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Review Article

Short-Term Outcomes of ACURATE neo2

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ABSTRACT

Inferior outcomes with ACURATE neo, a self-expanding transcatheter heart valve (THV) for the treatment of severe aortic stenosis, were mainly driven by higher rates of moderate/severe paravalvular leak (PVL). To overcome this limitation, the next-generation ACURATE neo2 features a 60% larger external sealing skirt. Data on long-term performance are limited; however, clinical evidence suggests improved short-term performance which is comparable to contemporary THVs. This report reviews data on short-term clinical and echocardiographic outcomes of ACURATE neo2. A PubMed search yielded 13 studies, including 5 single arm and 8 nonrandomized comparative studies with other THVs which reported in-hospital or 30-day clinical and echocardiographic outcomes. In-hospital or 30-day all-cause mortality was ≤3.3%, which is comparable to other contemporary THVs. The rates of postprocedural ≧moderate PVL ranged 0.6%-4.7%. In multicenter propensity-matched analyses, neo2 significantly reduced the rate of ≧moderate PVL compared to neo (3.5% vs. 11.3%, $p < 0.01$), whereas rates were comparable to Evolut Pro/Pro+ (Neo2: 2.0% vs. Pro/Pro+: 3.1%, $p = 0.28$) and SAPIEN 3 Ultra (Neo2: 0.6% vs. Ultra: 1.1%, $p = 0.72$). The rate of permanent pacemaker implantation with neo2 was consistently low (3.3%-8.6%) except in one study, and in propensity-matched analyses were significantly lower than Evolut Pro/Pro+ (6.7% vs. 16.7%, $p < 0.01$), and comparable to SAPIEN 3 Ultra (8.1% vs. 10.3%, $p = 0.29$). In conclusion, ACURATE neo2 showed better short-term performance by considerably reducing PVL compared to its predecessor, with short-term clinical and echocardiographic outcomes comparable to contemporary THVs.

ABBREVIATIONS

AKI, acute kidney injury; AS, aortic stenosis; HALT, hypo-attenuated leaflet thickening; PPI, permanent pacemaker implantation; PVL, paravalvular leak; STS, society of thoracic surgeons; TAVI, transcatheter aortic valve implantation; THV, transcatheter heart valve.

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Introduction

Transcatheter aortic valve implantation (TAVI) is an established treatment option for patients with severe aortic stenosis (AS) and its indication has now been expanded to lower risk and younger patients.[1] Whilst its safety and efficacy are equivalent, or even superior, to those of surgical aortic valve replacement,[2,3] the incidence of paravalvular leak (PVL) and permanent pacemaker implantation (PPI) is higher, and given their negative impact on long-term outcomes, there is a pressing need to overcome these shortcomings.[4,5]

The ACURATE neo (Boston Scientific, USA) is a self-expanding transcatheter heart valve (THV), which failed to show noninferiority compared to SAPIEN 3 and CoreValve Evolut in the SCOPE I and II trials, respectively, primarily due to the higher rates of moderate or severe PVL with ACURATE neo.[6,7] The ACURATE neo2 (Boston Scientific, USA) is a next-generation self-expanding THV, which received its Conformité Européenne mark in 2020. Whilst data on long-term performance are limited, clinical evidence suggests its short-term performance is more favorable than its predecessor, ACURATE neo, with reduced rates of PVL, and low rates of PPI compared to contemporary devices.[8] This paper reviews the features and short-term outcomes of ACURATE neo2 for the treatment of AS.

Features of ACURATE neo2

ACURATE neo2 is the third generation device in the ACURATE series (Figure 1).[9] The history of the first (ACURATE TA) and second (ACURATE neo) generation devices are summarized in Supplemental Table 1. ACURATE neo2 is a self-expanding THV which consists of a nitinol frame, supra-annular porcine pericardial leaflets with anticalcification treatment and a porcine pericardial sealing skirt. On top, it has axial stabilization arches which help maintain coaxiality with the native annulus, whilst its open cell design facilitates easy access to the coronary arteries. The upper crown is designed to anchor and cap the native leaflets, stabilizing the valve position and reducing the risk of coronary obstruction. There is minimal protrusion of the lower crown into the left ventricle, which together with the relatively low radial force of the valve frame, mitigates interference with the conduction system. In contrast to other self-expanding THVs, the ACURATE series THVs are released from the top down with a 2-step procedure: step 1 release of the stabilization arches and upper crown, and step 2 release of the lower crown (Figure 2).[10]

There were two key design changes during the evolution from neo to neo2. First, the height of the sealing skirt was increased by 60% in neo2 to overcome the higher incidence of moderate or severe PVL that was observed with neo. Second, a radiopaque marker was added to the delivery system to facilitate initial valve positioning, which potentially reduces the amount of contrast dye and consequently the incidence of acute kidney injury.

ACURATE neo2 is deliverable using a 14 Fr expandable sheath via the femoral artery and due to the relatively low radial force, predilatation is strongly recommended. It is available in three sizes (S - 23mm, M - 25mm and L - 27mm) and is suitable for aortic annulus diameters from 21 to 27 mm (Figure 3).

Short-Term Outcomes of ACURATE neo2

Study Selection

A review of published articles was conducted with a search of PubMed using the term "ACURATE neo2". We only included single arm or comparative studies which enrolled at least 30 patients in the ACURATE neo2 cohort, and reported in-hospital or 30-day clinical and echocardiographic outcomes. We excluded studies with less than 30 patients in the neo2 cohort, studies without clinical or echocardiographic outcomes, and case reports.

As of November 2023, there are no data from randomized controlled trials (RCTs) comparing ACURATE neo2 to other THVs; however, there are 13 studies, including 5 single arm and 8 non-RCTs with other devices,

	TA	neo	neo2
Access	Apical	Femoral / apical	Femoral
Outer diameter	30 Fr	TF: 18 Fr / TA: 22 Fr	18Fr
Sheath size	Sheathless	TF: 14Fr expandable TA: Sheathless	14Fr expandable
Leaflet	Intra-annular Porcine native leaflet	Supra-annular Porcine pericardium	Supra-annular Porcine pericardium
Skirt	Polyethylene terephtalate	Porcine pericardium	Porcine pericardium 60% higher than neo

Figure 1. ACURATE family.
Abbreviations: TF, transfemoral; TA, transapical.
Images were provided courtesy of Boston Scientific.

