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ORIGINAL RESEARCH

Myocardial Injury After Balloon Predilatation Versus Direct Transcatheter Aortic Valve Replacement: Insights From the DIRECTAVI Trial

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BACKGROUND: Myocardial injury is associated with higher mortality after transcatheter aortic valve replacement (TAVR) and might be increased by prior balloon aortic valvuloplasty (BAV). We aimed to evaluate the impact of prior BAV versus direct prosthesis implantation on myocardial injury occurring after (TAVR) with balloon-expandable prostheses.

METHODS AND RESULTS: The DIRECTAVI (Direct Transcatheter Aortic Valve Implantation) trial, an open-label randomized study, demonstrated noninferiority of TAVR without BAV (direct TAVR group) compared with systematic BAV (BAV group) with the Edwards SAPIEN 3 valve. High-sensitivity troponin was assessed before and the day after the procedure. Incidence of myocardial injury after the procedure (high-sensitivity troponin elevation >15× the upper reference limit [14 ng/L]) was the main end point. Impact of myocardial injury on 1-month adverse events (all-cause mortality, stroke, major bleeding, major vascular complications, transfusion, acute kidney injury, heart failure, pacemaker implantation, and aortic regurgitation) was evaluated. Preprocedure and postprocedure high-sensitivity troponin levels were available in 211 patients. The mean age of patients was 83 years (78–87 years), with 129 men (61.1%). Mean postprocedure high-sensitivity troponin was 124.9±81.4 ng/L in the direct TAVR group versus 170.4±127.7 ng/L in the BAV group (P=0.007). Myocardial injury occurred in 42 patients (19.9%), including 13 patients (12.2%) in the direct TAVR group and 29 (27.9%) in the BAV group (P=0.004). BAV increased by 2.8-fold (95% CI, 1.4–5.8) myocardial injury probability. Myocardial injury was associated with 1-month adverse events (P=0.03).

CONCLUSIONS: BAV increased the incidence and magnitude of myocardial injury after TAVR with new-generation balloon-expandable valves. Myocardial injury was associated with 1-month adverse events. These results argue in favor of direct SAPIEN 3 valve implantation.

REGISTRATION: URL: https://www.Clinicaltrials.gov; Unique identifier: NCT02729519.

Key Words: balloon aortic valvuloplasty ■ direct implantation ■ myocardial injury ■ transcatheter aortic valve replacement ■ troponin

Systematic balloon aortic valvuloplasty (BAV) before device implantation was considered as the standard of care in the initial transcatheter aortic valve replacement (TAVR) experience to allow both insertion and optimal expansion of the prosthesis.[1] However, regarding improvements in device profiles and increased operators' experience, this step is not currently systematically performed.[2–7] This strategy of direct TAVR was shown to be feasible in observational studies and more recently in a randomized study with the CoreValve

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CLINICAL PERSPECTIVE

What Is New?

- Direct prosthesis implantation may decrease the incidence and severity of myocardial injury compared with prior balloon aortic valvuloplasty in patients undergoing transcatheter aortic valve replacement with balloon-expandable devices.
- Myocardial injury may be associated with an increased risk of conduction disorders and pacemaker implantations.

What Are the Clinical Implications?

- Direct valve implantation should be utilized to decrease the risk of myocardial injury in patients undergoing transcatheter aortic valve replacement with new-generation balloon-expandable devices.

Nonstandard Abbreviations and Acronyms

BAV	balloon aortic valvuloplasty
DIRECTAVI	Direct Transcatheter Aortic Valve Implantation
EuroSCORE	European System for Cardiac Operative Risk Evaluation
hs-TnT	high-sensitivity troponin T
TAVR	transcatheter aortic valve replacement
VARC-2	Valve Academic Research Consortium-2

