

# Presence of Moderate or Severe Regurgitation after Transcatheter Aortic Valve Implant with the Cusp Overlap Strategy

*Presencia de regurgitación moderada o grave luego del implante percutáneo de la válvula aórtica con la estrategia de "Cusp Overlap"*

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## ABSTRACT

**Background:** The aim of this study is to whether higher transcatheter aortic valve implantation (TAVI) with self-expandable valves using the right and left cusp overlap strategy (Cusp Overlap, COVL) is associated with a lower incidence of moderate or severe paravalvular regurgitation (PVR), compared with the conventional strategy (CON).

**Methods:** A total of 206 consecutive patients undergoing TAVI with self-expandable valves between August 2019 and May 2022 were analyzed. The CON technique was used in the first 101 patients (49%) and COVL was used in 105 (51%).

The primary endpoint (PEP) was the presence of moderate or severe paravalvular regurgitation at 30 days.

**Results:** There were no clinical differences between the groups in terms of mean age, sex or comorbidities, except for a trend towards more patients with diabetes and previous percutaneous coronary intervention in the COVL group.

The STS score was greater in the COVL group ( $6.9 \pm 2.2$  vs.  $5.8 \pm 2.4$  in the CON group;  $p = 0.01$ ).

There was no difference in the PEP at 30 days with 2% incidence of moderate PVR in the CON group and 0.9% in the COVL group, and none of them presented severe PVR. There were no differences in mortality, myocardial infarction, coronary artery obstruction, stroke, major bleeding or vascular complications. The need for permanent pacemaker was lower with the COVL strategy (6.7% vs. 17.8%,  $p = 0.01$ ) and a new left bundle branch block occurred in 5.7% vs. 12.9% ( $p = 0.07$ ).

**Conclusions:** In this single-center series, the strategy of high transcatheter aortic valve implantation using the COVL strategy showed no difference in the presence of moderate or severe regurgitation compared with the conventional strategy, with no differences in complications, and was associated with a lower need for definitive pacemaker and with a trend towards lower incidence of left bundle branch block at 30 days.

**Key words:** Aortic Valve Insufficiency - Self Expandable Metallic Stents - Transcatheter Aortic Valve Replacement

## RESUMEN

**Introducción:** Analizar si la estrategia del implante alto usando superposición de las cúspides derechas e izquierdas (Cusp Overlap, COVL) en el implante percutáneo de la válvula aórtica (TAVI) se relaciona con menor incidencia de regurgitación paravalvular (RPV) moderada o grave, comparada con la estrategia convencional (CON).

**Material y métodos:** Se analizaron 206 pacientes consecutivos que recibieron TAVI con válvulas autoexpandibles entre agosto de 2019 y mayo de 2022. Se utilizó una estrategia CON en 101 pacientes (49%) y COVL en 105 (51%).

El Punto Final Primario (PFP) fue la presencia de regurgitación paravalvular moderada y grave a 30 días.

**Resultados:** No hubo diferencia clínica entre los grupos en cuanto a la edad media, sexo ni comorbilidades; excepto una tendencia a más diabetes y angioplastia coronaria previa en el grupo COVL. El STS score fue mayor en el grupo de COVL ( $6,9 \pm 2,2$  vs.  $5,8 \pm 2,4$  en CON,  $p = 0,01$ ).

A 30 días no hubo diferencia en el PFP (RPV moderada en 2% en CON, y 0,9% en COVL; ninguno presentó RPV grave). Tampoco hubo diferencia en mortalidad, infarto, oclusión coronaria, accidente cerebrovascular, sangrado mayor y complicación vascular. La necesidad de marcapasos definitivo fue menor con la estrategia de COVL (6,7% vs. 17,8%,  $p = 0,01$ ) y un nuevo bloqueo de rama izquierda ocurrió en 5,7% vs. 12,9% ( $p = 0,07$ ).