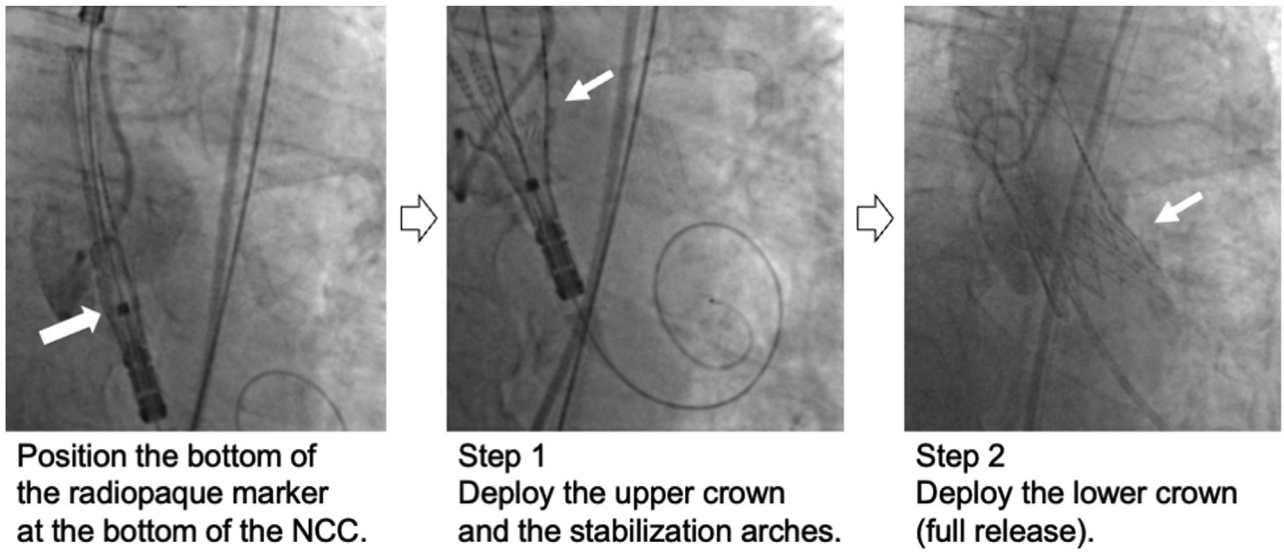


Figure 2. Implantation steps of ACURATE neo2. The images are reproduced and modified from the paper of Wong I, et al.[10]
Abbreviation: NCC, noncoronary cusp.

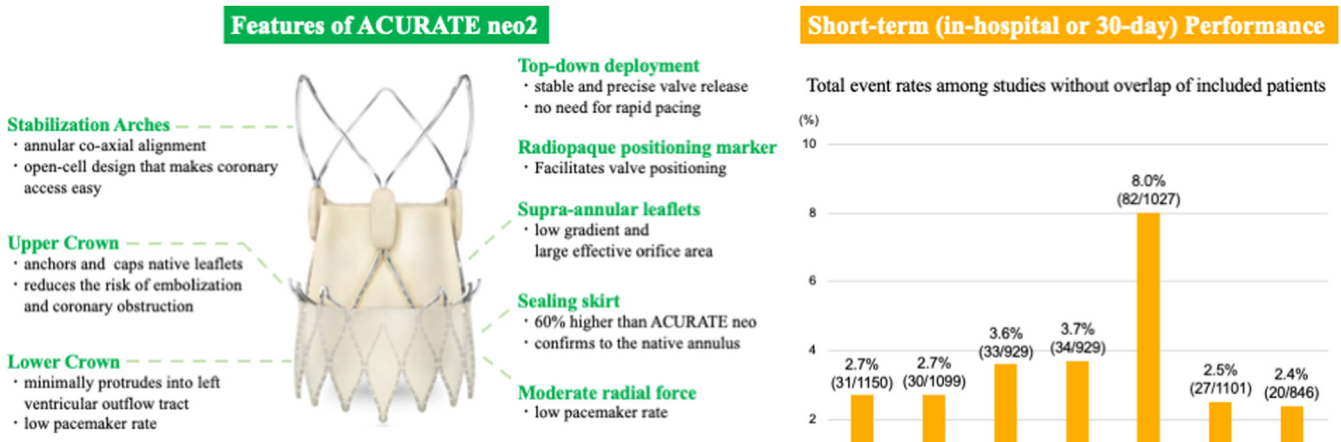
which have enrolled at least 30 patients in the neo2 cohort and have reported prospective or retrospective in-hospital or 30-day clinical and hemodynamic outcomes of ACURATE neo2 (Tables 1 and 2).[11–24] Data on long-term follow-up are limited, with the ITAL-neo registry reporting clinical outcomes at 90-days, and the ACURATE neo AS study and the post marketing surveillance study reporting clinical outcomes at 1-year.[11,14,17] Two studies from the NEOPRO-2 registry report outcomes from the same patient cohort,[21,22] whilst there is likely to be overlap amongst patients included in the other studies. Supplemental Table 2 and Figure 3 show the total event rates from the four studies where there is no overlap of included patients.[11,15,20,22] Five comparative studies reported the results of propensity-matched analyses, and their clinical and echocardiographic outcomes are summarized in Tables 3 and 4, respectively.[17,20,22–24]

In-Hospital or 30-Day All-Cause Mortality

In-hospital or 30-day all-cause mortality after neo2 implantation ranged from 0.0%–3.3% among all studies (Table 1), which is in line with the low to intermediate risk patient cohorts that were mainly included, and comparable to 30-day mortality after TAVI in this patient risk group in landmark trials such as PARTNER 2A (3.9%), PARTNER 3 (0.4%), SURTAVI (2.2%), and self-expanding low risk (0.5%).[25–28] The total event rate among the 4 studies without overlap of included patients was 2.7% (31/1150, Supplemental Table 2). Eight comparative studies reported similar in-hospital or 30-day mortalities between ACURATE neo2 and neo, Evolut PRO/PRO + or SAPIEN 3 Ultra.[17–24] Notably, there were also no significant differences in propensity-matched comparisons (Table 3), with 30-day mortality with ACURATE neo2 comparable to that of Evolut PRO/PRO+ (2.7 vs. 1.6%, $p = 0.27$) in the NEOPRO-2 registry,[22] and SAPIEN 3 Ultra (1.7 vs. 2.4%, $p = 0.65$) as reported by Pellegrini C, et al.[24]

