2019)	30일	32	2	6.3	58	4	6.9		0.93	0.17,5.10	
		1년	32	3	9.4	58	4	6.9		1.39	0.31,6.21	
In patients with no concomitant procedures												
Death from any cause, stroke, or rehospitalization	Mack (2019)	30일	457	19	4.2	334	30	9.0		0.45	0.26,0.81	
		1년	457	39	8.5	334	51	15.4		0.53	0.35,0.81	
Death from any cause	Mack (2019)	30일	457	2	0.4	334	3	0.9		0.45	0.08,2.91	
		1년	457	5	1.1	334	8	2.4		0.45	0.15,1.37	
Stroke	Mack (2019)	30일	457	3	0.7	334	7	2.1		0.31	0.08,1.20	
		1년	457	6	1.3	334	9	2.7		0.48	0.17,1.34	
Rehospitalization	Mack (2019)	30일	457	15	3.3	334	22	6.7		0.49	0.26,0.95	
		1년	457	33	7.3	334	38	11.6		0.61	0.38,0.97	

2) 연속형 변수

결과변수	1저자 (연도)	시점	TAVR			SAVR			두 군간 변화량차이		P value	RR (HR)	95% CI	S/
			N	Mean	SD	N	Mean	SD	M5ea	SD				
length of index hospitalization (days)	Mack (2019)		496	3.0		454	7.0				<0.001	-4.0	-4.0, -3.0	
6-minute walk test distance	Mack (2019)	30일	478	32.0		405	7.4							
		1년	454	32.2		369	17.1							
KCCQ overall summary score	Mack (2019)	30일	490	37.8		429	12.8							
		1년	479	39.7		400	38.7							
Six-minute walk test distance(m) change from baseline	Mack (2019)	30일	496	17.2	4.63	454	-15.2	6.27	33.7	19.9 47.				
		1년	496	15.4	5.30	454	15.1	5.85	-1.4	-15. 12.				

결과변수	1저자 (연도)	시점	TAVR			SAVR			두 군간 변화량차이		P value	RR (HR)	95% CI	S/
			N	Mean	SD	N	Mean	SD	M5ea	SD				
KCCQ-OS score change from baseline	Mack (2019)	30일	496	18.5	0.83	454	2.5	1.05	16.1	14. 18.				
		1년	496	19.4	0.87	454	17.4	0.99	1.8	0.2 3.4				
Echocardiographic Results														
Systolic blood pressure, mmHg	Pibarot (2020)	baseline	495	136.6	18.7	453	136.4	18.0						
		30일	495	138.5	18.6	453	133.0	20.2			0.0008			
		1년	495	140.0	18.8	453	139.6	19.3			0.7700			
Diastolic blood pressure, mmHg	Pibarot (2020)	baseline	495	73.8	10.0	453	73.7	9.8						
		30일	495	72.3	10.0	453	73.0	10.7			0.3916			
		1년	495	74.2	10.5	453	75.9	9.5			0.0076			
Peak aortic velocity, m/s	Pibarot (2020)	baseline	495	4.47	0.53	453	4.44	0.52						
		30일	495	2.41	0.39	453	2.25	0.43			0.1639			
		1년	495	2.46	0.46	453	2.26	0.45			0.0024			
Peak gradient, mmHg	Pibarot (2020)	baseline	495	80.9	19.7	453	79.9	18.9						
		30일	495	23.8	8.0	453	21.0	8.0			0.4242			
		1년	495	25.0	10.1	453	21.3	8.8			0.0427			
Mean gradient, mmHg	Pibarot (2020)	baseline	495	49.4	12.7	453	48.3	11.8						
		30일	495	12.8	4.3	453	11.2	4.3			0.4958			
		1년	495	13.7	5.6	453	11.6	5.0			0.1209			
Mean gradient ≥ 20mmHg	Pibarot (2020)	baseline	473	473 (100%)		428	427 (99.8%)							
		30일	482	33 (6.8%)		413	17 (4.1%)				0.0812			
		1년	460	46 (10.0%)		379	21 (5.5%)				0.0208			
Aortic valve area, ㎠	Pibarot (2020)	baseline	495	0.77	0.16	453	0.77	0.15						
		30일	495	1.74	0.36	453	1.79	0.41			0.9567			
		1년	495	1.72	0.37	453	1.76	0.42			0.1204			
Indexed aortic valve area, ㎠/㎡	Pibarot (2020)	baseline	495	0.38	0.08	453	0.38	0.08						
		30일	495	0.87	0.18	453	0.89	0.21			0.9449			
		1년	495	0.85	0.18	453	0.87	0.21			0.1433			
Doppler velocity index	Pibarot (2020)	baseline	495	0.19	0.05	453	0.20	0.04						
		30일	495	0.41	0.07	453	0.45	0.08			0.0032			
		1년	495	0.40	0.07	453	0.44	0.08			<0.0001			
Energy loss index, ㎠/㎡	Pibarot (2020)	baseline	495	0.42	0.10	453	0.42	0.09						
		30일	495	1.17	0.64	453	1.17	0.48			0.3550			
		1년	495	1.09	0.30	453	1.15	0.43			0.1189			
Valvulo-arterial impedance, mmHg/mL/㎡	Pibarot (2020)	baseline	495	4.7	1.0	453	4.8	1.0						
		30일	495	3.7	0.8	453	3.9	0.9			0.0005			
		1년	495	3.7	0.8	453	3.9	0.9			<0.0001			
≥Moderate paravalvular aortic regurgitation	Pibarot (2020)	baseline	495	NA	NA	453	NA	NA						
		30일	487	4 (0.8%)	0.8	421	0 (0.0%)	0			0.1281			
		1년	466	3 (0.6%)	0.6	381	2 (0.5%)	0.5			>0.9999			
≥ Moderate total aortic regurgitation	Pibarot (2020)	baseline	483	19 (3.9%)	3.9	445	11 (2.5%)	2.5						
		30일	490	4 (0.8%)	0.8	428	1 (0.2%)	0.2			0.3793			
		1년	470	5 (1.1%)	1.1	389	2 (0.5%)	0.5			0.4658			
LV end diastolic diameter, ㎝	Pibarot (2020)	baseline	495	4.9	0.52	453	4.9	0.51						
		30일	495	4.9	0.50	453	4.8	0.51			<0.0001			
		1년	495	4.9	0.53	453	4.8	0.51			<0.0001			
LV end systolic diameter, ㎝	Pibarot (2020)	baseline	495	3.0	0.62	453	3.0	0.63						
		30일	495	3.0	0.59	453	3.0	0.59			0.2011			
		1년	495	2.9	0.59	453	2.9	0.56			0.9827			
LV mass index, g/㎡	Pibarot (2020)	baseline	495	104.6	25.7	453	101.6	25.4						
		30일	495	99.0	23.7	453	94.1	25.9			0.0684			
		1년	495	91.9	22.6	453	89.0	28.0			0.5610			

결과변수	1저자 (연도)	시점	TAVR			SAVR			두 군간 변화량차이		P value	RR (HR)	95% CI	S/
			N	Mean	SD	N	Mean	SD	M5ea	SD				
LV hypertrophy	Pibarot (2020)	baseline	475	198 (41.7%)		434	138 (31.8%)							
		30일	478	152 (31.8%)		407	95 (23.3%)				0.0054			
		1년	462	94 (20.3%)		382	60 (15.7%)				0.0892			
Relative wall thickness	Pibarot (2020)	baseline	495	0.46	0.09	453	0.45	0.08						
		30일	495	0.45	0.08	453	0.45	0.09			0.1407			
		1년	495	0.43	0.08	453	0.44	0.09			0.0005			
LV ejection fraction, %	Pibarot (2020)	baseline	495	65.7	9.0	453	66.2	8.6						
		30일	495	65.7	8.2	453	65.5	8.9			0.2657			
		1년	495	66.4	7.9	453	66.5	7.8			0.2267			
LV ejection fraction 〈 50%	Pibarot (2020)	baseline	462	21 (4.5%)		422	21 (5.0%)							
		30일	471	19 (4.0%)		395	19 (4.8%)				0.6195			
		1년	441	13 (2.9%)		354	12 (3.4%)				0.8386			
LV stroke volume, mL	Pibarot (2020)	baseline	495	81.7	15.3	453	80.9	15.5						
		30일	495	84.2	15.4	453	76.6	16.2			〈0.0001			
		1년	495	87.0	16.5	453	80.6	16.3			〈0.0001			
LV stroke volume index, mL/㎡	Pibarot (2020)	baseline	495	40.7	7.65	453	40.1	7.68						
		30일	495	41.9	7.55	453	38.0	7.97			〈0.0001			
		1년	495	43.2	8.14	453	40.1	8.09			〈0.0001			
LV stroke volume index 〈 35 mL/㎡	Pibarot (2020)	baseline	449	106 (23.6%)		411	110 (26.8%)							
		30일	464	99 (21.3%)		390	142 (36.4)				〈0.0001			
		1년	441	75 (17.0%)		362	106 (29.3%)				〈0.0001			
≥ Mild mitral regurgitation	Pibarot (2020)	baseline	476	174 (36.6%)		436	154 (35.3%)							
		30일	490	128 (26.1%)		424	142 (33.5%)				0.0164			
		1년	467	141 (30.2%)		386	141 (36.5%)				0.0572			
≥ Moderate mitral regurgitaion	Pibarot (2020)	baseline	476	6 (1.3%)		436	14 (3.2%)							
		30일	490	3 (0.6%)		424	15 (3.5%)				0.0015			
		1년	467	4 (0.9%)		386	10 (2.6%)				0.0587			
RV TAPSE, ㎝	Pibarot (2020)	baseline	495	2.1	0.4	453	2.1	0.4						
		30일	495	2.1	0.4	453	1.4	0.4			〈0.0001			
		1년	495	2.1	0.5	453	1.6	0.4			〈0.0001			
≥ Mild tricuspid regurgitation	Pibarot (2020)	baseline	472	152 (32.2%)		430	140 (32.6%)							
		30일	483	135 (28.0%)		427	179 (41.9%)				〈0.0001			
		1년	460	144 (31.3%)		381	178 (46.7%)				〈0.0001			
≥ Moderate tricuspid regurgitation	Pibarot (2020)	baseline	472	8 (1.7%)		430	10 (2.3%)							
		30일	483	4 (0.8%)		427	22 (5.2%)				〈0.0001			
		1년	460	8 (1.7%)		381	21 (5.5%)				0.0038			
Tricuspid regurgitation peak gradient, mmHg	Pibarot (2020)	baseline	495	27.4	10.0	453	28.6	9.7						
		30일	495	25.4	7.35	453	24.9	7.1			0.8528			
		1년	495	25.6	7.7	453	24.5	7.6			0.5467			