**Conclusiones:** En esta serie de un solo centro, la estrategia del implante alto de la válvula aórtica percutánea usando la técnica de COVL no demostró diferencia en la presencia de regurgitaciones moderadas o graves comparada con la estrategia convencional, sin presentar diferencia en las complicaciones, y se asoció a una menor necesidad de marcapasos definitivo y a una tendencia de menos bloqueos de rama izquierda a 30 días.

**Palabras clave:** Insuficiencia de la Válvula Aórtica - Stents Metálicos Autoexpandibles - Reemplazo de la Válvula Aórtica Transcáteter

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## INTRODUCTION

Transcatheter aortic valve implantation (TAVI) has shown its benefit in high-risk or inoperable patients, (1,2) those at intermediate risk (3,4) and also in low-risk patients. (5,6)

According to different analyses, the presence of mild paravalvular regurgitation (PVR) occurs in 20% to 40% of the cases, (7) while moderate or severe PVR in about 3% to 12% (2) and has been associated with higher mortality rates. (8,9) Although the incidence of PVR has decreased with the learning curve of the operators and the new devices, it represents a complication that should be avoided or managed during the procedure.

Another issue with self-expandable valves is the need for implantation of a permanent pacemaker (PPM), with an incidence of about 17%-30% in large, randomized studies. (2-6)

To overcome these limitations, higher implant of percutaneous aortic valves using a view where the right and left cusps are overlapped (Cusp-overlap, COVL) is a technique developed to reduce contact with the membranous septum and conduction system and thereby reduce the need for PPM. (10)

This strategy has demonstrated a significant decrease in the need for PPM in some observational series, (11-13) but the impact on the incidence of perivalvular leaks leading to moderate or severe regurgitation has not been clearly evaluated.

## METHODS

We analyzed 206 consecutive patients undergoing TAVI with self-expandable valves between August 2019 and May 2022. The conventional technique (CON) was used in the first 101 patients (49%) and the COVL strategy in the subsequent 105 (51%).

Patients with previous surgical bioprosthetic valves, prior PPM, bicuspid aortic valve or pure or predominant aortic regurgitation as indication of TAVI or implant of a balloon-expandable valve were excluded from the study.

The primary endpoint (PEP) was the presence of moderate or severe PVR at 30 days, defined according to the criteria of the VARC-3. (14) The incidence of the following events was also analyzed: all-cause mortality, acute myocardial infarction (MI), acute coronary artery obstruction due to TAVI, stroke, major bleeding (as defined by VARC), vascular complication, emergency cardiac surgery, reintervention, need for PPM implantation, and new-onset left bundle branch block (LBBB) persistent at 30 days.

Implant success (IS) was defined as adequate valve implant with a residual gradient <10 mm Hg at the end of the procedure in the absence of severe regurgitation, and clinical success (CS) as IS in the absence of death, acute MI, stroke, reintervention or urgent valve surgery.

All the patients were evaluated by the hospital "Valve Heart Team", with Doppler-echocardiography, coronary angiography with aortography, and a multi-slice contrast-enhanced computed tomography angiography with 3D reconstruction of the aortic valve, thoracic aorta, abdominal aorta, and subclavian, iliac and femoral arteries. An electrocardiogram (ECG) was recorded before TAVI, at 24 hours and at 30 days. Color Doppler-echocardiography was performed before TAVI, immediately after and at 30 days.

Anesthesia with conscious sedation was used, except for those in whom a percutaneous femoral access was not used and thus required general anesthesia. All patients received dual antiplatelet therapy with aspirin and clopidogrel; in those patients receiving oral anticoagulants for any other reason, only clopidogrel was indicated.

Anticoagulation with heparin 100 U/Kg was used during the procedure, with values controlled during its course.

In patients receiving implants with the CON strategy, the valve was positioned and implanted using the coplanar 3-cusp projection according to the computed tomography angiography and usually corrected by the left anterior oblique slightly cranial angiographic projection. The implantation was performed having as target an implant depth of approximately 2-4 mm below the aortic annulus under high stimulation frequency (120 bpm) with temporary pacing, at the operator's discretion.