Postprocedural Paravalvular Leak

The design changes in ACURATE neo2 succeeded in reducing PVL, with postprocedural echocardiographic assessment showing the



Valve size	S (23 mm)	M (25 mm)	L (27 mm)
Sheath	14 Fr expandable sheath		
Aortic annulus diameter	21-23 mm	23-25 mm	25-27 mm
Aortic annulus perimeter	66-72 mm	72-79 mm	79-85 mm

Figure 3. The features of ACURATE neo2 (left) and total event rates of the four studies without overlap of included patients (right).
Abbreviations: PPI, permanent pacemaker implantation; PVL, paravalvular leak.

Table 1
In-hospital or 30-d clinical outcomes after TAVI with ACURATE neo2

Study	THV	N	STS score (S) or EuroSCORE II (E)	Predilatation	All-cause mortality		All stroke		Bleeding (VARC-3 type 3-4)		AKI		Major vascular complication		PPI*	
					Rate	*p* value	**Rate**	*p* value	**Rate**	*p* value	**Rate**	*p* value	**Rate**	*p* value	**Rate**	*p* value
ACURATE neo AS (2021)[11]	*30-d* neo2	120	4.8 (S)	95.8%	3.3%	–	2.5%	–	5.0%†	–	VARC2 St. 2-3 0.8%	–	3.3%	–	16.1%	–
Multicenter, prospective	*1 y* neo2	118	–	–	11.9%‡	–	2.5%‡	–	8.5%†‡	–	–	–	3.3%‡	–	17.8%‡§	–
Kim WK (2022)[12] Single-center, retrospective	neo2	448	2.9 (E)	83.5%	2.4%	–	3.4%	–	9.2%#	–	VARC3 St. 2-4 2.9%	–	5.4%	–	6.9%§	–
PMS (2023)[13,14] Multicenter, prospective	30-d neo2	250	2.9 (S)	96.8%	0.8%	–	0.8%	–	2.9%†	–	VARC2 St. 2-3 0%	–	3.2%‖	–	6.5%	–
	1-y neo2	223	–	–	5.1%‡**	–	3.0%‡**	–	3.7%†‡**	–	–	–	–	–	8.3%‡**	–
NeoAlign (2023)[15] Single-center, prospective	neo2	170	2.9 (E)	–	1.8%	–	1.2%	–	–	–	10.0%††	–	–	–	6.2%‖	–
Early neo2 (2023)[16] Multicenter, prospective	neo2	554	4.0 (S)	87.0%	1.3%	–	2.7%	–	–	–	VARC2 St.2-3 2.1%	–	3.4%‖	–	6.8%	–
ITAL-neo (2022)[17]	*In-hospital*										VARC3 St.2-4					
Multicenter, retrospective	neo2	205	3.40 (S)	92.2%	1.5%‖	0.62	1.0%‖	–	1.5%‖	–	3.0%	–	3.4%‖	–	7.6%‖	0.71
	neo	205	3.33 (S)	69.0%	0.5%‖		1.0%‖		1.5%‖		3.0%		3.9%‖		9.1%‖	
	90-d		–	–	4.5%‡‡	1.00	2.5%‡‡	–	2.0%‡‡	–	–	–	–	–	7.7%‡‡	0.37
	neo2	200	–	–	4.0%‡‡		1.2%‡‡		2.3%‡‡		–		–		10.9%‡‡	
	neo	175														
PREDICT PVL (2022)[18] Single-center, prospective	neo2	30	3.1 (S)	90.0%	0.0%	–	0.0%	–	0.0%§§	0.3	–	–	0%	–	3.6%	–
	neo	30	3.0 (S)	93.3%	0.0%		0.0%		3.3%§§				–		0.0%	
Kim WK (2022)[19] Multicenter, retrospective	neo2	810	3.3 (E)	90.9%	3.3%	>0.99	3.6%	0.22	14.8%#	<0.01	VARC3 St. 2-4 3.3% 4.4%	0.21	6.9% 8.7%	0.13	8.6%§ 9.3%§	0.61
	neo	2055	3.4 (E)	73.2%	2.8%		2.7%		19.8%#							
Miyashita H (2023)[20] Single-center, retrospective	neo2	100	3.5 (S)	100.0%	2.0%	0.62	5.0%‖	0.86	7.0%‖‖	0.22	–	–	7.0%‖	0.67	3.3%‖	0.73
	neo	348	4.2 (S)	98.6%	1.2%		5.5%‖		11.2%‖‖				8.3%‖		4.1%‖	
NEOPRO/NEOPRO-2 (2022)[21] Multicenter, retrospective	neo2	763	3.5 (S)	85.9%	2.9%	0.90	–	–	2.8%	–	VARC3 St. 2-3 2.8% 2.9%	0.95	3.2% 5.9%	–	7.7% 8.7%	0.46
	neo	1263	4.1 (S)	83.2%	3.1%		–		4.4%							
NEOPRO-2 (2023)[22] Multicenter, retrospective	neo2	763	4.2 (S)	85.9%	2.9%	0.33	2.8%	0.60	2.8%	–	VARC3 St. 3-4 2.5% 1.2%	0.02	3.2% 4.0%	–	7.7% 15.6%	<0.001
	PRO/PRO+	1412	4.2 (S)	44.3%	2.2%		2.9%		2.0%							

(*continued on next page*)

Table 1 (*continued*)