3) Paired Difference (*paired differences reflect changes with baseline)

결과변수	1저자 (연도)	시점	TAVR				SAVR				두 군간 변화량 차이			S/N
			N	Paired difference	95% CI	P Value	N	Paired difference	95% CI	P Value	Mean	95% CI	P value	
KCCQ Overall Summary	Baron 2019	1개월	490	18.5	16.9,20.1	<0.001	429	2.5	0.5,4.6	0.016	16.0	14.2,17.8	<0.001	
		6개월	484	20.2	18.5,21.9	<0.001	402	17.4	15.5,19.3	<0.001	2.6	1.0,4.3	0.002	
		12개월	479	19.4	17.7,21.1	<0.001	400	17.4	15.4,19.3	<0.001	1.8	0.1,3.5	0.033	
KCCQ Physical Limitations	Baron 2019	1개월	479	13.4	11.8,15.1	<0.001	423	-0.6	-2.7,1.5	0.589	14.0	12.0,15.9	<0.001	
		6개월	470	14.0	12.3,15.8	<0.001	398	10.6	8.7,12.6	<0.001	2.9	1.1,4.8	0.002	
		12개월	466	12.7	10.9,14.5	<0.001	395	11.1	9.2,13.1	<0.001	1.2	-0.7,3.1	0.216	
KCCQ Total Symptoms	Baron 2019	1개월	490	13.4	11.7,15.2	<0.001	428	4.4	2.3,6.5	<0.001	9.9	8.1,11.8	<0.001	
		6개월	483	13.4	11.7,15.2	<0.001	401	12.1	10.1,14.0	<0.001	1.9	0.1,3.6	0.035	
		12개월	479	12.6	10.8,14.4	<0.001	399	12.3	10.2,14.3	<0.001	0.8	-1.1,2.7	0.404	
KCCQ Quality of Life	Baron 2019	1개월	489	29.8	27.7,32.0	<0.001	427	11.7	9.1,14.4	<0.001	17.7	15.4,20.0	<0.001	
		6개월	484	33.7	31.5,35.9	<0.001	400	29.3	26.8,31.9	<0.001	3.9	1.8,6.0	<0.001	
		12개월	477	33.2	30.9,35.4	<0.001	398	29.7	27.1,32.3	<0.001	2.8	0.8,4.9	0.007	
KCCQ Social Limitation	Baron 2019	1개월	436	17.9	15.4,20.4	<0.001	380	-6.5	-9.8,-3.2	<0.001	23.9	21.1,26.6	<0.001	
		6개월	435	19.8	17.2,22.3	<0.001	362	17.8	15.2,20.4	<0.001	1.9	-0.5,4.2	0.120	
		12개월	424	19.4	16.8,22.0	<0.001	348	16.8	14.0,19.6	<0.001	2.5	0.1,4.8	0.038	
SF-36 Physical Summary	Baron 2019	1개월	479	5.0	4.3,5.7	<0.001	416	-2.7	-3.6,-1.9	<0.001	7.7	6.8,8.6	<0.001	
		6개월	474	5.9	5.2,6.7	<0.001	393	5.1	4.3,5.9	<0.001	0.6	-0.3,1.6	0.167	
		12개월	469	5.2	4.4,6.0	<0.001	389	5.0	4.2,5.9	<0.001	0.0	-1.0,1.0	0.958	
SF-36 Mental Summary	Baron 2019	1개월	483	3.4	2.6,4.2	<0.001	417	0.1	-1.0,1.1	0.921	4.1	3.1,5.1	<0.001	
		6개월	476	3.5	2.8,4.3	<0.001	394	4.5	3.5,5.4	<0.001	0.0	-0.9,0.9	0.996	
		12개월	473	3.5	2.7,4.3	<0.001	391	4.0	3.1,4.9	<0.001	0.3	-0.5,1.2	0.445	
EQ-5D Utilities	Baron 2019	1개월	484	0.06	0.05,0.07	<0.001	419	-0.01	-0.03,0.00	0.062	0.07	0.06,0.09	<0.001	
		6개월	477	0.05	0.04,0.06	<0.001	390	0.05	0.04,0.07	<0.001	0.00	-0.02,0.01	0.774	
		12개월	475	0.04	0.03,0.05	<0.001	391	0.04	0.03,0.06	<0.001	0.00	-0.02,0.01	0.766	

4) 기타 - 범주형 결과지표 등 (최대한 표로 표시, 그래프 캡쳐)

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P값	RR (HR)	95% CI	S/NS
				N	event	%	N	event	%				
Acute Kidney Injury													
Acute kidney injury stages	Mack (2019)	30일	Stage I	496	5	1.0	454	31	6.8		-5.8	-8.30, -3.34	
Acute kidney injury stages	Mack (2019)	30일	Stage II	496	0	0.0	454	5	1.1		-1.1	NA	
Acute kidney injury stages	Mack (2019)	30일	Stage III	496	2	0.4	454	3	0.7		-0.3	-1.19, 0.67	
Vascular Injury													
Vascular injury	Mack (2019)	30일	Major	496	10	2.0	454	6	1.3		1.53	0.55, 4.22	
Vascular injury	Mack (2019)	30일	Minor	496	21	4.2	454	4	0.9		4.92	1.68, 14.37	
Access-Site Complications													
Access-Site Complications	Mack (2019)	30일	Major	496	1	0.2	454	1	0.2		0.92	0.06, 14.65	
Access-Site Complications	Mack (2019)	30일	Minor	496	2	0.4	454	11	2.4		0.16	0.04, 0.74	
Bleeding Complications													
bleeding (VARC-2)	Mack (2019)	30일	life-threatening/disabling or major	496	18	3.6	454	111	24.5		0.12	0.07, 0.21	

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P value	RR (HR)	95% CI	SMD
				N	event	%	N	event	%				
bleeding (VARC-2)	Mack (2019)		life-threatening /disabling	496	6	1.2	454	54	11.9		0.09	0.04, 0.22	
bleeding (VARC-2)	Mack (2019)		Major	496	13	2.6	454	61	13.5		0.18	0.10, 0.33	
bleeding (VARC-2)	Mack (2019)		Minor	496	24	4.8	454	34	7.5		0.63	0.37, 1.07	
bleeding (VARC-2)	Mack (2019)	1년	life-threatening/disabling or major	496	38	7.7	454	117	25.9		0.25	0.17,0.37	
bleeding (VARC-2)	Mack (2019)	1년	life-threatening /disabling	496	14	2.8	454	58	12.8		0.20	0.11,0.36	
bleeding (VARC-2)	Mack (2019)	1년	Major	496	26	5.3	454	64	14.2		0.34	0.22,0.54	
bleeding (VARC-2)	Mack (2019)	1년	Minor	496	38	7.7	454	43	9.6		0.79	0.51,1.22	
bleeding (BARC)	Mack (2019)	30일	Type 1	496	4	0.8	454	12	2.6		0.30	0.10,0.93	
bleeding (BARC)	Mack (2019)	30일	Type 2	496	20	4.0	454	13	2.9		1.42	0.71,2.86	
bleeding (BARC)	Mack (2019)	30일	Type 3A	496	10	2.0	454	45	9.9		0.19	0.10,0.38	
bleeding (BARC)	Mack (2019)	30일	Type 3B	496	7	1.4	454	63	13.9		0.09	0.04,0.20	
bleeding (BARC)	Mack (2019)	30일	Type 3C	496	0	0	454	1	0.2		NA	NA	
bleeding (BARC)	Mack (2019)	30일	Type 4	496	2	0.4	454	19	4.2		0.09	0.02,0.40	
bleeding (BARC)	Mack (2019)	30일	Type 5	496	2	0.4	454	0	0		NA	NA	
bleeding (BARC)	Mack (2019)	1년	Type 1	496	8	1.6	454	12	2.6		0.60	0.24,1.46	
bleeding (BARC)	Mack (2019)	1년	Type 2	496	32	6.5	454	23	5.2		1.27	0.74,2.17	
bleeding (BARC)	Mack (2019)	1년	Type 3A	496	20	4.0	454	49	10.9		0.35	0.21,0.59	
bleeding (BARC)	Mack (2019)	1년	Type 3B	496	13	2.6	454	66	14.6		0.16	0.09,0.30	
bleeding (BARC)	Mack (2019)	1년	Type 3C	496	4	0.8	454	2	0.5		1.77	0.32,9.67	
bleeding (BARC)	Mack (2019)	1년	Type 4	496	3	0.6	454	19	4.2		0.14	0.04,0.48	
bleeding (BARC)	Mack (2019)	1년	Type 5	496	3	0.6	454	1	0.2		2.70	0.28,25.94	
Echocardiography Results													
Patient-Prosthesis mismatch	Mack (2019)	baseline	Moderate	NA	NA	NA	NA	NA	NA				
Patient-Prosthesis mismatch	Mack (2019)	baseline	Severe	NA	NA	NA	NA	NA	NA				
Patient-Prosthesis mismatch	Mack (2019)	30일	Moderate	470	140	29.8	395	92	23.3		6.5	0.6,12.4	
Patient-Prosthesis mismatch	Mack (2019)	30일	Severe	470	20	4.3	395	25	6.3		-2.1	-5.1,0.9	
Patient-Prosthesis mismatch	Mack (2019)	1년	Moderate	NA	NA	NA	NA	NA	NA				
Patient-Prosthesis mismatch	Mack (2019)	1년	Severe	NA	NA	NA	NA	NA	NA				
Atrial fibrillation	Mack (2019)	첫 입원	new onset AF	417	17	4.1	369	131	35.5				