In those undergoing the COVL strategy, the computed tomography angiography was previously analyzed in detail, identifying the projection where there was right and left cusp overlap, in opposition to the non-coronary cusp, and this was chosen as the projection for the implantation. In case of difficulties or differences, corrections were made according to the previous angiography.

When this was not feasible, positioning was performed using two pigtail or Amplatz AL2 catheters placed in the right and left sinuses, and then the angiographic projection showing cusp overlap was sought.

Usually, the COVL projection coincides with a caudally oriented right oblique projection.

The target was implantation approximately 2-3 mm below the aortic annulus with respect to the non-coronary sinus.

At the time of the final deployment, overstimulation with temporary pacemaker at 120 beats per minute was used to achieve system stability.

Both pre-dilation with a balloon diameter lower than that of the aortic annulus and post-dilation were performed according to the operator's criterion.

All the patients were followed-up at 30 days with a face-to-face visit and analysis of PVR by Doppler-echocardiography performed 30 days after the implant.

## Ethical considerations

The study was conducted following the recommendations of the Declaration of Helsinki and the International Conference of Good Clinical Practice. All patients signed an informed consent form before participating in the study. Their identity was preserved for the moment of the analysis.

## Statistical analysis

Continuous variables are presented as mean and standard deviation and categorical variables as absolute value and percentage. The Student's t test was used to compare continuous variables and the chi-square test or Fisher's exact test was used for categorical variables. A p value < 0.05 was considered statistically significant.

## RESULTS

The clinical characteristics of the populations were similar; age was  $79.8 \pm 7.9$  years vs.  $80.4 \pm 6.9$  years in the CON strategy vs. COVL strategy, and 48.5% were male vs. 55%. There was no difference in the prevalence of hypertension, previous MI, history of coronary artery surgery, percutaneous coronary intervention (PCI) before TAVI, chronic obstructive pul-

monary disease (COPD), renal function, and dialysis. Diabetes and PCI were slightly more common in the COVL group (20.8% vs. 32.3%,  $p = 0.06$ , and 31.7% vs. 44.8%  $p = 0.05$ , respectively).

The STS risk score was greater in the COVL group ( $5.8 \pm 2.4$  vs.  $6.9 \pm 2.2$ ,  $p = 0.01$ ).

There were no differences in the baseline ECG in terms of previous conduction disorders as atrioventricular (AV) block, right bundle branch block (RBBB), LBBB, or atrial fibrillation.

There was also no difference in left ventricular ejection fraction, mean trans-aortic gradient or aortic valve area.

Femoral access was used in all the p except for 2 p. in the COVL group who underwent subclavian access. Pre-dilation was greater in this group (87.6% vs. 57.4%,  $p < 0.001$ ) with no differences in the use of post-dilation. There was no difference in the use of percutaneous closure, which was done with any of the following devices: PROSTAR XL® (ABBOTT Vascular, Santa Clara, California) and Proglide® (ABBOTT Vascular, Santa Clara, California). (Table 1).

Self-expanding valves were implanted in all the pa-

tients. (Table 2)

There was no difference in the PEP at 30 days between both strategies (Figure 1), with 2% incidence of moderate PVR in the CON group and 0.9% in the COVL group, and there were no cases of severe PVR. There was no difference in mortality, acute MI, coronary obstruction, stroke, cardiac surgery, reoperation, vascular complication or major bleeding.