self-expandable device.[8] BAV may be associated with specific complications as annulus rupture, aortic regurgitation, and cerebral embolization.[2,9–12] Furthermore, rapid pacing, required for BAV, may increase myocardial injury and induce hemodynamic instability after TAVR, particularly in patients with previous left ventricular dysfunction or coronary artery disease.[13,14] Likewise, myocardial injury, defined as troponin elevation >15× the upper reference limit,[15] is a well-known prognostic factor of mortality in patients undergoing TAVR.[16–18] Several factors such as rapid pacing duration, hypotension, embolization, and prosthesis positioning may induce myocardial injury during TAVR procedure. Only 1 observational study evaluated the impact of BAV on postprocedure myocardial injury showing a significant decrease in troponin elevation in patients without BAV with self-expandable Medtronic CoreValve implantation.[19] In this study, troponin elevation after TAVR was associated with poorer prognosis. Our team recently conducted the DIRECTAVI (Direct Transcatheter Aortic Valve Implantation) trial, a randomized trial comparing direct TAVR versus prior BAV in 236 patients with the last-generation Edwards SAPIEN 3 balloon-expandable prosthesis (Edwards Lifesciences).[20] In this study, we demonstrated the noninferiority of the direct TAVR strategy on device success and similar outcomes at 1 month between the 2 study groups.[20]

In the present ancillary study, we aimed to evaluate the impact of BAV on myocardial injury assessed by significant postprocedure troponin increase and subsequent clinical outcomes in patients included in the DIRECTAVI trial.

METHODS

Study Design

The DIRECTAVI trial was a prospective, randomized, single-center, open-label trial using the third-generation balloon-expandable Edwards SAPIEN 3 device. The main hypothesis was the noninferiority of direct TAVR in comparison to systematic BAV before prosthesis implantation. The study protocol was approved by an independent ethics committee (Comité de Protection des Personnes Sud Méditerranée, Montpellier, France, ID RCB: 2015-A01823-46) and all patients provided written informed consent. An independent and out-of-region located safety monitoring committee oversaw the study. The trial was conducted according to the World Medical Association Declaration of Helsinki and all data and materials have been made publicly available at clinicaltrial.gov (NCT02729519).[20]

Patient Population

From May 2016 to May 2018, all patients included in the DIRECTAVI trial (N=236) with available preprocedure and postprocedure high-sensitivity troponin T (hs-TnT) values were included in the present ancillary study. Inclusion and exclusion criteria were previously published and all patients were randomized between the 2 strategies as previously described[20] Figure 1.

Procedure

All TAVR procedures were performed under general anesthesia with the Edwards SAPIEN 3 device and a transfemoral default strategy. Rapid right ventricular pacing (160–200 beats per minute during 10 seconds) was performed through a femoral venous access in both groups for valve deployment and for BAV in the BAV group as previously reported in the DIRECTAVI trial.[20]

hs-TnT Assessment and Follow-Up

Preprocedure and postprocedure hs-TnT measurements were prospectively collected. hs-TnT measurement was

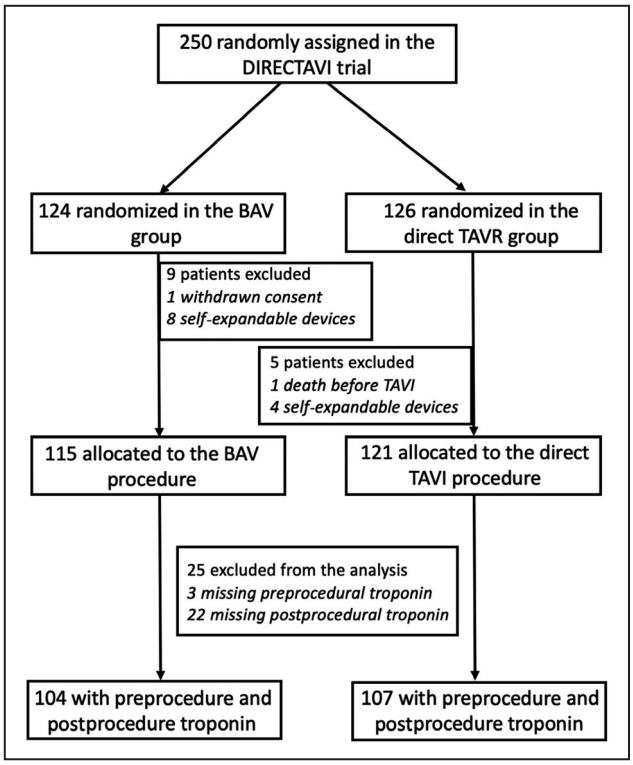

Figure 1. Flow chart of the DIRECTAVI (Direct Transcatheter Aortic Valve Implantation) trial and of the myocardial injury ancillary study.
Among the 236 patients allocated to randomization in the DIRECTAVI trial, preprocedure and postprocedure troponin were available in 211 patients (89.4%) (104 [90.4%] in the balloon aortic valvuloplasty [BAV] group and 107 [88.4%] in the direct transcatheter aortic valve replacement [TAVR] group). TAVI indicates transcatheter aortic valve implantation.