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P-value	RR (HR)	95% CI	SMD
				N	event	%	N	event	%				
Atrial fibrillation	Mack (2019)		present on 30 Day ECG	17	1	5.9	131	3	2.3				
Atrial fibrillation	Mack (2019)		Not present on 30 Day ECG	17	16	94.1	131	120	91.6				
Atrial fibrillation	Mack (2019)		30 Day ECG missing	17	0	0	131	8	6.1				
Atrial fibrillation	Mack (2019)	30일	new onset AF	417	21	5.0	369	145	39.3				
Atrial fibrillation	Mack (2019)	30일	present on 30 Day ECG	NA	NA	NA	NA	NA	NA				
Atrial fibrillation	Mack (2019)	30일	Not present on 30 Day ECG	NA	NA	NA	NA	NA	NA				
Atrial fibrillation	Mack (2019)	30일	30 Day ECG missing	NA	NA	NA	NA	NA	NA				
Atrial fibrillation	Mack (2019)	1년	new onset AF	417	29	7.0	369	150	40.7				
Atrial fibrillation	Mack (2019)	1년	present on 30 Day ECG	NA	NA	NA	NA	NA	NA				
Atrial fibrillation	Mack (2019)	1년	Not present on 30 Day ECG	NA	NA	NA	NA	NA	NA				
Atrial fibrillation	Mack (2019)	1년	30 Day ECG missing	NA	NA	NA	NA	NA	NA				
AF duration	Mack (2019)	첫 입원	≤ 24hrs	17	11	64.7	131	41	31.3				
AF duration	Mack (2019)	첫 입원	〉24hrs	17	5	29.4	131	51	38.9				
AF duration	Mack (2019)	첫 입원	Unknown	17	1	5.9	131	39	29.8				
AF duration	Mack (2019)	30일	≤ 24hrs	21	11	52.4	145	46	31.7				
AF duration	Mack (2019)	30일	〉24hrs	21	6	28.6	145	54	37.2				
AF duration	Mack (2019)	30일	Unknown	21	4	19.0	145	45	31.0				
AF duration	Mack (2019)	1년	≤ 24hrs	29	12	41.4	150	46	30.7				
AF duration	Mack (2019)	1년	〉24hrs	29	8	27.6	150	56	37.3				
AF duration	Mack (2019)	1년	Unknown	29	9	31.0	150	48	32.0				
AF treatment	Mack (2019)	첫 입원	Electrical cardioversion	17	7	41.2	131	11	8.4				
AF treatment	Mack (2019)	첫 입원	Electrical cautery/ablation	17	1	5.9	131	0	0				
AF treatment	Mack (2019)	첫 입원	Medical cardioversion	17	1	5.9	131	8	6.1				
AF treatment	Mack (2019)	첫 입원	New medication	17	4	23.5	131	100	76.3				
AF treatment	Mack (2019)	첫 입원	Other	17	1	5.9	131	0	0				
AF treatment	Mack (2019)	첫 입원	No action	17	3	17.6	131	12	9.2				
AF treatment	Mack (2019)	30일	Electrical cardioversion	21	7	33.3	145	13	9.0				
AF treatment	Mack (2019)	30일	Electrical cautery/ablation	21	1	4.8	145	0	0.0				
AF treatment	Mack (2019)	30일	Medical cardioversion	21	1	4.8	145	8	5.5				
AF treatment	Mack (2019)	30일	New medication	21	7	33.3	145	110	75.9				

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P-value	RR (HR)	95% CI	SMS
				N	event	%	N	event	%				
AF treatment	Mack (2019)		Other	21	1	4.8	145	1	0.7				
AF treatment	Mack (2019)		No action	21	4	19.0	145	13	9.0				
AF treatment	Mack (2019)	1년	Electrical cardioversion	29	7	24.1	150	13	8.7				
AF treatment	Mack (2019)		Electrical cautery/ablation	29	1	3.4	150	0	0				
AF treatment	Mack (2019)		Medical cardioversion	29	1	3.4	150	9	6.0				
AF treatment	Mack (2019)		New medication	29	12	41.4	150	113	75.3				
AF treatment	Mack (2019)		Other	29	1	3.4	150	1	0.7				
AF treatment	Mack (2019)		No action	29	7	24.1	150	14	9.3				
Echo Paravalvular Regurgitation													
Paravalvular aortic regurgitation	Mack (2019)	30일	None/Trace	487	343	70.4	421	409	97.1				
Paravalvular aortic regurgitation	Mack (2019)		Mild	487	140	28.7	421	12	2.9				
Paravalvular aortic regurgitation	Mack (2019)		≧moderate	487	4	0.8	421	0	0				
Paravalvular aortic regurgitation	Mack (2019)	1년	None/Trace	466	326	70.0	381	371	97.4				
Paravalvular aortic regurgitation	Mack (2019)		Mild	466	137	29.4	381	8	2.1				
Paravalvular aortic regurgitation	Mack (2019)		≧moderate	466	3	0.6	381	2	0.5				
Echo Total Aortic Regurgitation													
Total AR	Mack (2019)	30일	None/Trace	490	345	70.4	428	409	95.6				
Total AR	Mack (2019)		Mild	490	141	28.8	428	18	4.2				
Total AR	Mack (2019)		≧moderate	490	4	0.8	428	1	0.2				
Total AR	Mack (2019)	1년	None/Trace	470	322	68.5	389	365	93.8				
Total AR	Mack (2019)		Mild	470	143	30.4	389	22	5.7				
Total AR	Mack (2019)		≧moderate	470	5	1.1	389	2	0.5				
NYHA Class (Mack 2019, Figure S7)													
NYHA Ⅰ	Mack (2019)	baseline	1	496	2	0.4	454	7	1.5				
NYHA Ⅱ	Mack (2019)		2	496	339	68.3	454	339	74.7				
NYHA Ⅲ	Mack (2019)		3	496	152	30.6	454	103	22.7				
NYHA Ⅳ	Mack (2019)		4	496	3	0.6	454	5	1.1				
NYHA Ⅰ	Mack (2019)	30일	1	493	396	80.3	433	289	66.7				
NYHA Ⅱ	Mack (2019)		2	493	91	18.5	433	125	28.9				
NYHA Ⅲ	Mack (2019)		3	493	6	1.2	433	19	4.4				
NYHA Ⅳ	Mack (2019)		4	493	0	0	433	0	0				
NYHA Ⅰ	Mack (2019)	1년	1	480	395	82.3	407	339	83.3				
NYHA Ⅱ	Mack (2019)		2	480	80	16.7	407	62	15.2				

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P값	RR (HR)	95% CI	SAS
				N	event	%	N	event	%				
NYHA Ⅲ	Mack (2019)		3	480	5	1.0	407	6	1.5				
NYHA Ⅳ	Mack (2019)		4	480	0	0	407	0	0				
KCCQ-OS (Baron 2019, supplementary table 5)											OR		
KCCQ-OS	Baron (2019)	1개월	Large Improvement	494	216	43.7	449	86	19.1				
KCCQ-OS	Baron (2019)		Moderate Improvement	494	90	18.3	449	64	14.3				
KCCQ-OS	Baron (2019)		Small Improvement	494	57	11.6	449	46	10.3				
KCCQ-OS	Baron (2019)		No Change	494	95	19.3	449	102	22.8				
KCCQ-OS	Baron (2019)		Worse	494	33	6.7	449	145	32.2				
KCCQ-OS	Baron (2019)		Dead	494	2	0.4	449	6	1.4				
KCCQ-OS	Baron (2019)	6개월	Large Improvement	494	218	44.2	449	167	37.1				
KCCQ-OS	Baron (2019)		Moderate Improvement	494	102	20.6	449	97	21.6				
KCCQ-OS	Baron (2019)		Small Improvement	494	73	14.8	449	75	16.7				
KCCQ-OS	Baron (2019)		No Change	494	78	15.8	449	71	15.8				
KCCQ-OS	Baron (2019)		Worse	494	20	4.1	449	28	6.3				
KCCQ-OS	Baron (2019)		Dead	494	2	0.4	449	11	2.4				
KCCQ-OS	Baron (2019)	12개월	Large Improvement	494	218	44.2	449	172	38.4				
KCCQ-OS	Baron (2019)		Moderate Improvement	494	92	18.6	449	92	20.4				
KCCQ-OS	Baron (2019)		Small Improvement	494	74	14.9	449	55	12.2				
KCCQ-OS	Baron (2019)		No Change	494	82	16.5	449	85	19.0				
KCCQ-OS	Baron (2019)		Worse	494	24	4.8	449	33	7.3				
KCCQ-OS	Baron (2019)		Dead	494	5	1.0	449	12	2.7				