The COVL strategy resulted in a significant reduction in conduction disorders after implantation, with a lower need for PPM (6.7% vs. 17.8%;  $p = 0.01$ ) and a trend towards less development of new LBBB (5.7% vs. 12.9%;  $p = 0.07$ ). Of the patients requiring PPM, 6 were  $\geq 80$  years and only one patient presented normal sinus rhythm. One patient had previous atrial fibrillation, one presented first degree AV block, another had LBBB, and one had trifascicular block. (Table 3) (Figure 2)

## DISCUSSION

In our series, TAVI with the COVL technique was not significantly associated with a difference in the presence of PVR compared with the conventional strategy,

**Table 1.** Characteristics of the population

	CON (101 p.)	COVL (105 p.)	p value
Age, years, (mean $\pm$ SD)	79.8 $\pm$ 7.9	80.4 $\pm$ 6.9	0.41
Men	49 (48.5)	58 (55.2)	0.33
Hypertension	90 (89.1)	98 (93.3)	0.20
Diabetes	21 (20.8)	34 (32.3)	0.06
Previous MI	23 (22.7)	18 (17.1)	0.31
Previous CABGS	19 (18.8)	16 (15.2)	0.42
Previous PCI	32 (31.7)	47 (44.5)	0.05
PCI before TAVI	22 (21.8)	30 (28.6)	0.18
COPD	19 (18.8)	13 (12.4)	0.22
Stroke	5 (4.9)	4 (3.8)	0.68
eGFR	60.1 $\pm$ 19.3	61.8 $\pm$ 20.1	0.44
Dialysis	3 (3)	4(3.8)	0.73
Mortality according to STS score	5.8 $\pm$ 2.4	6.7 $\pm$ 2.2	0.01
Atrial fibrillation	16 (15.8)	25 (23.8)	0.43
AV block	6 (5.9)	7 (6.7)	0.83
RBBB	10 (9.9)	9 (8.6)	0.73
LBBB	10 (9.9)	15 (14.3)	0.33
LVEF (%)	52.7 $\pm$ 13.4	53.1 $\pm$ 12.6	0.45
AVA	0.71 $\pm$ 0.15	0.73 $\pm$ 0.9	0.43
Mean gradient (mm Hg)	40.8 $\pm$ 10.7	41.3 $\pm$ 10.2	0.35
Femoral access	101 (100)	103 (98.1)	0.16
Subclavian access	-	2 (1.9)	0.16
Pre-dilation	58 (57.4)	92 (87.6)	<0.001
Post-dilation	25 (24.5)	36 (34.3)	0.92
Pop-Up	-	-	
Percutaneous closure	100 (99)	103 (98.1)	0.58

AV: atrioventricular. AVA: aortic valve area. CABG: coronary artery bypass grafting. CON: conventional COPD: chronic obstructive pulmonary disease. COVL: Cusp overlap. eGFR: estimated glomerular filtration rate LBBB: left bundle branch block. LVEF: left ventricular ejection fraction. MI: myocardial infarction. p.: patients. PCI: percutaneous coronary intervention. RBBB: right bundle branch block. SD: standard deviation. STS: Society of Thoracic Surgeons. TAVI: transcatheter aortic valve implantation. Categorical variables are presented as n(%) and continuous variables as mean  $\pm$  SD.

but there was less need for PPM and lower incidence of LBBB, with no differences in mortality, acute MI, stroke, coronary obstruction, major vascular complications and major bleeding, cardiac surgery or reintervention.

Of the 7 p. in our series requiring PPM, 6 were ≥ 80 years and 5 presented a significant conduction disorder.

The presence of PVR has been related to valvular calcification with a generally asymmetrical pattern with dominating non-coronary leaflet and sinus calcification in most p. (15) Different studies have analyzed the presence of calcium and its quantity in the implant site (16,17) and demonstrated that asymmetry in calcification is related to PVR. (18) Some authors analyzed the presence of calcium in the left ventricular outflow tract which could be a risk factor for PVR. However, we must also consider that calcification of the annulus may contribute to annular rupture, especially in balloon-expandable valves in case of aggressive pre-dilation or post-dilation and need for a second valve. (19-21)

Total device landing zone calcium volume could predict the degree of PVR: none with 389 mm<sup>3</sup>, mild with 371 mm<sup>3</sup>, moderate with 690 mm<sup>3</sup> and severe PVR with 777 mm<sup>3</sup>. We should also analyze asymmetry in the CT scan as it is a predictor of PVR. (22)

The risk of moderate or severe PVR is lower in women; this seems to be related to a smaller diameter annulus that facilitates perivalvular sealing. (23)

The presence of moderate to severe regurgitation was more common at the beginning of the experience and with the first-generation devices. The learning curve of the operators, which has improved the implants, and the new devices with a perivalvular "skirt" at the base to improve sealing, have led to a significant reduction of this phenomenon.