performed on the Cobas 8000/e602 analyzer (Roche Diagnostics) the day before and the day after the procedure. The 99% upper reference limit for this kit is 14 ng/L. For patients requiring revascularization, percutaneous coronary intervention was performed at least 1 week before TAVR. Myocardial injury was defined according to Valve Academic Research Consortium-2 (VARC-2) recommendations as hs-TnT elevation >15× the upper reference limit and at least a 50% increase compared with the preprocedure value.[14] Baseline characteristics and clinical, biological, and procedural data were collected at the time of randomization in the DIRECTAVI trial.[20] Clinical follow-up was performed at 72 hours and 1 month.

Study End Points

The primary end point was the incidence of myocardial injury depending on the group of patients (direct implantation versus BAV). Magnitude of myocardial injury was assessed by mean postprocedure hs-TnT in both groups.

The prognostic impact of preprocedure and postprocedure hs-TnT on 1-month clinical events assessed in the DIRECTAVI trial was also evaluated. These clinical events included all-cause mortality, stroke, major bleeding, major vascular complications, transfusion, acute kidney injury, heart failure, pacemaker implantation, and aortic regurgitation according to VARC-2 criteria.[15] Predictive factors of myocardial injury were also studied.

Statistical Analysis

Patients' characteristics are presented with proportions for categorical variables and as mean±SD and median (interquartile range) for quantitative variables. Characteristics were compared between both groups with the Student *t* test or the Mann–Whiney *U* test for continuous variables, and with chi-square or Fisher exact test for categorical variables. Logistic regressions were executed to analyze predictive factors of myocardial injury. The patients' group was considered as a predictive variable, as well as baseline variables. Univariate models were first performed, and the variables with a *P* value <0.20 were selected for a multivariable logistic model. The variables with a *P* value <0.05 in the multivariate model after a stepwise selection of variables were then considered statistically significant. The occurrence of myocardial injury was included in a Cox survival model and its predictive impact on outcomes was assessed. Statistical analyses were performed using SAS 9.1 software (SAS Institute Inc), and the statistical significance threshold was set at 5%.

RESULTS

Study Population

Between May 2016 and May 2018, preprocedure and postprocedure hs-TnT levels were available in 211 patients (89.4%) included in the DIRECTAVI trial, 104 (90.4%) in the BAV group, and 107 (88.4%) in the direct TAVR group (Figure 1). The median age was 83 years (78–87 years), 129 were men (61.1%), and the mean European System for Cardiac Operative Risk Evaluation (EuroSCORE) II was 2.7% (2–4%). Population baseline characteristics are shown in Table 1. BAV was necessary in 6 patients (5.6%) allocated to direct implantation as a result of medical decision regarding aortic valve heavy calcifications (n=4; 3.7%) or failure to cross the valve (n=2; 1.9%). Preprocedure hs-TnT, C-reactive protein, hemoglobin, and creatinine were not statistically different between both groups (Table 2). Postprocedure hemoglobin count was similar between both groups (11.8 g/dL [95% CI, 11–12.9] in the BAV group versus 11.9 g/dL [95% CI, 10.8–12.8] in the direct TAVR group, *P*=0.9). Postprocedure creatinine level was similar between both groups (90 µmol/L [95% CI, 70–110] in the BAV