녹색 계산하여 입력한 값

저자의 결론	수술 저위험군의 중증 대동맥판 협착증 환자에서 풍선확장형 SAPIEN3을 이용한 TAVR 시행은 SAVR 과 비교하여 1년 평가 시, 사망, 뇌졸중, 재입원의 복합적인 비율에서 유의하게 낮은 결과를 나타냄(Mack, 2019). 또한 중재 후 초기 건강상태 평가에서 SAVR 에 비하여 향상된 결과를 보였으며, 이후 1년간에도 SAVR과 비교시 지속적인 이점이 관찰됨(Baron, 2019) 중재 후 두 군 간의 심장초음파 결과를 비교하였을 때 TAVR 중재군에서 mild AR이 더 빈번하게 나타났지만 이는 1년 시점의 결과와 관련이 없는 것을 확인함. 또한 SAVR 중재군에서 우심실 기능저하 및 삼첨판 역류 등이 1년간 지속된 결과 등을 확인함(Pibarot, 2020)
기타(funding 등)	Edwards Lifesciences 가 모든 임상시험 관련 활동에 자금을 지원하고, 지역 선택, 데이터 수집 및 모니터링, 통계 분석에 참여함
기타 참고사항	

1.3. Evolute 연구 자료추출

<table>
<tr><td rowspan="6">기본
정보</td><td>Trial</td><td>Evolute</td></tr>
<tr><td>1저자(연도)</td><td>Popma (2019)</td></tr>
<tr><td>NCT no.</td><td>NCT02701283</td></tr>
<tr><td>연구디자인</td><td>RCT</td></tr>
<tr><td>연구국가</td><td>다국가(호주, 캐나다, 프랑스, 일본, 네덜란드, 뉴질랜드, 미국)</td></tr>
<tr><td>모집기관</td><td>86개 센터</td></tr>
<tr><td rowspan="2">연구
방법</td><td>연구목적</td><td>저위험군에서 TAVR vs. SAVR의 결과확인</td></tr>
<tr><td>연구대상자</td><td>
<table>
<tr><td>모집기간</td><td>2016.03-2018.11.</td></tr>
<tr><td>질환</td><td>☑ Severe AS (☑ with symptom, ☑ without symptom)</td></tr>
<tr><td>risk</td><td>☐ Intermediate risk group
☑ Low risk group (기준: 30일 예측 사망위험 3% 미만)
☐ 기타 (_____)</td></tr>
<tr><td>선택기준</td><td>• 30일 예측 수술사망위험 3% 미만(각 사이트의 심장팀에서 평가
• Severe aortic stenosis
증상이 있는 경우: 휴식상태 심초음파상 대동맥판면적 ≤1.0 cm2, or mean gradient ≥40 mmHg, or maximal aortic valve velocity ≥4.0 m/sec
증상이 없는 경우:
- 휴식상태 심초음파상 대동맥판면적 ≤1.0 cm2, and mean gradient ≥40 mmHg, or maximal aortic valve velocity ≥4.0 m/sec
- 휴식상태 심초음파상 대동맥판면적 ≤1.0 cm2, AND a mean gradient ≥40 mmHg or maximal aortic valve velocity ≥4.0 m/sec AND an exercise tolerance test that demonstrates a limited exercise capacity, abnormal blood pressure response, or arrhythmia
- 휴식상태 심초음파상 대동맥판면적 ≤1.0 cm2, AND mean gradient ≥40 mmHg, or maximal aortic valve velocity ≥4.0 m/sec, AND a left ventricular ejection fraction 〈50%</td></tr>
<tr><td>배제기준</td><td>다음중 하나라도 해당되면 임상시험 참여 안됨
1. 생체판막 금기 상태
2. 아스피린, 헤파린, bivalirudin, ticlopidine, clopidogrel, Nitinol, 조영제 등 사전 투약약물 금기환자
3. 백혈구 감소증, 혈소판 감소증, 출혈장애 등 혈액장애 환자
4. 활동성 심내막염을 포함한 패혈증
5. 무작위배정전 30일 이내 bare metal stent를 받거나 180일 이내 drug eluting stent 시술을 받은 환자
6. 다혈관질환: Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score 〉22
7. 심평팀 평가 10주 이내 경동맥, 척추동맥 질환 또는 치료경험이 있는 환자
8. 심인성 쇼크 환자
9. 최근 2개월내 뇌졸중 또는 TIA
10. 위장관출혈
11. 수혈거부 환자
12. 중증치매
13. 기대수명 24개월 미만 환자
14. 프로토콜 준수가 어려운 의학적, 사회적, 심리상태
15. 다른 임상시험 참여자
16. 중재 30일 이전 급성 심근경색</td></tr>
</table>
</td></tr>
</table>

		17. 응급 수술이 필요한 환자 18. 임신 또는 수유중인 환자 19. 미성년자 또는 법적으로 취약한 대상 해부학적 배제기준 20. 이전 인공심장판막 시술을 받은 환자 21. 수술 또는 성형술이 필요한 중증 승모판 역류 22. 수술 또는 성형술이 필요한 중증 삼첨판 역류 23. 수술 또는 성형술이 필요한 중등도~중증 승모판 협착 24. 폐쇄성 심근비대증 25. 이첨판 26. 최심실 석회화 27. self expanding bioprosthesis 배치하기에 부적당한 Valsalva 직경 28. Aortic annulus diameter 〈18mm 또는 〉30mm 29. 대퇴하 또는 쇄골하 접근이 어려운 심각한 대동맥병증 30. Access vessel mean diameter 〈5.0 mm: Evolut 23R, 26R, or 29R access vessel mean diameter 〈5.5 mm: Evolut 34R mm or Evolut PRO left internal mammary artery graft access vessel mean diameter 〈5.5 mm: Evolut 23R, 26R, 29R left internal mammary artery graft access vessel mean diameter 〈6mm: CoreValve 31 mm, Evolut R 34R or Evolut PRO
	심장팀 논의	☑ 유(□전원동의 □일부동의 ☑ 불확실) □무 □ 기타 (_____)
	심장팀 구성	각 사이트의 다학제 심장팀이라고만 표기됨
	합의 기준	30일 예측 수술사망위험 3% 미만 등 선택/배제에 대한 평가를 각 사이트의 심장팀에 평가한다고만 기술, 합의기준 없음

연구 중재	중재명	TAVR
	Device	☑ Corevale (상세 제품 : CoreValve, Evolut R, Evolut PRO) □ Sapien (상세 제품 :) □ lotus (상세 제품 :) □ 기타 _____ (상세 제품 :)
	세대구분	□ SAPIEN XT, CoreValve® ■ SAPIEN 3, Corevalve Evolut R
	접근 경로	☑ TF ☑ TA □ 기타( ) □ NR
	상세 중재설명	• random 추출 후 접근방법 및 valve사이즈 결정
비교중재	중재명	surgery
	Device	☑ tissue valve (상세 제품 : bioprosthetic heart valve) □ 기타 (상세 제품 :)
	상세 중재설명	수술의 밸브의 종류 및 사이즈는 흉부외과 전문의가 결정

결과변수 정의	**지표명**	**정의**	**기준**
	cardiovascular death	proximate cardiac cause, non-coronary vascular conditions, All procedure-related deaths, All valve-related deaths, Sudden or unwitnessed death, Death of unknown cause	
	Non-cardiovascular death	primary cause of death is clearly related to another condition (eg, trauma, cancer, suicide)	
	STROKE AND TRANSIENT ISCHEMIC ATTACK (TIA)	Serial neurological examinations using the modified Rankin Scale (mRS) were performed by certified observers before and after the procedure Stroke: duration of a focal or global neurological deficit ≥24 h; OR	