Study	THV	N	STS score (S) or EuroSCORE II (E)	Predilatation	All-cause mortality		All stroke		Bleeding (VARC-3 type 3-4)		AKI		Major vascular complication		PPI*	
					Rate	*p* value	Rate	*p* value	Rate	*p* value	Rate	*p* value	Rate	*p* value	Rate	*p* value
Rheude T (2023)[23]	neo2	155	–	94.2%	–	–	1.9%	0.50	5.8%	0.16	VARC3 St. 2-3	0.27	11.6%	0.02	7.5%	0.002
Multicenter,	PRO	155	–	56.1%	–		3.9%		2.6%		5.8%		4.5%		20.6%	
retrospective											3.2%					
Pellegrini C (2023)[24]	neo2	608	3.0 (E)	87.8%	1.8%	0.57	3.0%	1.00	4.3%‖	1.00	VARC3 St. 2-4	1.00	6.4%‖	0.12	7.7%	0.09
Multicenter,	S3 Ultra	748	3.0 (E)	35.8%	2.5%		3.1%		4.4%‖		3.0%		8.8%‖		10.5%	
retrospective											3.1%					

30-d outcomes are shown without annotations.
There could be some overlap of the included patients among studies.
Abbreviations: PMS, post marketing surveillance; PPI, permanent pacemaker implantation; STS, Society of Thoracic Surgeons; THV, transcatheter heart valve; VARC, valve academic research consortium.
* PPI was calculated in the patients without permanent pacemaker at baseline.
† VARC-2 life-threatening or disabling bleeding.
‡ 1-y outcomes.
§ Percentage in the entire cohort including patients with a permanent pacemaker at baseline.
‖ In-hospital outcomes.
VARC-3 type2-4.
** Kaplan-Meier time-to-event estimate.
†† AKI was defined as an increase of 26 mmol/L serum creatinine.
‡‡ 90-d outcomes.
§§ Any bleeding.
‖‖ VARC-2 bleeding ≧major.

incidence of moderate or severe PVL with ACURATE neo2 to be 0.6%-4.7% among all studies (Tables 2) and 2.5% (27/1001) among the 4 studies without overlap of enrolled patients (Supplemental Table 2 and Figure 3), which is far lower than the 9.4 and 9.6% seen with its predecessor in the SCOPE I and II studies, respectively.[6,7] This improvement was also seen in the five head-to-head studies comparing ACURATE neo2 to neo,[17–21] and confirmed by quantitative video-densitometric angiography immediately post procedure.[29] Propensity-matched analyses showed similar results, and whilst the reduction in moderate or severe PVL with neo2 compared to neo was significant in the multicenter retrospective ITAL-neo study (3.5% [7/202] in neo2, and 11.3% [23/204] in neo, $p < 0.01$),[17] it was only numerically lower in the study by Miyashita H, et al. (4.3% [4/94] in neo2, and 8.5% [8/94] in neo, $p = 0.23$).[20] This latter finding was likely to be due to the relatively low number of included patients.

In the comparisons with other devices, Rheude T, et al reported significantly lower rates of postprocedural moderate or severe PVL with ACURATE neo2 compared to Evolut Pro (0.6 vs. 4.6%, $p = 0.036$) in a matched cohort.[23] However, in the NEOPRO-2 registry comparing neo2 to Evolut Pro/Pro+, the same result was only seen in the full population (1.7 vs. 4.1%, $p = 0.003$) and not in the matched sub-group (2.0 vs. 3.1%, $p = 0.28$),[22] which is probably due to a selection bias as patients in the Evolut Pro/Pro+ arm had more calcified anatomies. Rates of post-procedural moderate or severe PVL were similar with ACURATE neo2 compared to SAPIEN 3 Ultra (Entire cohort: 0.7 vs. 0.8%, $p = 1.00$, and matched cohort: 0.6 vs. 1.1%, $p = 0.72$); however, mild PVL, which may also have a negative impact on mortality,[5] was significantly lower with SAPIEN 3 Ultra (Entire: 32.6 vs. 19.2%, $p < 0.001$ and matched: 32.8 vs. 20.0%, $p < 0.001$).[24]

In the NEOPRO-2 registry, there was a tendency for higher rates of moderate or severe PVL to be seen in patients with increasing levels of aortic valve calcification (1.1% in non or mild calcification, 2.6% in moderate calcification, and 3.1% in severe calcification).[22] A greater degree of aortic valve calcification is a well-recognized predictor of PVL after TAVI; however, one meta-analysis suggests that this is no longer seen with the newer generation THVs with a sealing skirt.[30] Notably, a multivariable analysis by Kim WK, et al showed that higher calcium density was associated with more relevant PVL after implantation of the ACURATE neo but not with neo2.[19]

The PREDICT PVL study investigated the precise location of PVL after implanting an ACURATE neo2 and reported that it was most frequently observed in the commissures adjacent to the left coronary cusp, as also seen with neo.[18,31] As the THV catheter proceeds through the outer side of the ascending aorta and the THV is positioned in the commissure between the non and right coronary cusp at the start of deployment, PVL presumably occurs at the opposite side of the initial position. Despite the PREDICT PVL study providing detailed assessments of PVL, the study was small, and therefore the relationship between the amount and distribution of aortic valve calcification and the severity and localization of PVL needs to be more formally investigated in future analyses with larger populations.

In-Hospital or 30-Day Permanent Pacemaker Implantation

As with ACURATE neo, neo2 was associated with a lower rate of PPI, with consistent rates between 3.3% and 8.6% in all studies bar one, where the rate was 16.1% (Table 1). The total rate of PPI in studies without overlap of enrolled patients was 8.0% (82/1027, Supplemental Table 2 and Figure 3), which is lower than that observed with ACURATE neo in SCOPE I (10.0%) and II (11.0%).[6,7] Two propensity-matched studies comparing ACURATE neo to neo2 reported no significant differences in the rate of PPI,[17,20] whilst significantly lower rates were seen with neo2 compared to Evolut PRO (7.5 vs. 20.6%, $p = 0.002$),[23] and Evolut PRO/PRO+ (6.7 vs. 16.7%, $p < 0.001$) in matched cohorts (Table 3).[22] Of note, the rates of PPI after implanting an Evolut PRO or PRO+ in these studies were similar to those seen in RCTs of the

