



Editorial

New-Onset Left Bundle Branch Block Post-TAVI: No More an Innocent Bystander

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See article by Eschalier et al., pages 1386–1393 of this issue.

Transcatheter aortic valve implantation (TAVI) has brought a new era in the treatment of aortic stenosis. During the last years, the successive iterations of transcatheter heart valve (THV) systems and the growing experience of centres/operators have translated into a progressive reduction in peri-procedural complications. However, conduction disturbances, such as high-degree atrioventricular block and new-onset left bundle branch block (LBBB), have not decreased over time and remain the most frequent drawback of the procedure.¹ The incidence of new-onset LBBB with the use of newer-generation THVs has ranged from 6% to 77%.² The use of different definitions of new-onset LBBB (mainly different time points), along with differences in baseline and procedural characteristics (including valve type, valve positioning), may explain this large variability in incidence.

Multiple studies have evaluated the relationship between new-onset LBBB and midterm clinical outcomes. Although inconsistent results were reported regarding association with all-cause mortality,^{1–6} there has been a more consistent association with an increased risk (about 2-fold) of high-degree conduction disturbances leading to permanent pacemaker implantation (PPM) across studies.^{1–4,6} In addition, several studies have evaluated the relationship between new-onset LBBB post-TAVR and changes in left ventricular ejection fraction (LVEF)^{4,6–12} (Table 1). Overall, a consistent association with deterioration in left ventricular (LV) function (vs patients with no LBBB) was observed across studies. Some studies have also shown a relationship between new-onset LBBB post-TAVR and rehospitalizations at midterm follow-up.^{4,5}

In this issue of the *Canadian Journal of Cardiology*, Eschalier et al.¹³ contribute another piece of information regarding the association between new-onset LBBB and LV function. The work is a secondary analysis of the LBBB-TAVI

study (NCT02482844),¹⁴ which consists of prespecified management of patients with new-onset LBBB with an electrophysiological study (EPS), followed by continuous electrocardiographic (ECG) monitoring in those with no (in-hospital) PPM post-TAVI. In-hospital PPM need was indicated by the presence of a His-ventricular interval > 70 ms on EPS. The study included 40 patients with new-onset LBBB (that persisted at 24 hours post-TAVI) compared with 40 matched (by LVEF and age) patients from the same period who did not develop LBBB. Baseline and procedural characteristics were generally well-balanced between the 2 groups, but patients with new-onset LBBB more frequently had hypertension and were more frequently treated with self-expanding valves (vs balloon-expandable). After a mean follow-up of 8 months, new-onset LBBB was associated with a 5%-point decrease in LVEF, in contrast to the non-LBBB group (increase of 1.5%-point in LVEF, $P < 0.001$). In addition, this reduction in LVEF was more prominent in patients with previous LV dysfunction (LVEF < 50%) and when LBBB persisted beyond 6 months after the TAVI procedure. No differences in clinical outcomes (hospitalization for heart failure or mortality) were observed between groups.

Although multiple previous studies have already determined the negative impact of new-onset LBBB post-TAVI on ventricular function^{4,6–12} (Table 1), this is the first prospective matched analysis of this topic. Interestingly, the results regarding the degree of LVEF deterioration at follow-up were similar to those reported in previous studies (Table 1).

Definition, Incidence of New-Onset LBBB

Eschalier et al. defined new-onset LBBB when it persisted for at least 24 hours post-TAVI.¹³ As previously mentioned, multiple definitions of new-onset LBBB have been used across studies, and no clear consensus exists on the most appropriate definition. It is well known that a proportion of conduction disturbances resolve within the days following the procedure, and a more conservative definition (eg, LBBB that persists up to 3 days or at hospital discharge; the most common definitions used to date) would have probably been more accurate to avoid the inclusion of patients with early LBBB regression.

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Table 1. Impact of new-onset LBBB post-TAVI on LVEF