Although the use of the COVL technique seems to help in the same sense (in fact, in our series PVR decreased by 50%), a greater number of patients would be needed to obtain considerable higher differences than those of our experience.

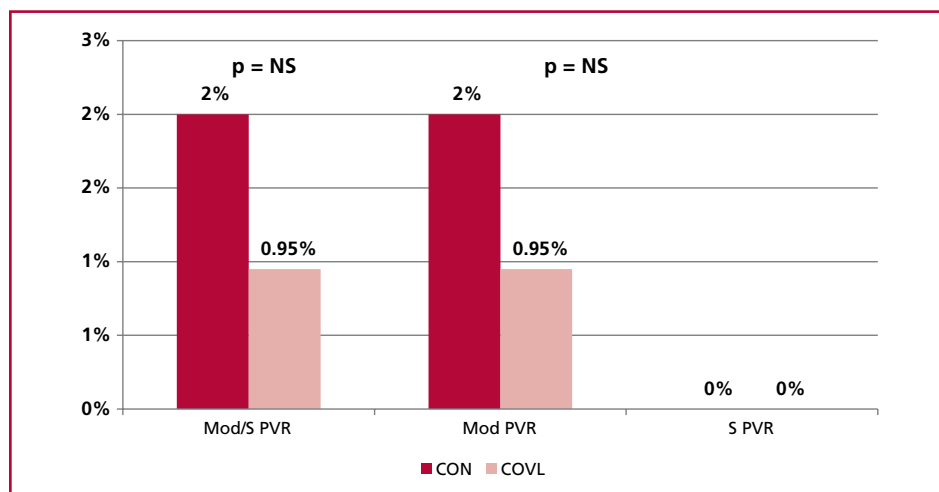
The presence of moderate or severe PVR is often associated with low functional class dyspnea or even hemolysis. One of the treatments proposed to avoid surgery is closure of PVR with plugs under transesophageal Doppler echocardiography. Although this strategy is not easy to perform and is not frequently used, it has demonstrated favorable outcome in some publications with a low rate of complications. (25)

An important meta-analysis evaluated the outcome of patients with PVR at 4 years. Those with moderate to severe PVR had higher mortality than those with mild or minimal PVR. But when first-generation valves were compared with second-generation valves, the incidence of PVR was significantly lower with second-generation valves. Mild PVR had higher 4-year mortality rate than minimal PVR. For this reason, it is currently necessary to be extremely accurate at the time of implantation, choosing the most suitable device and performing post-dilations if necessary to leave the minimal regurgitation possible; ideally, absolutely no regurgitation.

Our group started several years ago with the implantation of self-expandable valves with the COVL strategy. In our publications, we demonstrated a significant decrease in the need for PPM after implantation and a trend towards lower LBBB without increasing the incidence of complications or valve

**Table 2.** Prosthetic valves implanted

	CON n (%)	COVL n (%)
Evolut-Evolut R®/PRO®	101 (100%)	79 (74.5)
Accurate Neo®	-	15 (14.3)
PORTICO®	-	11 (11.2)