Table 2

Postprocedural echocardiographic measurement after TAVI with ACURATE neo2

Study	THV	N*	PVL					≧moderate PVL		Mean PG (mmHg)		Mean PG ≧20mmHg		EOA (cm^2)	
			None/trace	Mild	Moderate	Severe	*p* value	**Rate**	*p* value	Value	*p* value	**Rate**	*p* value	Value	*p* value
ACURATE neo AS (2021)[11] Multicenter, prospective	neo2	80	36.3%†	61.3%†	2.5%†	0.0%†	–	2.5%†	–	8.0 ± 3.4†	–	–	–	1.6 ± 0.4†	–
Kim WK (2022)[12] Single-center, retrospective	neo2	448	–	–	–	–	–	1.3%‡	–	9.0 (7.0-12.0)	–	–	–	1.7 (1.5-2.0)	–
PMS (2023)[13] Multicenter, prospective	neo2	171-192	77.2%	22.2%	0.6%	0.0%	–	0.6%	–	9.7 ± 5.4	–	–	–	1.6 ± 0.4	–
NeoAlign (2023)[15] Single-center, prospective	neo2	170	43.5%	50.6%§	4.7%	0.0%	–	4.7%	–	9.5 ± 3.9	–	–	–	–	–
Early neo2 registry (2023)[16] Multicenter, prospective	neo2	466	57.8%	37.3%	2.8%	0.0%	–	2.8%	–	7.6 ± 3.3	–	0.0%	–	2.24 ± 0.64	–
ITAL-neo (2022)[17]	neo2	202	50.0%	46.5%	3.5%	0.0%	<0.001	3.5%	–	7.0 (6.0-10.0)	0.09	–	–	1.88 (1.60-2.19)	0.35
Multicenter, retrospective	neo	204	30.0%	58.8%	10.7%	0.5%		11.3%		6.0 (5.0-9.0)				1.76 (1.56-2.02)	
PREDICT PVL (2022)[18]	neo2	30	60.0%	36.7%§	3.3%	0.0%	0.07	3.3%	–	8.9 ± 3.8	0.50	–	–	2.3 ± 0.6	0.20
Single-center, prospective	neo	30	26.7%	66.7%§	6.7%	0.0%		6.7%		8.3 ± 2.7				2.1 ± 0.5	
Kim WK (2022)[19]	neo2	805-810	65.8%	31.7%	2.5%	0.0%	–	2.5%	0.06	8.5 (6.0-11.0)	0.02	–	–	1.7 (1.5-2.0)	0.08
Multicenter, retrospective	neo	2046-2055	43.9%	52.2%	3.9%	0.0%		4.0%		8.0 (6.0-11.0)				1.7 (1.5-2.0)	
Miyashita H (2023)[20]	neo2	99	55.6%	40.4%	4.0%	0.0%	0.58	4.0%	0.13	10.5 ± 4.7	0.006	6.1%	0.25	–	–
Single-center, retrospective	neo	346	54.9%	36.4%	8.1%	0.6%		8.7%		9.0 ± 4.9		3.5%			
NEOPRO/NEOPRO-2 (2022)[21]	neo2	763	59%	39%	2%	0%	<0.01	1.7%	<0.001	8.9 ± 4.1†	<0.001	–	–	1.8 ± 0.4†	0.83
Multicenter, retrospective	neo	1263	38%	57%	5%	0.1%		4.9%		8 ± 3.3†		–		1.8 ± 0.4†	
NEOPRO-2 (2023)[22]	neo2	747-763	59.0%	39.3%	1.7%	0.0%	0.02	1.7%	0.003	9.1 ± 4.2	<0.001	1.9%	0.58	1.79 ± 0.46	<0.001
Multicenter, retrospective	PRO/PRO+	1356-1412	59.3%	36.6%	3.8%	0.3%		4.1%		7.7 ± 4.0		1.6%		1.94 ± 0.54	
Rheude T (2023)[23]	neo2	153-154	–	–	–	–	–	0.6%	0.04	9 (7-12)	0.001	1.9%	0.06	–	–
Multicenter, retrospective	PRO	148-153						4.6%		8 (6-11)		0.0%			
Pellegrini C (2023)[24]	neo2	608	66.8%	32.6%	0.7%	0.0%	–	0.7%	1.00	9 ± 4	<0.001	1.8%	<0.001	Indexed EOA	<0.001
Multicenter, retrospective	S3 Ultra	748	80.0%	19.2%	0.8%	0.0%		0.8%		13 ± 5		9.3%		0.92 (0.79-1.05) 0.78 (0.68-0.90)	

Postprocedural or predischarge outcomes are shown without annotations.

There must be some overlap of the included patients among studies.

Abbreviations: –, not available; EOA, effective orifice area; PG, pressure gradient; PMS, post marketing survey; PVL, paravalvular leak; THV, transcatheter heart valve.

* Number of patients who underwent postprocedural echocardiographic assessment.

† Measurement at 30 d.

‡ Relevant PVL (≧moderate PVL at discharge, the implantation of a second valve, or surgical aortic valve replacement for PVL ≧moderate within 30 d).

§ Including mild-moderate PVL.

Table 3
In-hospital or 30-d clinical outcomes in comparative studies with propensity-matched cohorts