Study	n	Type of valve	Incidence of new-onset LBBB	Baseline LVEF (%)			Follow-up	Δ LVEF (%)		
				New-onset LBBB	No LBBB	<i>P</i> value		New-onset LBBB	No LBBB	<i>P</i> value
Urena et al. 2012 ⁷	202	Balloon expandable (100%)	38 (18.8%)	57 ± 12	58 ± 11	0.44	1 year	-4.75	+2.52	0.001
Testa et al. 2013 ⁸	818	Balloon expandable (100%)	354 (43.3%)	53 ± 11	51 ± 13	0.83	1 year	+3	+4	0.56
Urena et al. 2014 ⁹	668	Balloon expandable (100%)	128 (19.2%)	56 ± 13	56 ± 11	0.841	1 year	+0	+4	0.007
Nazif et al. 2014 ¹⁰	1151	Balloon expandable (100%)	121 (10.5%)	54.4 ± 11	55.4 ± 11.8	0.24	1 year	-1.8	+2.9	< 0.001
Carraba et al. 2015 ¹¹	92	Self-expanding (100%)	34 (37%)	48 ± 12	48 ± 15	0.818	1 year	+1	+4.5	< 0.05
Dobson et al. 2017 ¹²	48	Self-expanding: 17 (71%) Mechanically expandable: 7 (29%)	24*	56.6 ± 10.5	54.1 ± 11.5	0.386	6 months	-2.2	+4.6	0.002
Chamandi et al. 2019 ⁶	1020	Self-expanding: 470 (46.1%) Balloon expandable: 526 (51.6%)	212 (20.7%)	62 ± 12	58 ± 12	0.607	3 years	-1.4	+1.9	< 0.001
Nazif et al. 2019 ⁴	1179	Balloon expandable (100%)	179 (15.2%)	59.7 ± 10.1	58.5 ± 11	0.18	2 years	-4.3	+0.1	< 0.001

LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; TAVI, transcatheter aortic valve implantation.

* Matched with 24 non-LBBB patients.

Nevertheless, the rate of LBBB persistence at 6-month follow-up (58%) was similar to that observed in the MARE trial at 1-year follow-up (62%),¹⁵ when new-onset LBBB was defined as the one persisting for at least 3 days post-TAVI. However, the incidence of new-onset LBBB (9.6%) shown in the work by Eschalier et al.¹³ was surprisingly low compared with most recent studies using newer generation transcatheter valves.²

Sample Size Issues, Lack of Echocardiography Core Lab

As the investigators themselves recognize, it is important to note that the sample size of the work by Eschalier et al. was very small. In addition to the small number of patients included initially, a significant proportion of conduction disturbances had resolved at follow-up (17 of 40, 43.5%), with only 23 patients maintaining the LBBB abnormality at the 8-month echocardiographic assessment. Thus, some unmeasured confounders and/or bias cannot be excluded with such a small number of patients. More specifically, only 7 patients per group had LV dysfunction (LVEF < 50%) at baseline. Thus, the results from this study must be interpreted with caution and should be considered as primarily hypothesis generating. In addition, the lack of echocardiography core lab was an important limitation, particularly considering both the limited sample size and the primary outcome (LVEF changes) of the study.

Patient Selection

Approximately 25% of TAVI candidates have atrial fibrillation (AF; pre-existing and new-onset), which has indeed been associated with poorer outcomes.¹⁶ Patients with AF were excluded in the study by Eschalier et al., and no specific reason was provided to justify such a decision. This limits the generalization of the results (limited to those patients in sinus rhythm).

Patients with new-onset LBBB and (in-hospital) PPM had been included in the new-onset LBBB group when the ventricular pacing rate was < 5%. However, the initial percentage of patients with PPM and LBBB was not reported nor was the ventricular pacing rate at follow-up in such patients. Considering that chronic right ventricular pacing can cause LV dysfunction, one may wonder whether this issue (the potential presence of paced patients during follow up in the LBBB group) might have influenced the results.

PPM During the Follow-up Period

The 0% PPM rate during the follow-up period in the new-onset LBBB group was a very surprising finding. As previously discussed, a consistently increased risk of PPM in patients with new-onset LBBB has been reported in previous studies,^{3,4} with PPM rates of 10% to 15% at 1-year follow-up. The fact that all patients had EPS with PPM indication in those with HV interval > 70 ms probably explains such unique results. We can assume that a significant proportion of LBBB patients had PPM implantation before hospital discharge (not reported), and the group with HV interval < 70 ms probably constituted a low-risk group. These results anticipate the likely global results from the LBBB-TAVI study (NCT02482844),¹⁴ with a very original prespecified strategy for managing patients with new-onset LBBB. However, the possibility of overtreatment (ie, high in-hospital PPM rate and low pacing rates at follow-up) will need to be determined.

Conclusion

The results from the study by Eschalier et al. reinforce the concept of new-onset LBBB indicating an increased risk of LVEF-impairment post-TAVI. A causal relationship needs to be considered in light of the well-known negative impact of electromechanical dyssynchrony on LV function, particularly in patients with ventricular dysfunction. In addition to

continued efforts to prevent such a complication, the Eschaliere data highlight the importance of close follow-up of these patients, particularly for those with low LVEF pre-TAVI. In addition, the potential need for implementing such additional measures as resynchronization therapy in these patients should be considered. In an era when TAVI use is expected to expand toward the treatment of the majority of patients with aortic stenoses, studies like the work from Eschaliere et al. emphasize the importance of conduction abnormalities post-TAVI (particularly new-onset LBBB), and underline the fact that they should no more be considered “innocent bystanders.”

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