Table 1. Baseline Characteristics of the Population

	BAV Group	Direct TAVR Group
	n=104	n=107
Women	39 (37.5)	43 (40.2)
Age, y	3 (79–86)	83 (78–87)
Body mass index, kg/m^2	25.9 (24.2–29.2)	26.7 (24.5–30.1)
Diabetes mellitus	38 (36.5)	41 (38.3)
Previous PCI	45 (43.3)	48 (44.9)
Previous CABG	5 (4.8)	6 (5.6)
Previous BAV	10 (9.6)	10 (9.3)
Cerebrovascular disease	4 (3.8)	4 (3.7)
Peripheral vascular disease	13 (12.5)	9 (8.4)
COPD	7 (6.7)	16 (14.9)
Atrial fibrillation	27 (26.0)	39 (36.4)
Anticoagulant therapy	29 (27.9)	42 (39.5)
Permanent pacemaker	15 (14.4)	13 (12.1)
Pulmonary hypertension	2 (1.9)	2 (1.9)
Creatinine, µmol/L	101 (82–125)	104 (84–131)
Hemoglobin, g/Dl	12.5 (11.8–13.7)	12.3 (11.4–13.4)
C-reactive protein, mg/L	3.2 (1.5–6.3)	4 (1.3–7.8)
hs-TnT, ng/L	27.4 (16.6–39.4)	23.8 (16.2–39.5)
Hypertension	72 (69.2)	65 (60.8)
EuroSCORE I	10 (7–14)	0 (7–14)
EuroSCORE II	2.9 (2–4)	2.3 (2–4)
NYHA class		
I or II	51 (49.0)	50 (46.7)
III or IV	53 (50.9)	57 (53.3)
LVEF, %	60 (50–60)	60 (50–60)
Aortic valve area, cm^2	0.7 (0.6–0.9)	0.8 (0.6–0.9)
Mean aortic valve gradient, mm Hg	6 (40–55)	49.5 (40–58)

Values are expressed as median (interquartile range) or number (percentage). BAV indicates balloon aortic valvuloplasty; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; hs-TnT, high-sensitivity troponin T; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; and TAVR, transcatheter aortic valve replacement.

Table 2. Baseline Characteristics of the Population According to Myocardial Injury

	Myocardial Injury	No Myocardial Injury	
	n=42	n=169	*P* Value
Women	19 (45.24)	63 (37.28)	0.35
Age, y	84.5 (81–87)	83 (78–87)	0.11
Body mass index, kg/m^2	26.6 (24.6–29.4)	26.0 (24.3–29.6)	0.83
Diabetes mellitus	17 (40.5)	62 (36.7)	0.65
Previous PCI	18 (42.9)	75 (44.9)	0.52
Previous CABG	2 (4.8)	9 (5.3)	0.27
Previous BAV	1 (2.4)	19 (11.2)	0.54
Cerebrovascular disease	2 (4.8)	6 (3.5)	0.66
Peripheral vascular disease	5 (11.9)	17 (10.1)	0.78
COPD	0 (0.0)	23 (13.6)	0.01
Atrial fibrillation	5 (11.9)	61 (36.1)	<0.01
Anticoagulant therapy	6 (14.3)	65 (38.5)	<0.01
Permanent pacemaker	5 (11.9)	23 (13.6)	0.77
Pulmonary hypertension	1 (2.4)	3 (1.8)	0.99
Creatinine, µmol/L	103.5 (86–126)	103.0 (82–126)	0.39
Hemoglobin, g/dL	12.5 (12–13.1)	12.3 (11.4–13.7)	0.64
C-reactive protein, mg/L	3.6 (1.8–5.9)	3.3 (1.3–7.7)	0.73
hs-TnT, ng/L	28.8 (18.7–50.6)	24.9 (15.7–38.6)	0.12
Hypertension	35.0 (83.3)	102 (60.4)	<0.01
EuroSCORE I	10 (7–14)	10 (7–14)	0.78
EuroSCORE II	2 (2–3.4)	3 (2–4)	0.39
NYHA class			0.76
I or II	21 (50.0)	80 (47.3)	
III or IV	21 (50.0)	80 (52.7)	
LVEF, %	60 (52.5–60)	60 (46–60)	0.10
Aortic valve area, cm^2	0.7 (0.5–0.8)	0.8 (0.6–0.9)	0.07
Mean aortic valve gradient, mm Hg	46 (40–60)	48 (40–56)	0.96

Values are expressed as median (interquartile range) or number (percentage). BAV indicates balloon aortic valvuloplasty; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; hs-TnT, high-sensitivity troponin T; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and PCI, percutaneous coronary intervention.

group versus 91 µmol/L [95% CI, 70–115] in the direct TAVR group, *P*=0.6).