지표명	정의	기준
	〈24 h if available neuroimaging documents a new hemorrhage or infarct; OR the neurological deficit results in death Disabling stroke: an mRS score of ≥ 2 at 90 days and an increase in at least 1 mRS category from an individual's pre-stroke baseline Non-disabling stroke: an mRS score of 〈2 at 90 days or one that does not result in an increase in at least 1 mRS category from an individual's pre-stroke baseline TIA: Duration of a focal or global neurological deficit 〈24 h, any variable neuroimaging does not demonstrate a new hemorrhage or infarct 뇌종양, 외상, 저혈당 등과 같은 비뇌졸중 원인이 없는 경우 신경과 전문의에 의한 진단, 뇌이미지 촬영	
MYOCARDIAL INFARCTION	**1. 72간 이내에 발현된 아래와 같은 증상 :Peri-Procedural MI** · New ischemic symptoms (e.g. chest pain or shortness of breath), OR · New ischemic signs (e.g. ventricular arrhythmias, new or worsening heart failure, new ST-segment deviations - either elevation 〉1 mm or depression 〉1 mm in two or more contiguous leads, hemodynamic instability, or imaging evidence of new loss of viable myocardium or new wall motion abnormality), AND · Confirmatory biomarker evidence, consisting of two or more samples for CK-MB that are 6-8 hours apart with a 20% increase in the second sample and a peak value exceeding 10x the 99th percentile upper reference limit (URL), or a peak value exceeding 5x the 99th percentile URL and with new pathological Q waves in at least 2 contiguous leads. **2.72시간 이후에 발현된 아래와 같은 증상 : Spontaneous MI** ·Detection of rise and/or fall of cardiacbiomarkers (preferably troponin) with at least one value above the 99th percentile URL, together with evidence of myocardial ischemia with at least one of the following: · ECG changes indicative of new ischemia (new ST-T changes or new left bundle branch block [LBBB]); · development of pathological Q waves in at least 2 contiguous leads; · imaging evidence of new loss of viable myocardium or new regional wall motion abnormality · Sudden, unexpected cardiac death, involving cardiac arrest, often with symptoms suggestive of myocardial ischemia, and accompanied by presumably new ST elevation, or new LBBB, and/or evidence of fresh thrombus by coronary angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood. · Pathological findings of an acute myocardial infarction. IfthepatienthasahistoryofMI,indicate"Yes"ontheBaselineCRF.	VARC
Life-threatening or Disabling Bleeding	Life-threatening or Disabling Bleeding - 치명적 출혈 - 중요 장기(뇌내, 안구내, 심장맥 등)의 출혈 - 저혈량/저혈당/지혈(vasopressors)/수술을 야기하는 출혈 - hemoglobin of ≥5 g/dl 감소 또는 RBC 수혈 ≥4 units	VARC
Major Bleeding	Overt bleeding either associated with a drop in the hemoglobin level of at least 3.0 g/dL or requiring transfusion of 2-3 units of whole blood/RBC AND **Does not meet criteria of life-threatening or disabling bleeding** - hemoglobin of ≥3 g/dl 감소 또는 RBCs 수혈 2-3 units - Life-threatening or Disabling Bleeding 출혈이 아님	
Minor Bleeding	Any bleeding worthy of clinical mention (e.g. access site hematoma) that does not qualify as life-threatening, disabling or major - life-threatening, disabling or major가 아닌 출혈	
Renal Failure (Acute Kidney Injury)	- 시술전과 비교하여 혈청 크레아티닌 변화 및 소변량 확인 Stage 1: Increase in serum creatinine to 150-199% (1.5-1.99 x increase compared with baseline) or increase	VARC

지표명	정의	기준
	of ≥ 0.3 mg/dl (≥26.4 μmol/L) Urine output 〈0.5 mL/kg/h for 〉6 but 〈12 h Stage 2: Increase in serum creatinine to 200% to 299% (2.0 to 2.99 X increase compared with baseline) Urine output 〈0.5 mL/kg/h for 〉12 but 〈24 h Stage 3: Increase in serum creatinine to≥300% 〈〉 3 x increase compared with baseline) or serum creatinine of≥ 4.0 mg/d (≥354 μmol/L) with an acute increase of at least 0.5 mg/dl (44 μmol/L) Urine output 〈0.3 ml/kg/h for ≥24 h Anuria for ≥12 h	
Major Vascular Complications	- 대동맥박리, 대동맥 파열, left ventricle perforation, or new apical aneurysm/ pseudoaneurysm - Access site or access-related vascular injury leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment - Distal embolization (noncerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage OR - The use of unplanned endovascular or surgical intervention - Any new ipsilateral lower extremity ischemia - Surgery for access site-related nerve injury - Permanent access site-related nerve injury	VARC
Minor Vascular Complications	- Access site or access-related vascular injury not leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment OR - Distal embolization treated with embolectomy and/or thrombectomy and not resulting in amputation or irreversible end-organ damage OR - Any unplanned endovascular stenting or unplanned surgical intervention not meeting the criteria for a major vascular complication OR - Vascular repair or the need for vascular repair	
Percutaneous closure device failure	Failure of a closure device to achieve hemostasis at the arteriotomy site leading to alternative treatment	
VALVE DYSFUNCTION REQUIRING REPEAT PROCEDURE	Any valve dysfunction that requires repeat procedure (eg, balloon valvuloplasty, TAVR, snare repositioning, placement of vascular plug paravalvular leak, or surgical AVR)	
HEART FAILURE HOSPITALIZATION	아래 사유로 인한 재입원 syncope, dizziness, shortness of breath, orthopnea, hepatomegaly, pulmonary rales, hypotension, elevated BNP, jugular vein distension, low serum sodium concentration, exercise intolerance, chest pain, renal or hepatic dysfunction, peripheral edema, paroxysmal nocturnal dyspnea, abdominaljugular reflex, narrow pulse pressure, radiographic evidence of pulmonary edema	

연구 결과

대상자수

	총 수	TAVR	SVAR
스크리닝수(enroll)	2,032		
randomised	2,032	1011	1021
수술/시술 수행자	1,938	994	944
분석대상자	1,910	974	936
탈락율 (2년)	1,505(21.2%)	789 (19%)	716 (23.5%)

대상자 특성

■ **연구대상 특성**

문헌	중재	N	평균 연령	남자 (%)	평균 STS	평균 LES	NYHA 3/4	이전시술/수술 CABG	PCI	Pace maker	AVR*
Popma (2020) -AT	TAVR	725	74.1	64	1.9	NR	25.1	2.5	14.2	3.2	0
	SAVR	678	73.6	66.2	1.9	NR	28.4	2.1	12.8	3.8	0
Popma (2020) -ITT	TAVR	734	74.0	63.8	1.9	NR	24.6	2.5	13.9	3.4	0
	SAVR	734	73.8	66.4	1.9	NR	27.9	2.3	12.7	3.8	0

문헌	중재	기저질환									
		CAD	PVD	뇌혈관 질환	AF	MI	당뇨병	고혈압	신장질환	간질환	COPD
Popma (2020) -AT	TAVR	10.2	7.5	10.2	15.4	6.6	31.4	84.8	0.4	NR	15.0
	SAVR	11.8	8.3	11.8	14.5	4.9	30.5	82.6	0.1	NR	18.0
Popma (2020) -ITT	TAVR	10.1	7.6	10.1	15.5	6.7	31.1	84.9	0.4	NR	15.1
	SAVR	11.4	8.5	11.4	14.9	5.3	30.5	82.9	0.1	NR	17.2

STS, Society of Thoracic Surgeons score; LES, Logistic EuroScore I; NYHA, New York Heart; CABG, coronary-artery bypass grafting; PCI, percutaneous coronary intervention; AVR, aortic-valve; CAD, coronary artery disease; PVD, peripheral vascular disease; AF, atrial fibrillation; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease.
†neurological event, §AF와 atrial flutter를 합친 대상자
** 이전 심장판막 수술 환자는 제외기준임

추적관찰 기간

평균추적관찰 기간 : 년

결과

1) 이분형 변수

As Treated

결과변수	1저자 (연도)	시점	TAVR			SAVR			difference, 95% CI
			N	event*	%	N	event*	%	
Death from any cause or disabling stroke	Popma (2019)	1	725	6	0.8	678	18	2.6	−1.8 (−3.2 to −0.5)
Death from any cause	Popma (2019)	1	725	4	0.5	678	9	1.3	−0.8 (−1.9 to 0.2)
Death from cardiovascular cause	Popma (2019)	1	725	4	0.5	678	9	1.3	−0.8 (−1.9 to 0.2)
All stroke	Popma (2019)	1	725	25	3.4	678	23	3.4	0.0 (−1.9 to 1.9)
Disabling	Popma (2019)	1	725	4	0.5	678	12	1.7	−1.2 (−2.4 to −0.2)
Nondisabling	Popma (2019)	1	725	22	3.0	678	12	1.7	1.2 (−0.3 to 2.9)
Transient ischemic attack	Popma (2019)	1	725	4	0.6	678	5	0.8	−0.2 (−1.2 to 0.7)
30-Day composite safety end point†	Popma (2019)	1	725	38	5.3	678	73	10.7	−5.4 (−8.3 to −2.6)
Life-threatening or disabling bleeding	Popma (2019)	1	725	17	2.4	678	51	7.5	−5.1 (−7.5 to −2.9)
Major vascular complication	Popma (2019)	1	725	28	3.8	678	22	3.2	0.6 (−1.4 to 2.5)
Acute kidney injury stage 2 or 3	Popma (2019)	1	725	7	0.9	678	19	2.8	−1.8 (−3.4 to −0.5)
Atrial fibrillation	Popma (2019)	1	725	56	7.7	678	240	35.4	−27.7 (−31.8 to −23.6)
Permanent pacemaker implantation	Popma (2019)	1	725	126	17.4	678	41	6.1	11.3 (8.0 to 14.7)
Myocardial infarction	Popma (2019)	1	725	7	0.9	678	9	1.3	−0.4 (−1.5 to 0.7)
Coronary-artery obstruction	Popma (2019)	1	725	7	0.9	678	3	0.4	0.5 (−0.3 to 1.4)
Endocarditis	Popma (2019)	1	725	1	0.1	678	1	0.2	−0.1 (−0.7 to 0.3)