Study	THV	N	STS score (S) or EuroSCOREII (E)		Predilatation		All-cause mortality		All stroke		Bleeding (VARC-3 type 3-4)		AKI		Major vascular complication		PPI*	
			Score	*p* value	**Rate**	*p* value	**Rate**	*p* value	**Rate**	*p* value	**Rate**	*p* value	**Rate**	*p* value	**Rate**	*p* value	**Rate**	*p* value
ITAL-neo (2022)[17]	neo2	205	3.4 (S)	0.68	92.2%	<0.001	1.5%†	0.62	1.0%†	–	1.5%†	–	VARC3 St.2-4	–	3.4%†	–	7.6%†	0.71
Multicenter, retrospective	neo	205	3.3 (S)		69.0%		0.5%†		1.0%†		1.5%†		3.0% 3.0%		3.9%†		9.1%†	
Miyashita H (2023)[20]	neo2	94	3.4 (S)	0.90	100.0%	1.00	1.1%	1.00	5.3%†	0.39	7.5%†‡	0.79	–		6.4%†	0.76	3.5%†	0.50
Single-center, retrospective	neo	94	3.4 (S)		98.9%		0.0%		8.5%†		8.5%†‡		–		5.3%†		7.1%†	
NEOPRO-2 (2023)[22]	neo2	452	3.8 (S)	0.33	86.7%	<0.001	2.7%	0.27	3.3%	0.67	3.3%	–	VARC3 St. 3-4	0.002	4.0%	–	6.7%	<0.001
Multicenter, retrospective	PRO/PRO+	452	4.0 (S)		36.5%		1.6%		3.9%		1.1%		3.3% 0.5%		3.4%		16.7%	
Rheude T (2023)[23]	neo2	155	–	–	94.2%	<0.001	–	–	1.9%	0.50	5.8%	0.16	VARC3 St. 2-3	0.27	11.6%	0.02	7.5%	0.002
Multicenter, retrospective	PRO	155	–		56.1%		–		3.9%		2.6%		5.8% 3.2%		4.5%		20.6%	
Pellegrini C (2023)[24]	S3 Ultra	472	3.0 (E)	0.83	91.9%	<0.001	1.7%	0.65	3.4%	0.44	3.8%†	1.00	VARC3 St. 2-4	1.00	6.1%†	0.07	8.1%	0.29
Multicenter, retrospective	neo2	472	3.1 (E)		31.4%		2.4%		2.4%		3.6%†		3.2% 3.2%		9.5%†		10.3%	

30-d outcomes are shown without annotations.
There could be some overlap of the included patients among studies.
Abbreviations: –, not available; AKI, acute kidney injury; PPI, permanent pacemaker implantation; STS, Society of Thoracic Surgeons; THV, transcatheter heart valve; VARC, valve academic research consortium.
* PPI was calculated in the patients without permanent pacemaker at baseline.
† In-hospital outcomes.
‡ VARC-2 bleeding ≥major.

Table 4
Postprocedural echocardiographic measurement in comparative studies with propensity-matched cohorts

Study	THV	N* (neo2)	PVL					≥moderate PVL		Mean PG (mmHg)		Mean PG ≥20mmHg		EOA (cm^2)	
			None/trace	Mild	Moderate	Severe	*p* value	**Rate**	*p* value	Value	*p* value	**Rate**	*p* value	Value	*p* value
ITAL-neo (2022)[17]	neo2	202	50.0%	46.5%	3.5%	0.0%	<0.001	3.5%	–	7.0 (6.0-10.0)	0.09	–	–	1.88 (1.60-2.19)	0.35
Multicenter, retrospective	neo	204	30.0%	58.8%	10.7%	0.5%		11.3%		6.0 (5.0-9.0)		–		1.76 (1.56-2.02)	
Miyashita H (2023)[20]	neo2	94	57.4%	38.3%	4.3%	0.0%	0.66	4.3%	0.23	10.6 ± 4.8	0.045	6.4%	1.00	–	–
Single-center, retrospective	neo	94	52.1%	39.4%	8.5%	0.0%		8.5%		9.0 ± 6.1		6.4%		–	
NEOPRO-2 (2023)[22]	neo2	452	58.4%	39.6%	2.0%	0.0%	0.56	2.0%	0.28	9.0 ± 4.0	<0.001	1.3%	0.35	1.75 ± 0.4	<0.001
Multicenter, retrospective	PRO/PRO+	452	57.9%	39.0%	3.1%	0.0%		3.1%		7.7 ± 4.0		0.7%		1.91 ± 0.5	
Rheude T (2023)[23]	neo2	155	–	–	–	–	–	0.6%	0.04	9 (7-12)	0.001	1.9%	0.06	–	–
Multicenter, retrospective	PRO	155	–	–	–	–		4.6%		8 (6-11)		0%		–	
Pellegrini C (2023)[24]	neo2	472	66.5%	32.8%	0.6%	0.0%	–	0.6%	0.72	9 ± 4	<0.001	2.4%	<0.001	Indexed EOA	<0.001
Multicenter, retrospective	S3 Ultra	472	78.9%	20.0%	1.1%	0.0%		1.1%		13 ± 4		7.7%		0.92 (0.79-1.05) 0.78 (0.67-0.91)	

Postprocedural or predischarge outcomes are shown.
There could be some overlap of the included patients among studies.
Abbreviations: –, not available; EOA, effective orifice area; PG, pressure gradient; PVL, paravalvular leak; THV, transcatheter heart valve.
* Number of patients who underwent postprocedural echocardiographic assessment.