Postprocedure hs-TnT Elevation and Myocardial injury

The mean hs-TnT value after TAVR procedure was 124.9±81.4 ng/L in the direct TAVR group versus 170.4±127.7 ng/L in the BAV group (*P*=0.007) (Figure 2). Mean postprocedure hs-TnT elevation was 4.4-fold in the whole population, 3.8-fold in the direct TAVR group, and 5-fold in the BAV group. Myocardial injury occurred in 42 patients (19.9%), including 13 patients (12.2%) in the direct TAVR group and 29 (27.9%) in the BAV group (*P*=0.004) (Figure 3. In univariate analysis, BAV increased by 2.8 for the probability of myocardial injury in comparison to the direct TAVR group (odds ratio [OR], 2.8; 95% CI, 1.4–5.8). Baseline characteristics of patients according to presence of myocardial injury are detailed in Table 2. Patients without myocardial injury more frequently had a medical history of chronic obstructive pulmonary disease and atrial fibrillation. A higher rate of hypertension was observed in patients with myocardial injury.

Secondary End Points

Preprocedural hs-TnT mean value was not predictive of 1-month clinical adverse events (as previously defined) in either group of patients (*P*=0.4). According to Cox

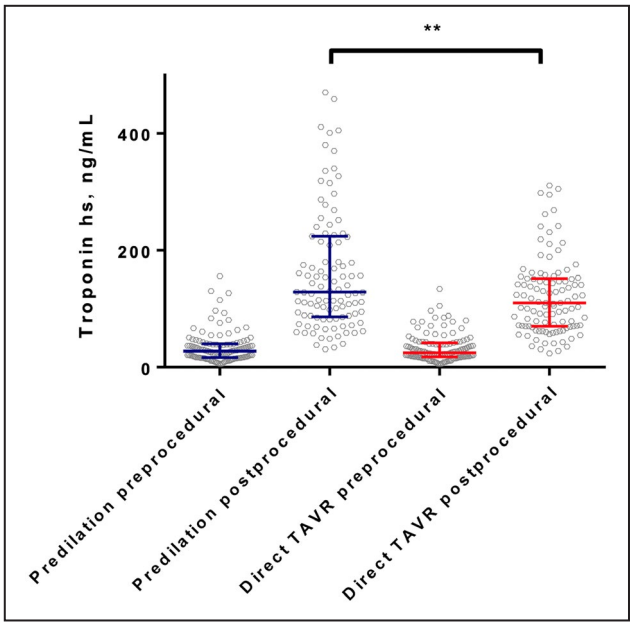

Figure 2. Preprocedure and postprocedure troponin according to the group of patients (predilatation [balloon aortic valvuloplasty (BAV)] and direct transcatheter aortic valve replacement [TAVR]).
Mean preprocedure troponin level was similar between both groups (*P*=0.3). Mean postprocedure troponin level was significantly higher in the predilatation (BAV) group in comparison to the direct TAVR group (*P*=0.007). *TAVR: Transcatheter aortic valve replacemen. **Data are outside the axis limits: Hs-TnT=858 ng/mL, Hs-TnT=630 ng/mL and Hs-TnT=546 ng/mL

survival model, the probability of 1-month outcomes was increased by 2.4-fold in patients with myocardial injury (hazard ratio, 2.4; 95% CI, 1.1–5.3 [*P*=0.03]). Conversely, myocardial injury after TAVR was associated with a numerically higher rate of total 1-month clinical adverse events (*P*=0.09) and with a significantly higher rate of pacemaker implantations (*P*=0.01) (Table 3).

Predictive Factors of Myocardial Injury

Predictive factors of myocardial injury in univariate and multivariate analysis are presented in Table 4. In multivariate analysis, BAV was still predictive of myocardial injury (OR, 2.09; 95% CI, 1.02–4.7 [*P*=0.04]), along with hypertension (OR, 3.2; 95% CI, 1.2–9.1 [*P*=0.02]). Medical history of AF (OR, 0.284; 95% CI, 0.09–0.87 [*P*=0.03]) was protective for myocardial injury. Medical history of coronary disease, procedural length, or postdilatation were not predictive of myocardial injury.