결과변수	1저자 (연도)	시점	TAVR			SAVR			difference, 95% CI
			N	event*	%	N	event*	%	
Valve thrombosis	Popma (2019)	1	725	1	0.1	678	1	0.1	0.0 (−0.4 to 0.4)
Aortic reintervention	Popma (2019)	1	725	3	0.4	678	3	0.4	0.0 (−0.8 to 0.7)
Hospitalization for heart failure	Popma (2019)	1	725	9	1.2	678	17	2.5	−1.3 (−2.8 to 0.1)
Death from any cause or disabling stroke	Popma (2019)	12	725	21	2.9	678	31	4.6	−1.8 (−4.0 to 0.4)
Death from any cause	Popma (2019)	12	725	17	2.4	678	20	3.0	−0.6 (−2.6 to 1.3)
Death from cardiovascular cause	Popma (2019)	12	725	12	1.7	678	18	2.6	−0.9 (−2.7 to 0.7)
All stroke	Popma (2019)	12	725	30	4.1	678	29	4.3	−0.2 (−2.4 to 1.9)
Disabling	Popma (2019)	12	725	6	0.8	678	16	2.4	−1.6 (−3.1 to −0.3)
Nondisabling	Popma (2019)	12	725	25	3.4	678	15	2.2	1.1 (−0.6 to 2.9)
Transient ischemic attack	Popma (2019)	12	725	12	1.7	678	12	1.8	−0.2 (−1.6 to 1.3)
Life-threatening or disabling bleeding	Popma (2019)	12	725	23	3.2	678	60	8.9	−5.7 (−8.4 to −3.1)
Major vascular complication	Popma (2019)	12	725	28	3.8	678	24	3.5	0.3 (−1.7 to 2.3)
Acute kidney injury stage 2 or 3	Popma (2019)	12	725	7	0.9	678	19	2.8	−1.8 (−3.4 to −0.5)
Atrial fibrillation	Popma (2019)	12	725	71	9.8	678	260	38.3	28.5 (−32.8 to −24.1)
Permanent pacemaker implantation	Popma (2019)	12	725	141	19.4	678	45	6.7	12.6 (9.2 to 16.2)
Myocardial infarction	Popma (2019)	12	725	12	1.7	678	11	1.6	0.1 (−1.3 to 1.5)
Coronary-artery obstruction	Popma (2019)	12	725	7	0.9	678	3	0.4	0.5 (−0.3 to 1.4)
Endocarditis	Popma (2019)	12	725	1	0.2	678	3	0.4	−0.2 (−0.9 to 0.5)
Valve thrombosis	Popma (2019)	12	725	1	0.2	678	2	0.3	−0.1 (−0.9 to 0.5)
Aortic reintervention	Popma (2019)	12	725	5	0.7	678	4	0.6	0.0 (−1.0 to 0.9)
Hospitalization for heart failure	Popma (2019)	12	725	23	3.2	678	44	6.5	−3.4 (−5.9 to −1.0)

* event %에서 추출됨
* Values represent the estimated incidence (median of the posterior probability distribution as calculated by Bayesian analysis). Caution should be exercised regarding drawing inferences about absolute treatment effects with the 95% Bayesian credible interval (BCI), owing to multiple secondary end-point comparisons
† The 30-day composite safety end point was a composite of death, disabling stroke, life-threatening bleeding, major vascular complication, or stage 2 or 3 acute kidney injury.

(2) ITT 전체대상자

결과변수	1저자 (연도)	시점	TAVR			SAVR			difference, 95% CI
			N	event*	%	N	event*	%	
Death from any cause - %	Popma (2019)	1	734	4	0.5	734	6	0.8	-0.3 (-1.2, 0.6)
Cardiovascular - %	Popma (2019)	1	734	4	0.5	734	4	0.6	-0.1 (-1.0, 0.7)
All stroke - %	Popma (2019)	1	734	15	2.1	734	14	1.9	0.2 (-1.2, 1.7)
Disabling stroke - %	Popma (2019)	1	734	3	0.4	734	7	0.9	-0.5 (-1.5, 0.3)
Non-disabling stroke - %	Popma (2019)	1	734	14	1.9	734	8	1.1	0.8 (-0.4, 2.1)
Transient ischemic attack - %	Popma (2019)	1	734	4	0.5	734	1	0.2	0.3 (-0.4, 1.0)
Myocardial infarction - %	Popma (2019)	1	734	7	0.9	734	4	0.6	0.3 (-0.7, 1.2)
Endocarditis - %	Popma (2019)	1	734	1	0.1	734	1	0.2	-0.1 (-0.7, 0.3)
Valve thrombosis - %	Popma (2019)	1	734	1	0.1	734	1	0.1	0.0 (-0.4, 0.4)
Aortic reintervention - %	Popma (2019)	1	734	1	0.2	734	3	0.4	-0.1 (-0.8, 0.5)
Heart failure rehospitalization - %	Popma (2019)	1	734	7	0.9	734	8	1.1	-0.2 (-1.2, 0.9)
Death from any cause - %	Popma (2019)	12	734	18	2.4	734	21	2.9	-0.5 (-2.4, 1.3)
Cardiovascular - %	Popma (2019)	12	734	12	1.7	734	19	2.6	-0.9 (-2.6, 0.7)
All stroke - %	Popma (2019)	12	734	29	4	734	31	4.2	-0.2 (-2.4, 2.0)
Disabling stroke - %	Popma (2019)	12	734	6	0.8	734	15	2.1	-1.3 (-2.7, -0.0)
Non-disabling stroke - %	Popma (2019)	12	734	24	3.3	734	18	2.4	0.9 (-1.0, 2.7)
Transient ischemic attack - %	Popma (2019)	12	734	12	1.6	734	14	1.9	-0.3 (-1.8, 1.2)
Myocardial infarction - %	Popma (2019)	12	734	12	1.7	734	12	1.6	0.1 (-1.4, 1.5)
Endocarditis - %	Popma (2019)	12	734	1	0.2	734	3	0.4	-0.1 (-0.8, 0.5)
Valve thrombosis - %	Popma (2019)	12	734	2	0.3	734	2	0.3	-0.0 (-0.8, 0.7)
Aortic reintervention - %	Popma (2019)	12	734	5	0.7	734	4	0.6	0.1 (-0.9, 1.0)
Heart failure rehospitalization - %	Popma (2019)	12	734	26	3.6	734	49	6.7	-3.1 (-5.6, -0.6)

* event %에서 추출됨

* Values represent the estimated incidence (median of the posterior probability distribution as calculated by Bayesian analysis). Caution should be exercised regarding drawing inferences about absolute treatment effects with the 95% Bayesian credible interval (BCI), owing to multiple secondary end-point comparisons

†The 30-day composite safety end point was a composite of death, disabling stroke, life-threatening bleeding, major vascular complication, or stage 2 or 3 acute kidney injury.

2) 연속형 변수

결과변수	1저자 (연도)	시점	TAVR			SAVR			두 군간 변화량차이		P-value	95% CI	S/NS
			N	Mean	SD	N	Mean	SD	Mean	SD			
KCCQ change	Popma (2019)	12	428	22.2	20.3	347	20.9	21.0	1.3			−1.2, 3.8	
KCCQ change	Popma (2019)	1	713	20.2	21.1	636	9.1	22.3	10.9			8.6, 13.2	
KCCQ Overall Summary Score	Popma (2019)	1	714	88.7	14.2	637	78.6	18.9				8.6, 13.2	
KCCQ Overall Summary Score	Popma (2019)	6	633	90.3	13.4	547	90.2	13.8				−1.0, 3.8	
KCCQ Overall Summary Score	Popma (2019)	12	429	90.3	12.7	349	90.8	12.4				−1.6, 4.3	

3) 기타 – 범주형 결과지표 등

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P value	RR (HR)	95% CI	S/NS
				N	event	%	N	event	%				
Total aortic regurgitation	Popma (2019)	1	Moderate 이상	709	25	3.5	626	3	0.5				
Paravalvular leak	Popma (2019)	1	Moderate 이상	703	24	3.4	608	2	0.4				
Transvalvular regurgitation	Popma (2019)	1	Moderate 이상	695	0	0	609	1	0.2				
Patient-prosthesis mismatch	Popma (2019)	1	Moderate 이상	609	67	11.0	541	108	19.9				
Total aortic regurgitation	Popma (2019)	12	Moderate 이상	415	18	4.3	340	5	1.5				
Paravalvular leak	Popma (2019)	12	Moderate 이상	407	15	3.6	326	2	0.6				
Transvalvular regurgitation	Popma (2019)	12	Moderate 이상	405	0	0	327	0	0				
Patient-prosthesis mismatch	Popma (2019)	12	Moderate 이상	341	23	6.8	293	70	23.9				
Total aortic regurgitation	Popma (2019)	24	Moderate 이상	69	4	5.8	63	0	0				
Paravalvular leak	Popma (2019)	24	Moderate 이상	70	4	5.7	61	0	0				
Transvalvular regurgitation	Popma (2019)	24	Moderate 이상	69	0	0	61	0	0				
Patient-prosthesis mismatch	Popma (2019)	24	Moderate 이상	59	3	5.1	53	8	15.1				
NYHA Class III or IV	Popma (2019)	1	Moderate 이상	706	12	1.7	325	30	4.8				
NYHA Class III or IV	Popma (2019)	12	Moderate 이상	428	8	1.8	342	4	1.2				

저자의 결론	수술 저위험 AS 환자에서 self expanding TAVR는 24개월 결과지표(composite end point of death or disabling stroke at 24 months)에서 SAVR에 비해 열등하지 않음
기타(funding 등)	Supported by Medtronic