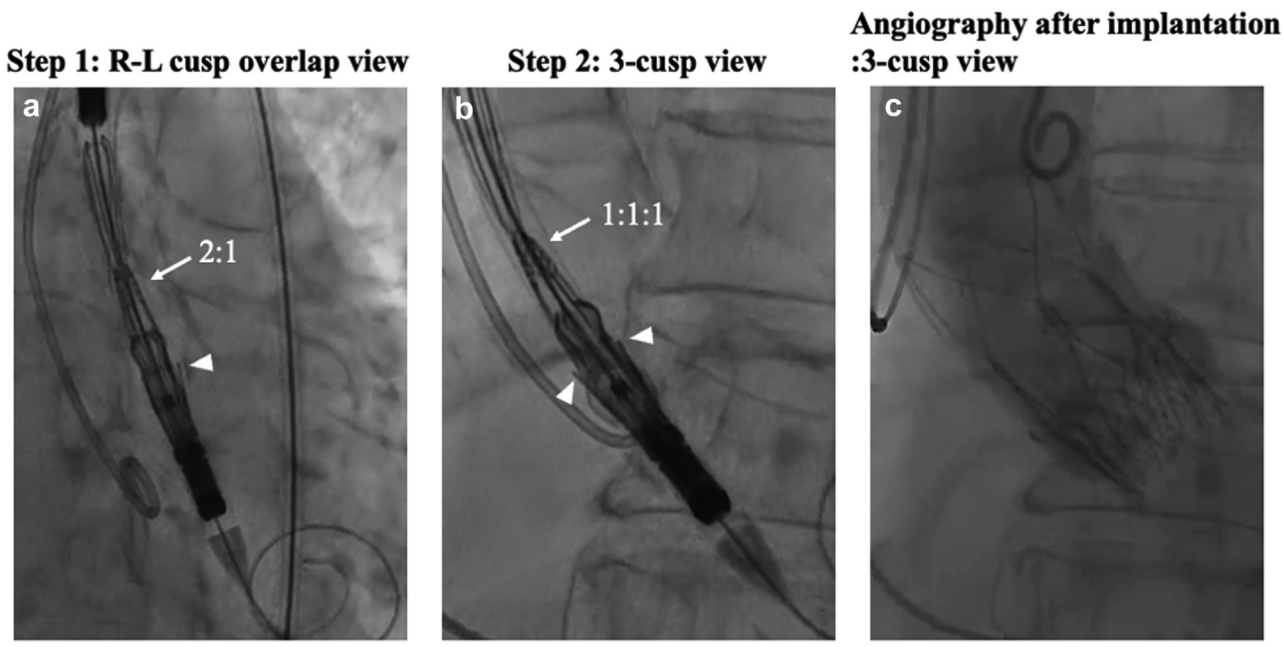


Figure 4. Karolinska commissural alignment technique. The delivery system is inserted into the sheath with the flush port positioned at 6 o'clock, and advanced without torque. First, the orientation of ACURATE neo2 is assessed in the R-L cusp overlap view, with the optimal position when you can see 2:1 stent posts and a wing on the right side (Step 1, A). Next, the orientation is assessed in the 3-cusp view, with the optimal orientation in this view 1:1:1 stent posts with 2 visible wings (Step 2, B). If the optimal orientation is not obtained in the 3-cusp view, the catheter is rotated clockwise or counterclockwise according to the initial orientation of the THV to obtain the 1:1:1 stent posts orientation; if the posts are seen 2:1, the catheter is rotated clockwise. Conversely if the posts are seen 1:2, the catheter is rotated counterclockwise. Lastly, the R-L cusp overlap view is checked again to confirm the 2:1 stent posts orientation. Angiography in the 3-cusp view after implantation of neo2 shows the 1:1:1 position of stent posts (C). arrow: stent post, arrowhead: wing. The images are reproduced and modified from the paper of Meduri CU, et al[15].

CoreValve in low-risk patients (17.4%).[28] Pellegrini C, et al reported similar rates of PPI with ACURATE neo2 and SAPIEN 3 Ultra in the entire (7.7 vs. 10.5%, $p = 0.09$) and matched cohorts (8.1 vs. 10.3%, $p = 0.29$)[24]; however, the rates with SAPIEN 3 Ultra were higher than those seen in the PARTNER 3 trial which used SAPIEN 3 in low-risk patients (6.6%),[26] or in real-world studies using SAPIEN 3 Ultra (2.3%-6.4%).[32,33]

The minimal protrusion into the left ventricular outflow tract and the relatively low radial force of the valve frame are considered to contribute to the lower rate of PPI seen with the ACURATE series. This is supported by the report of Hokken TW, et al who showed that the implantation depth with ACURATE neo was significantly shallower than SAPIEN3 and Evolut R/PRO (4.0 [3.0-5.0], 5.0 [3.7-6.8] and 5.0 [3.0-8.0] mm, respectively, $p < 0.01$), and that the length of the membranous septum, which is an established predictor of PPI after TAVI, was only associated with PPI after implantation of SAPIEN3 and Evolut R/PRO, and not neo.[34] Recently, implantation of THV using the left-right 2-cusp overlap view is advocated to achieve a higher valve position;[35] however, Kim WK, et al showed rates of PPI or implantation depth were not significantly different between the two views when implanting an ACURATE neo2. The top-down deployment system of neo2 in which the upper crown initially anchors the native leaflets inhibits it from going too deep, and thus the implantation depth is not affected or modified by the 2-cusp overlap view.[36]

Caution is needed when comparing rates of PPI as numerous factors such as baseline conduction disturbance, aortic valve calcification and valve oversizing, as well as implantation depth and membranous septum length can affect results.[37] In addition, the indication and threshold of PPI are different across centers. Thus, this needs to be formally evaluated by direct comparisons in RCTs.

Postprocedural Transvalvular Pressure Gradient

Postprocedural echocardiographic results are shown in Table 2. Three of five studies comparing ACURATE neo2 and neo reported similar mean postprocedural transvalvular pressure gradients,[17,18,21] whilst in two they were significantly higher with ACURATE neo2.[19,20] In propensity-matched analyses, a marginally higher pressure gradient was seen with neo2 compared to neo (10.6 ± 4.8 mmHg in neo2, and 9.0 ± 6.1 mmHg in neo, $p = 0.045$, Table 4),[20] which was speculated to be due to the longer sealing skirt of neo2 hindering full expansion of the THV frame. A similar finding was seen in the comparison between SAPIEN 3 and SAPIEN 3 Ultra, which has a 40% higher sealing skirt compared to SAPIEN 3.[20,38] Compared to SAPIEN 3 Ultra, ACURATE neo2 was associated with significantly lower postprocedural transvalvular mean pressure gradients (Entire cohort: 9 ± 4 vs. 13 ± 5 mmHg, $p < 0.001$, Matched cohort: 9 ± 4 vs. 13 ± 4 mmHg, $p < 0.001$) and a lower incidence of a mean pressure gradient ≧20 mmHg (Entire cohort:1.8 vs. 9.3%, $p < 0.001$, Matched cohort: 2.4 vs. 7.7%, $p < 0.001$).[24] These results are consistent with previous observations that supra-annular leaflet designs lead to lower pressure gradients compared to the intra-annular designs.[39] Notably, whilst the postprocedural transvalvular mean gradients in the two propensity-matched studies which compared ACURATE neo2 to Evolut PRO or PRO/PRO+ were low in both groups, they were still significantly higher with ACURATE neo2 (9 [7-12] vs. 8 [6-11] mmHg, $p = 0.001$, and 9.0 ± 4.0 vs. 7.7 ± 4.0 mmHg, $p < 0.001$, respectively).[22,23] This finding may be due to the relatively higher rate of use of the 29 mm valve in the Evolut groups.