DISCUSSION

This study, including patients from the prospective randomized DIRECTAVI study, evaluated for the first time the impact of BAV on myocardial injury with 4 main findings:

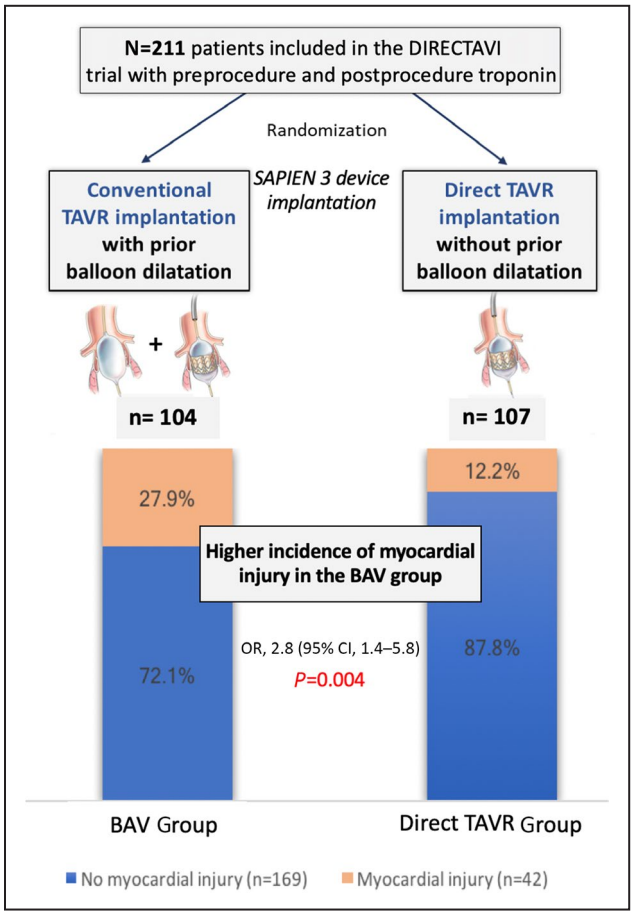

Figure 3. Primary end point: myocardial injury according to Valve Academic Research Consortium-2 criteria in the balloon aortic valvuloplasty (BAV) and direct transcatheter aortic valve replacement (TAVR) groups.
Myocardial injury was significantly more frequent in the BAV group compared with the direct TAVR group (*P*=0.004). DIRECTAVI indicates Direct Transcatheter Aortic Valve Implantation.

1. Myocardial injury remains frequent, occurring in ≈20% of patients after TAVR.
2. BAV was associated with a 3-fold increased probability and a higher magnitude of myocardial injury in comparison to direct device implantation.
3. In addition to BAV, hypertension and the absence of history of atrial fibrillation were predictive of myocardial injury.
4. Myocardial injury was associated with pacemaker implantation at 1-month follow-up.

Incidence of Myocardial Injury After TAVR

Previous studies reported myocardial injury after TAVR occurring in 30% to 50% of patients.[16–18] Indeed, in the largest cohort published evaluating 1300 patients undergoing TAVR, the incidence of myocardial injury was ≈50%.[18] In our study, myocardial injury occurred in approximately one fifth of patients, less frequently than

Table 3. Clinical Adverse Events at 1-Month Follow-Up According to Myocardial Injury

	Total Population (N=211)	Myocardial Injury (n=42, 19.9%)	No Myocardial Injury (n=169, 80.1%)	*P* Value
Total adverse events, n (%)*	81 (38.4)	23 (54.8)	58 (34.3)	0.09
All-cause mortality, n (%)	1 (0.47)	0 (0.00)	1 (0.59)	NA
Stroke, n (%)	3 (1.42)	1 (2.38)	2 (1.18)	0.55
Major vascular complications, n (%)	7 (3.32)	2 (4.76)	5 (2.96)	0.56
Major bleeding, n (%)	7 (3.32)	1 (2.38)	6 (3.55)	0.70
Transfusion, n (%)	4 (1.90)	2 (4.76)	2 (1.18)	0.13
Acute kidney injury, n (%)	4 (1.90)	2 (4.76)	2 (1.18)	0.13
Pacemaker implantation, n (%)	43 (20.38)	15 (35.71)	28 (16.57)	0.01
Heart failure, n (%)	3 (1.42)	1 (2.38)	2 (1.18)	0.55
Aortic regurgitation, n (%)				0.51
None (grade 0), n (%)	133 (63.03)	28 (66.67)	105 (62.13)	
Mild (grade 1), n (%)	65 (30.81)	13 (30.95)	52 (30.72)	
Moderate (grade 2), n (%)	13 (6.16)	1 (2.38)	12 (7.10)	
Severe (grade 3), n (%)	0 (0.00)	0 (0.00)	0 (0.00)	