1.4. STACCATO 연구 자료추출

<table>
<tr><td rowspan="6">기본
정보</td><td>Trial</td><td>STACCATO</td></tr>
<tr><td>1저자(연도)</td><td>Nielsen (2012)</td></tr>
<tr><td>NCT no.</td><td>NCT00986193 (※문헌에는 언급 없음)
https://clinicaltrials.gov/ct2/show/NCT00986193?cond=Aortic+Stenosis&cntry=DK&rank=3</td></tr>
<tr><td>연구디자인</td><td>RCT</td></tr>
<tr><td>연구국가</td><td>덴마크</td></tr>
<tr><td>모집기관</td><td>Departments of Cardiothoracic Surgery and Cardiology, Aarhus University Hospital (59명)
Departments of Thoracic Surgery and Cardiology, Odense University Hospital (11명)</td></tr>
<tr><td rowspan="2">연구
방법</td><td>연구목적</td><td>수술이 가능한 고령 환자에서의 transapical-TAVI와 SAVR 비교</td></tr>
<tr><td>연구대상자</td><td>
<table>
<tr><td>모집기간</td><td>2008.11-2011.05</td></tr>
<tr><td>질환</td><td>■ Severe AS (☐ with symptom, ☐ without symptom)</td></tr>
<tr><td>risk</td><td>☐ Intermediate risk group
■ Low risk group (기준: STS score 4% 이하)
☐ 기타 (_____)</td></tr>
<tr><td>선택기준</td><td>1. 초기에는 70세 이상을 대상자로 하였으나 75세 이상으로 변경
* 초기 11명 대상자 모집 후 3명에서 중대한 이상반응 발생하여 연구 보류하였고, 이후 75세 이상으로 변경하여 모집함
2. 대동맥판 면적 〈1㎠
3. a-TAVI, SAVR 가능한 상태
4. 성공적인 치료 후 기대 수명이 1년 초과
5. 연구 참여 승인한 환자</td></tr>
<tr><td>배제기준</td><td>1. PCI 혹은 CABG 받은 관상동맥질환(coronary artery disease)
2. 이전의 심근경색
3. 12개월 이내 PCI 시행
4. 이전 심장 수술
5. 수술 고위험군(high surgical risk)
6. 그 외 심장 수술의 필요성(이첨판, 삼첨판 판막 수술)
7. 응급수술(24시간 이내 수술의 적응증)
8. 불안정한 심장상태(수술시 심장 보조장치가 필요하거나, inotropes 또는 IV nitrates 요구되는 상태)
9. 항생제 치료가 필요한 지속적인 감염
10. 한달 이내의 뇌졸중
11. 혈액투석이 필요한 신부전
12. acetylsalicylic acid, clopidogrel, prasugrel 또는 x-ray 조영제 알러지</td></tr>
<tr><td>심장팀 논의</td><td>■ 유(☐전원동의 ☐일부동의 ■ 불확실) ☐무 ☐ 기타 (_____)</td></tr>
<tr><td>심장팀 구성</td><td>순환기내과 전문의, 심장외과 전문의, 마취통증의학과 전문의</td></tr>
<tr><td>합의 기준</td><td>Weekly Heart Team valve meeting 에 참석하여 과거 병력, 신체검사, 경흉부 심장초음파, 관상동맥조영술 및 폐기능 검사 결과를 기반으로 평가함</td></tr>
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연구 중재

중재명	a-TAVI
Device	☐ Corevale (상세 제품 :) ■ Sapien (상세 제품 : Edwards SAPIEN™ Transcatheter Heart Valve prosthesis, Edwards Lifesciences) ☐ lotus (상세 제품 :) ☐ 기타 (상세 제품 :)
세대구분	■ SAPIEN ☐ SAPIEN XT, CoreValve® ☐ SAPIEN 3, Corevalve Evolut R
접근 경로	☐ TF ■ TA ☐ 기타( ) ☐ NR
상세 중재설명	심장 카테터 수술실(cardiac catheterization laboratory)에서 2명의 심장외과(흉부외과) 전문의와 1명의 중재 순환기내과 전문의가 시행함. 23 또는 26 ㎜n Edwards SAPIEN™ 인공판막을 왼쪽의 최소한의 개흉술 및 심첨부위를 통해 앞으로 삽입됨 1. 좌심실 심첨부를 심초음파 화면으로 확인하면서 피부 절개 시행함 2. 경식도심초음파 및 형광투시법으로 정확한 위치를 확인한 후, 대동맥 판막 내 풍선 카테터를 확장하여 빠른 조율동안 인공판막을 삽입함 3. 심실 조율은 임시 심근 전극을 통해 수행함(분당 160-200) 4. 수술 후 국소 진통제 카테터는 흉강 내 위치하며, 개흉술을 종료하기 전에 흉관 배액관을 삽입함

비교중재

중재명	Surgery
Device	■ tissue valve (상세 제품 : PERIMOUNT™ aortic heart valve, Edwards Lifesciences) ☐ 기타 (상세 제품 :)
상세 중재설명	심폐우회술(cardio pulmonary bypass) 동안 흉골절개술 통해 시행됨 1. 대동맥 판막을 절제하고 정확한 생체인공판막 크기를 확인하기 위해 대동맥 판막륜(aortic annulus)을 측정함 2. 봉합 실을 판막륜 아래에 두고 인공판막을 묶어서 고정시킴 3. 경식도 심초음파를 통해 수술 전후 인공판막의 기능 확인함 좌심실 심첨부를 심초음파 화면으로 확인하면서 피부 절개 시행함

결과변수 정의

※ 프로토콜을 찾지 못함

지표명	정의기준	기타
일차 결과 변수		
composite of 30-day all-cause mortality, major stroke, and renal failure requiring dialysis	30일 측정시 모든 원인으로 인한 사망률, 주요 뇌졸중, 투석이 필요한 신부전을 복합적으로 평가	
이차 결과 변수		
all-cause death 모든 원인으로 인한 사망		
cardiac death 심장 원인으로 인한 사망		
stroke 뇌졸중		
myocardial infarction 심근경색		

지표명	정의기준	기타
New York Heart Association (NYHA) function test NYHA 기능분류 점수		
SF-36 composite physical and mental functional scores SF-36 복합 신체 및 정신 기능 점수		
aortic valve area 대동맥판 면적		
peak aortic valve gradient 대동맥판 최고압력차	-	
aortic valve leakage 대동맥판 누출		
left ventricular ejection fraction 좌심실구혈율		
duration of hospital stay 입원기간		
operation for bleeding 출혈로 인한 수술		
permanent pacemaker tratment 영구적 인공심박동기		

연구 결과

대상자수

	총 수	TAVR	SVAR
스크리닝수(enroll)	525	NR	NR
randomised	72	36	36
수술/시술 수행자	70	34	36
분석대상자	70	34	36
탈락율	NR	NR	NR

대상자 특성

■ 연구대상 특성

문헌	중재	N	평균 연령 (SD)	남자 (%)	평균 STS (SD)	평균 LES (SD)	NYHA ≧Ⅲ (%)	NYHA Ⅳ (%)	DM (%)	serum Cr >2 (%)	뇌혈관 질환 (%)	COPD (%)	말초혈관 질환 (%)	LV EF (SD)	Arotic valve area (SD)	Aortic valve peak gradient (SD))	SF36 복합신체 기능점수 (SD) T n=27 S n=32	SF 복합정신 기능점수 (SD) T n=27 S n=32
Nielsen 2012	a-TAVI	34	80 (3.6)	9 (26.5)	3.1 (1.5)	9.4 (3.9)	약18	NR	1 (2.9)	1 (2.9)	1 (2.9)	1 (2.9)	2 (5.9)	56.5 (9.7)	0.66 (0.17)	81 (26)	35 (10)	47 (10)
	대조 SAVR	36	82 (4.4)	12 (33.3)	3.4 (1.2)	10.3 (5.8)	약18	NR	3 (8.3)	0 (0.0)	1 (2.8)	1 (2.8)	3 (8.3)	56.3 (10)	0.71 (0.17)	66 (23)	37 (12)	46 (17)

추적관찰 기간

평균추적관찰 기간 : 3개월

결과

1) 이분형 변수

녹색 부분 계산하여 입력

결과변수	1저자 (연도)	시점	a-TAVI N	a-TAVI event	a-TAVI %	SAVR N	SAVR event	SAVR %	P value	RR (HR	95% CI	S/NS
Primary composite outcomes												
Primary composite outcomes	Nielsen (2012)	30일	34	5	14.7	36	1	2.8	0.07			NS

결과변수	1저자 (연도)	시점	a-TAVI			SAVR			P value	RR (HR)	95% CI	S/NS
			N	event	%	N	event	%				
30-day all-cause mortality	Nielsen (2012)	30일	34	2	5.88	36	0	0.0				
major stroke	Nielsen (2012)	30일	34	2	5.88	36	1	2.78				
renal failure requiring dialysis	Nielsen (2012)	30일	34	1	2.94	36	0	0.0				
Secondary outcomes												
all-cause death	Nielsen (2012)	3개월	34	4	11.76	36	NR	NR	NR			
cardiac death	Nielsen (2012)	3개월	NR	NR	NR	NR	NR	NR	NR			
stroke	Nielsen (2012)	3개월	NR	NR	NR	NR	NR	NR	NR			
myocardial infarction	Nielsen (2012)	3개월	34	0	0.00	36	0	0.0	NR			
permanent pacemaker treatment	Nielsen (2012)	3개월	34	2	5.88	36	1	2.78	NR			
device success, VARC1 기준	Nielsen (2012)	3개월	34	27	79	36	36	100	0.004			