**Fig. 1.** Primary end point

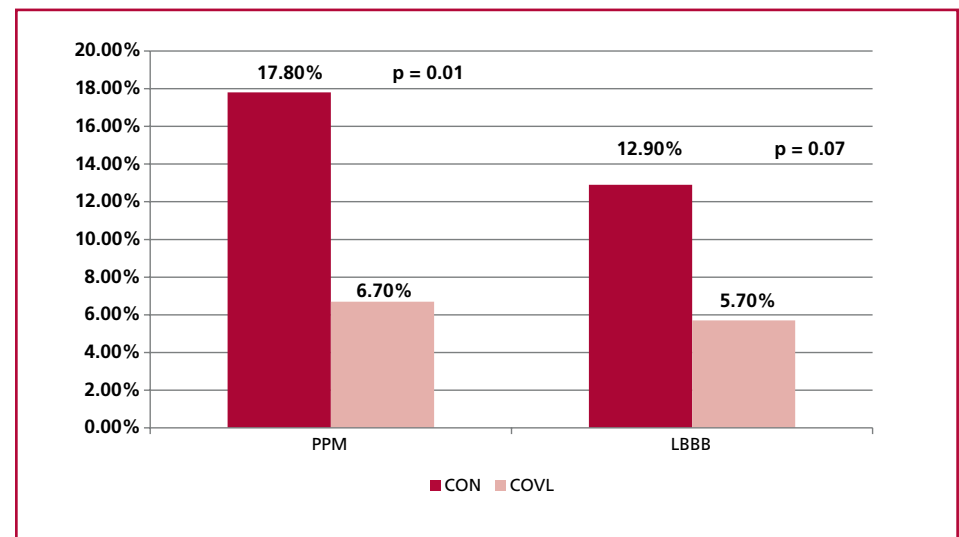
CON: conventional. COVL: Cusp overlap. Mod: moderate. PVR: paravalvular regurgitation. S: severe

**Table 3.** Outcomes at 30 days

	CON (101 p.) n (%)	COVL (105 p.) n (%)	p
Implant success	101 (100)	105 (100)	-
Clinical success	5 (4.9)	5 (4.8)	0.94
Moderate PVR	2 (2)	1 (0.95)	0.53
Severe PVR	-	-	-
Death	5 (4.9)	3 (2.8)	0.43
Infarction	-	1 (0.95)	1
Coronary obstruction	-	1 (0.95)	1
Stroke	-	1 (0.95)	1
Major bleeding	2 (2)	1 (0.95)	0.53
Vascular complication	2 (2)	4 (3.8)	0.43
PPM	18 (17.8)	7 (6.7%)	0.01
New-onset LBBB	13 (12.9)	6 (5.7)	0.07
Cardiac surgery	-	-	-
Reintervention	-	-	-

CON: conventional. COVL: Cusp overlap. LBBB: left bundle branch block. p.: patients. PPM: permanent pacemaker. PVR: paravalvular regurgitation

**Fig. 2.** Permanent pacemaker and new onset left bundle branch block.



CON: conventional. COVL: Cusp overlap. LBBB: left bundle branch block. PPM: permanent pacemaker.

embolization. In our publications, implants were performed with different self-expanding valves in the COVL group. (11,12)

We believe that this strategy offers benefits, and although we did not observe a significant difference in the incidence and severity of PVR that would have an impact on survival, the reduction in conduction disorders after implantation justifies its implementation, since conduction disorders also have an impact on survival and on hospital and long-term costs. (26,27)

**Study limitations**

The lack of randomization and the fact that this analysis was performed in a single center are the limitations of this study. In order to try to avoid the influence of the learning curve, a historical series of the last 101 patients treated with the CON strategy was compared

with the first 105 patients treated with the higher transcatheter aortic valve implantation strategy.

**CONCLUSIONS**

In this single-center series, the strategy of high transcatheter aortic valve implantation showed no difference in the presence of moderate or severe PVR compared with the conventional strategy with no differences in complications and was associated with a lower need for definitive pacemaker and a trend towards lower incidence of LBBB at 30 days.

**Conflicts of interest**

Oscar A. Mendiz is proctor in Latin America for Evolut, Accurate and Edwards Valves.

(See authors conflicts of interest forms in the website/ Supplementary material)

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