*Including all listed events except grade 0 and 1 aortic regurgitation (less than moderate).

previously reported. Moreover, mean postprocedure hs-TnT elevation was 4.4-fold in the whole population, less than the 7-fold previously described in other studies.[16,21–23] These differences may be explained by: (1) the population of patients included in our study with a lower risk profile, (2) TAVR procedure performed with last-generation devices, and (3) increasing the experience of operators. In the current TAVR era, with the evolution of the technique and of operators' experience, valve positioning may be more precise and quicker, leading to shorter procedural length with potentially less hemodynamic impairments.[24] Taking all of these considerations together, we can expect that the incidence of myocardial injury will further decrease over the years.

BAV and Myocardial Injury

Myocardial injury during TAVR may be induced by periprocedural conditions with a mismatch between myocardial oxygen supply and demand.[25] Among the factors involved in the occurrence of myocardial injury, BAV, but also acute aortic regurgitation, microembolism, or temporary hypotension during rapid ventricular pacing, were advocated.[16,19] New-generation TAVR devices with a lower profile sheath system and improved radial force provide adequate expansion in most cases.[2–7] Thus, systematic BAV before device implantation may not be a mandatory step in the current TAVR era, particularly with balloon-expandable prosthesis. Moreover, as BAV may be associated with specific complications involving aortic regurgitation, systemic embolism, and annulus rupture, avoiding BAV may be of interest.[3,4,12,19,20] Rapid pacing may induce myocardial injury through a hypotensive or a pro ischemic effect[13,14] and may also be associated with negative effects on microcirculation.[26] Thus, duration of rapid pacing, required for BAV and balloon-expandable valve positioning, may be reduced by a direct implantation strategy, with a positive impact on myocardial injury.[27] Our results argue with the impact of BAV not only on incidence but also on the magnitude of myocardial injury assessed by mean hs-TnT elevation levels. Only 1 observational study including 164 patients evaluated the effect of BAV on myocardial injury with a self-expandable device. The authors found that direct device implantation was associated with lower incidence of myocardial injury.[19] Therefore, direct TAVR, which is both feasible and safe, appears to be a useful option to simplify the TAVR procedure in the "minimalist TAVR" era and to reduce myocardial injury.[28,29]

Other Predictive Factors of Myocardial Injury

In our study, coronary artery disease was not related to incidence of myocardial injury, suggesting that myocardial ischemia was not the predominant mechanism of myocardial injury. In addition to BAV, hypertension was also predictive of myocardial injury. No similar data were found in the literature. However, one can hypothesize that patients with hypertension had potential left ventricular hypertrophy and may be more impacted by periprocedural-induced mismatch between myocardial oxygen supply and demand. Conversely, atrial fibrillation was negatively associated with myocardial injury in our study. One can hypothesis that preprocedural anticoagulant therapy in patients with atrial fibrillation might have played a role in microembolism during TAVR. However, an effect of anticoagulant therapy on myocardial injury cannot be definitively asserted as all patients are equally anticoagulated during the procedure.