2) 연속형 변수

결과변수	1저자 (연도)	시점	a-TAVI			SAVR			두 군간 변화량차이		P-value	95% CI	S/NS
			N	Mean	SD	N	Mean	SD	Mean	SD			
duration of hospital stay	Nielsen (2012)	3개월	34	8.8	6.7	36	7.6	2.4					
arotic valve area, ㎠	Nielsen (2012)	3개월	28	1.39	0.28	36	1.29	0.27					
peak aortic valve gradient, mmHg	Nielsen (2012)	3개월	28	20	6	36	24	11					
SF-36 composite physical functional scores, %	Nielsen (2012)	3개월	27	42	14	32	43	15			0.91		NS
SF-36 composite mental functional scores, %	Nielsen (2012)	3개월	27	53	14	32	50	17			0.44		NS

3) 기타 - 범주형 결과지표 등

결과변수	1저자 (연도)	시점	범주	TAVR			SAVR			P value	RR (HR)	95% CI	S/NS
				N	event	%	N	event	%				
paravalvular leakage	Nielsen (2012)	3개월	none	30	13	43	35	33	94				
paravalvular leakage	Nielsen (2012)		minimum	30	13	43	35	0	0				
paravalvular leakage	Nielsen (2012)		moderate /severe	30	4	13	35	2	6				

저자의 결론	소규모의 조기 종료된 연구의 제한점을 감안하여, 본 연구의 a-TAVI는 저위험군에서의 합병증 및 장치 삽입 성공률과 관련될 수 있으며, 대동맥 판막 협착증을 가진 고위험군에서 발견되는 것과 비슷하거나 열등함을 보임
기타(funding 등)	Aarhus University Hospital, Odense University Hospital, Danish Heart Association(study grant) 로부터 지원받음
기타 참고사항	

2. 비뚤림 위험평가

2.1. NOTION 연구 비뚤림 위험평가

Trial명	1저자, 출판연도	평가자	평가일
NOTION (저위험군)	Thyregod, 2015 Sondergaard, 2016 Thyregod, 2019 Sondergaard, 2019		2020.08.19., 2020.08.20

Domain	Risk of bias	Description
무작위 배정순서 생성	■ 낮음 □ 높음 □ 불확실	「Patients were randomized in a 1:1 ratio to treatment with TAVR or SAVR. Randomization was performed at the Copenhagen Trial Unit and was stratified accoriding to trail site」
배정순서 은폐	■ 낮음 □ 높음 □ 불확실	「The allocation sequence was arranged in permuted blocks, and block size was unknown to the investigators.」
연구참여자, 연구자에 대한 눈가림	■ 낮음 □ 높음 □ 불확실	눈가림이 중재결과에 영향을 미치지 않을 것으로 판단됨
결과평가에 대한 눈가림	■ 낮음 □ 높음 □ 불확실	눈가림이 결과평가에 영향을 미치지 않을 것으로 판단됨
불충분한 결과자료	■ 낮음 □ 높음 □ 불확실	- intention-to-treat (ITT) 기본 결과로 제시 - As-treatment 결과도 함께 제시 「The analysis for the primary outcome was performed in the intention-to-treat population with logistic regression...」 「The primary outcome was also analyzed in the as-treated population.」
선택적 보고	■ 낮음 □ 높음 □ 불확실	프로토콜이 존재하며, 연구에서 사전에 정의해 놓은 일차, 이차 중재 결과들의 정의 및 분석이 사전에 정해진 방법대로 다루어졌음을 확인할 수 있음
그 외 비뚤림(other bias) **민간 연구비 출처**	□ 낮음 ☑ 높음 ■ 불확실	기관 목적 확인되지 않음 「This work was supported by the Danish Heart Foundation」 * Siemieuniuk (2016) SR에서는 Free from industry funding에 비뚤림 위험이 높음으로 평가하였음 Disclosures Dr Ihlemann has received speaker fees from Medtronic. Dr Kjeldsen is a proctor for Edwards Lifesciences. Y. Chang is an employee and shareholder of Medtronic. Dr Franzen has received research contracts from Abbott Vascular and St. Jude Medical, and consulting fees from Edwards Lifesciences.

2.2. PARTNER 3 연구 비뚤림 위험평가

Trial명	1저자, 출판연도	평가자	평가일
PARTNER3 (저위험군)	Mack, 2019 Pibarot, 2020 Baron, 2019		2020.08.20., 2020.08.20
Domain	**Risk of bias**	**Description**	
무작위 배정순서 생성	■ 낮음 □ 높음 □ 불확실	「Patients were randomized 1:1 to undergo either transfemoral TAVR using the SAPIEN 3 balloon-expandable valve (Edwards LifeSciences, Irvine, California) or SAVR」 「Randomization was conducted with the use of an electronic system, with block sizes of four, and was stratified accoriding to site.」	
배정순서 은폐	□ 낮음 □ 높음 ■ 불확실	배정순서 은폐 방법에 대한 구체적 기술 확인되지 않음	
연구참여자, 연구자에 대한 눈가림	■ 낮음 □ 높음 □ 불확실	눈가림이 중재결과에 영향을 미치지 않을 것으로 판단됨	
결과평가에 대한 눈가림	■ 낮음 □ 높음 □ 불확실	눈가림이 결과평가에 영향을 미치지 않을 것으로 판단됨	
불충분한 결과자료	■ 낮음 □ 높음 □ 불확실	적절한 통계적 방법을 사용하여 결측치를 대체한 것으로 판단됨 「The primary analysis was performed in the as-treated population, which included patients who underwent randomization and in whom the index procedure was initiated」 「Sensitivity analyses of the primary end point were performed in the intention-to-treat population, as well as with the use of multiple imputation to account for missing data」	
선택적 보고	■ 낮음 □ 높음 □ 불확실	연구에서 사전에 정의해놓은 일차, 이차 중재결과들의 정의 및 분석이 사전에 정해진 방법대로 다루어졌음을 확인할 수 있음	
그 외 비뚤림(other bias) 민간 연구비 출처	□ 낮음 ■ 높음 □ 불확실	「The trial was sponsered by Edwards Lifesciences..」	

2.3. Evolute 연구 비뚤림 위험평가

Trial명	1저자, 출판연도	평가자	평가일
Evolute	Popma, 2019		2020.08.21., 2020.08.20
Domain	**Risk of bias**	**Description**	
무작위 배정순서 생성	■ 낮음 □ 높음 □ 불확실	"Randomization was performed in a 1:1 ratio, with variable block sizes, with an electronic ran\−domization system. Randomization was stratified by site and the need for coronary−artery revascu\−larization"	
배정순서 은폐	□ 낮음 □ 높음 ■ 불확실	배정순서 은폐 방법에 대한 구체적 기술 확인되지 않음	
연구참여자, 연구자에 대한 눈가림	☑ 낮음 □ 높음 ■ 불확실	눈가림이 중재결과에 영향을 미치지 않을 것으로 판단됨	
결과평가에 대한 눈가림	☑ 낮음 □ 높음 ■ 불확실	눈가림이 결과평가에 영향을 미치지 않을 것으로 판단됨	
불충분한 결과자료	■ 낮음 □ 높음 □ 불확실	적절한 통계적 방법을 사용하여 결측치를 대체한 것으로 판단됨 「The primary analysis cohort was the as-treated population, which comprised patients who were randomly assigned to a group and who underwent an attempted procedure.」 「Secondary analyses of the primary end point were also performed in the intention-to-treat population, the "implanted" population (patients in whom an aortic valve was implanted), and the per-protocol population.」	
선택적 보고	■ 낮음 □ 높음 □ 불확실	연구에서 사전에 정의해놓은 일차, 이차 중재결과들의 정의 및 분석이 사전에 정해진 방법대로 다루어졌음을 확인할 수 있음	
그 외 비뚤림(other bias) 민간 연구비 출처	□ 낮음 ■ 높음 □ 불확실	「Medtronic funded the trial and developed the protocol in collaboration with the executive committee.」	

2.4. STACCATO 연구 비뚤림 위험평가

Trial명	1저자, 출판연도	평가자	평가일
STACCATO (저위험군)	Nielsen, 2012		2020.08.20., 2020.08.20
Domain	**Risk of bias**	**Description**	
무작위 배정순서 생성	■ 낮음 □ 높음 □ 불확실	「The 1:1 randomisation between a-TAVI and SAVR was implemented using the web-based clinical trials support system, "TrialPartner".」	
배정순서 은폐	■ 낮음 □ 높음 □ 불확실	「TrialPartner permits, with a personal log-in, 24-hour randomisation.」	
연구참여자, 연구자에 대한 눈가림	■ 낮음 □ 높음 □ 불확실	눈가림이 중재결과에 영향을 미치지 않을 것으로 판단됨 Although there was lack of blinding in the studies, this did not affect mortality as an outcome between the two groups.	
결과평가에 대한 눈가림	■ 낮음 □ 높음 □ 불확실	눈가림이 결과평가에 영향을 미치지 않을 것으로 판단됨	
불충분한 결과자료	□ 낮음 ■ 높음 □ 불확실	「The RCT was prematurely terminated.」	
선택적 보고	□ 낮음 ■ 높음 □ 불확실	「The RCT was prematurely terminated.」	
그 외 비뚤림(other bias) 민간 연구비 출처	■ 낮음 □ 높음 □ 불확실	「The study was an academic study, designed and carried out by the involved cardiac surgeons, cardiologists and anaesthesiologists at Aarhus University Hospital, and Odense University Hospital, and primarily funded by the participating hospitals. Further, there was a study grant from the Danish Heart Association. There was no industry involvement.」	