Careful interpretation is needed when comparing postprocedural pressure gradients as it is significantly influenced by patient background as well as anatomical and procedural characteristics (e.g., annular and THV size, predilatation and postdilatation, valve expansion).

Commissural Alignment

Commissural alignment is an emerging topic in the field of TAVI, with its potential benefits easier coronary access and better valve performance.[40] All ACURATE series have three highly-visible commissural posts under fluoroscopy which facilitates the assessment of orientation.

The NeoAlign study assessed commissural alignment of the ACURATE neo2 in 170 consecutive patients using a specific technique (Karolinska commissural alignment technique).[15] In short, they assessed the orientation of the commissural posts and wings of neo2 in the right-left cusp overlap and 3-cusp views and torqued the catheter to achieve the optimal orientation before deployment of the THV (Figure 4). Postdeployment fluoroscopic assessment showed that 97% of patients achieved successful alignment (≦ mild misalignment), with the 3 easily identifiable commissural posts and the superior torque-ability of the neo2 delivery system contributing to the favorable result. The clinical impact of commissural alignment remains to be investigated in long-term follow-up.

Leaflet Thrombosis/Hypo-Attenuated Leaflet Thickening (HALT)

Leaflet thrombosis, which is identified as HALT by multidetector computed tomography (CT), is another emerging interest; however, its clinical significance is yet to be fully understood. A substudy of the PARTNER 3 trial reported the incidence of HALT after implantation of the SAPIEN3 THV to be 13% at 30 days and 28% at 1 year, with clinically significant valve thrombosis seen in 2%, and the presence of HALT at 30 days associated with a higher risk of composite thrombotic events during 1-year follow-up.[41] On the other hand, in the substudy of the Evolut low-risk trial, whilst the incidence of HALT was higher being 17% at 30 days and 30% at 1 year after TAVI, clinical valve thrombosis only occurred in 0.5%, and no association was seen between the presence of HALT at 30 days and clinical events up to 1 year.[42]

The rate of HALT at 6 months after implantation of ACURATE neo or neo2 in the population of the PREDICT PVL study was 16% (8/50), with no significant between-device difference (neo 14%, 4/28 vs. neo2 18.2%, 4/22).[43] The ACURATE neo2 postmarketing surveillance study reported that the incidence of HALT was 24.5% (50/204) at 30 days and 32.0% (49/153) at 1 year, with no association observed between its presence at 30 days or 1 year and echocardiographic or clinical outcomes at 1 year.[14] The incidence of HALT differs depending on the type of THV, timing of assessment, use of oral anticoagulant and patient comorbidity. The association between ACURATE neo2 and HALT needs to be formally investigated in a larger population with longer follow-up.

The GALILEO 4D CT substudy showed that compared to antiplatelets, rivaroxaban reduced the incidence of HALT at 3 months after implantation of a balloon-expandable or self-expanding THV.[44] However, in the main GALILEO trial, the rivaroxaban-based strategy was associated with higher risks of death, thromboembolic events and bleeding events compared to the antiplatelet-based strategy.[45] Notably the mean age of patients in the study was about 80 year old, and more than half the patients had intermediate or high STS risk. Furthermore, several types of THVs of different generations were included. The safety and efficacy of oral anticoagulant therapy may differ in younger patients with less comorbidities and specific THV. The ACURATE neo2 post marketing surveillance study reported that HALT was not detected at 30 days and 1 year follow-up in patients on oral anticoagulants, while in a sub-study of PREDICT PVL, 25% (2/8) of patients with HALT at 6 months received oral anticoagulation.[14,43] Clearly further investigations are needed to establish the optimal antithrombotic therapy after TAVI.

Ongoing Randomized Controlled Trials

To date, there are no completed RCTs involving ACURATE neo2; however, several trials are ongoing. ACURATE IDE (NCT03735667) is investigating 1-year clinical outcomes in patients with severe AS treated by ACURATE neo2 vs. SAPIEN3, Evolut R/PRO, or their new iterations. DOUBLE-CHOICE (NCT05036018) is comparing 30-day outcomes between ACURATE neo2 and Evolut PRO/PRO+, using a minimalist approach and standard of care.

ACURATE Prime XL

ACURATE Prime XL was developed to treat patients with a larger annulus diameter (26.5-29 mm). Its design is similar to neo2 but Prime XL has greater radial strength than neo2. Recently, the Prime XL human feasibility study reported favorable 30-day outcomes after implantation of Prime XL in 13 patients with severe AS.[46]

Limitation

This review has several limitations. First, most studies listed in Tables 1 and 2 were multi center studies, and since some institutions and study periods overlapped, it is likely that patients also did. Hence caution is needed in interpreting the event rates and overall averages could not be obtained. Instead, we calculated total event rates and the 95% confidence intervals of studies where there was no overlap of patients (Supplemental Table 2). Second, to date, no RCTs of ACURATE neo2 have been presented, thus only observational studies were included in this review. Comparative studies were not performed in the same population or at the same time. Many of the included studies lack clinical event adjudication by an independent committee or assessment by an echocardiographic core lab. Although propensity-matched analyses were conducted in the five comparative studies, there could still be biases related to patient, anatomical and procedural characteristics. Third, long-term follow-up data of ACURATE neo2 are scarce; the ACURATE neo AS study and post marketing surveillance study reported 1-year clinical outcomes; however, more research is needed to validate the long-term safety and efficacy of the device.[11,14]

Conclusions

ACURATE neo2, the new iteration of the ACURATE family, demonstrated favorable short-term performance by considerably reducing PVL compared to its predecessor, and having short-term clinical and echocardiographic outcomes which were comparable to contemporary THVs. The device has many of the most desirable properties of self-expanding and balloon expandable THVs, with lower pressure gradients and a low incidence of PPI. RCTs which directly compare outcomes against other THVs and long-term follow-up data are awaited.

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Authors did not use any AI technologies during the preparation of this work.

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Supplementary Material

Supplemental data for this article can be accessed on the publisher's website.

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