Table 4. Predictive Factors of Myocardial Injury in Univariate and Multivariate Analysis

	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Medical history						
COPD	<0.001	<0.001 to >999	NA			
Atrial fibrillation	0.239*	0.089 to 0.641*	0.0044*	0.284*	0.093–0.871*	0.0276*
Hypertension	3.284*	1.379 to 7.823*	0.0073*	3.246*	1.162–9.065*	0.0246*
NYHA III or IV	0.514*	0.242 to 1.092*	0.0835*			
Stroke	1.359	0.264 to 6.984	0.7137			
Coronary artery disease	1.224	0.622 to 2.407	0.5586			
Biological data						
Preprocedural hs-TnT	1.009	0.996 to 1.022	0.1875			
Preprocedural creatinine	1.004	0.999 to 1.009	0.1630			
Postprocedural creatinine	1.005*	1.000 to 1.011*	0.0669*			
Preprocedural hemoglobin	1.024	0.824 to 1.273	0.8283			
Postprocedural hemoglobin	0.974	0.784 to 1.210	0.8148			
Preprocedural C-reactive protein	0.955*	0.905 to 1.007*	0.0881*			
Postprocedural C-reactive protein	1.003	0.992 to 1.014	0.5951			
Procedural data						
BAV group	2.796*	1.359 to 5.751*	0.0052*	2.089*	1.022–4.734*	0.0476*
Procedure duration	0.982*	0.959 to 1.005*	0.1208*			
Postdilatation	1.350	0.137 to 13.313	0.7973			
Prosthesis diameter: 26 vs 23mm	0.696	0.327 to 1.485	0.3489			
Prosthesis diameter: 29 vs 23mm	0.788	0.303 to 2.046	0.6243			

*BAV indicates balloon aortic valvuloplasty; †COPD, chronic obstructive pulmonary disease; ‡hs-TnT, high-sensitivity troponin T; NA, not available; §NYHA, New York Heart Association; and OR, odds ratio.

Myocardial Injury and Prognostic

In the present study, preprocedure hs-TnT was not associated with 1-month events. Myocardial injury was associated with a trend in an increased risk of 1-month adverse outcomes without reaching significance except for pacemaker implantation rate. The prognostic impact of myocardial injury after TAVR was demonstrated in several studies with reduced left ventricular function improvement and increased risk of 1-month and 2-year mortality.[16,17,30,31] In a recent study with a large cohort of patients, myocardial injury was associated with long-term mortality only in patients with near-normal preprocedural troponin.[18] In our study, the pacemaker implantation rate was high, particularly in patients with myocardial injury regardless of preprocedural hs-TnT. This finding is consistent with a recent meta-analysis including 3442 patients in whom myocardial injury was predictive of post-TAVR permanent pacing.[32] The association between myocardial injury and need of pacemaker implantation may be explained by 2 main mechanisms. First, a relationship between myocardial injury and prosthesis implantation depth, a well-known risk factor for conduction disorder, was previously reported.[33,34] Second, a mechanical stretching during prosthesis implantation inducing both myocardial injury and myocardial fibrosis in the left ventricle outflow track as assessed by cardiac magnetic resonance imaging may have a potential impact on conductive pathways.[35]

Our study confirms for the first time the impact of BAV on myocardial injury in a randomized study. Indeed, previous studies were mainly historical comparisons, and nonrandomized and upstream selection of patients with more favorable anatomies for direct implantation cannot be excluded.

Study Limitations

The first limitation of this study is the relatively small sample size with a small number of adverse events not allowing significance to be reached reagarding the prognostic impact of myocardial injury on 1-month clinical adverse events. The second limitation was the ancillary character of the study with potential bias related to this design. Third, inflation duration was not collected precisely and may have played a role, as it is likely currently shorter compared with previous TAVI experience, in the lower incidence of myocardial injury found in the present study. Fourth, medical history of coronary disease, not found to be associated with myocardial injury, was heterogeneous data including previous percutaneous coronary intervention, previous coronary artery

bypass grafting, and medically managed coronary artery disease, not allowing a more precise analysis. Finally, the impact of BAV on myocardial injury was only studied with balloon-expandable valves and these results cannot be extended to others devices.

CONCLUSIONS

This ancillary study of the DIRECTAVI trial is the first randomized study to assess the impact of BAV on myocardial injury in patients undergoing TAVR with last-generation balloon-expandable Edwards SAPIEN 3 devices. Direct implantation significantly reduced the incidence and magnitude of myocardial injury, which was associated with a higher rate of pacemaker implantation. In addition to simplification of the procedure, direct TAVR may have a potential positive impact on pacemaker implantation by reducing the occurrence of myocardial injury.

ARTICLE INFORMATION

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