Prior Balloon Valvuloplasty Versus Direct Transcatheter Aortic Valve Replacement

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Prior Balloon Valvuloplasty Versus Direct Transcatheter Aortic Valve Replacement

Results From the DIRECTAVI Trial

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ABSTRACT

OBJECTIVES The aim of this study was to evaluate device success of transcatheter aortic valve replacement (TAVR) using new-generation balloon-expandable prostheses with or without balloon aortic valvuloplasty (BAV).

BACKGROUND Randomized studies are lacking comparing TAVR without BAV against the conventional technique of TAVR with BAV.

METHODS DIRECTAVI (Direct Transcatheter Aortic Valve Implantation) was an open-label noninferiority study that randomized patients undergoing TAVR using the Edwards SAPIEN 3 valve with or without prior balloon valvuloplasty. The primary endpoint was the device success rate according to Valve Academic Research Consortium-2 criteria, which was evaluated using a 7% noninferiority margin. The secondary endpoint included procedural and 30-day adverse events.

RESULTS Device success was recorded for 184 of 236 included patients (78.0%). The rate of device success in the direct implantation group (n = 97 [80.2%]) was noninferior to that in the BAV group (n = 87 [75.7%]) (mean difference 4.5%; 95% confidence interval: −4.4% to 13.4%; p = 0.02 for noninferiority). No severe prosthesis-patient mismatch or severe aortic regurgitation occurred in any group. In the direct implantation group, 7 patients (5.8%) required BAV to cross the valve. Adverse events were related mainly to pacemaker implantation (20.9% in the BAV group vs. 19.0% in the direct implantation group; p = 0.70). No significant difference was found between the 2 strategies in duration of procedure, contrast volume, radiation exposure, or rate of post-dilatation.

CONCLUSIONS Direct TAVR without prior BAV was noninferior to the conventional strategy using BAV with new-generation balloon-expandable valves, but without procedural simplification. BAV was needed to cross the valve in a few patients, suggesting a need for upstream selection on the basis of patient anatomy. (TAVI Without Balloon Predilatation [of the Aortic Valve] SAPIEN 3 [DIRECTAVI]; NCT02729519)

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Balloon aortic valvuloplasty (BAV) is typically considered a mandatory step in the transcatheter aortic valve replacement (TAVR) procedure both to facilitate implantation of the transcatheter heart valve (THV) and to reduce the radial counterforce for optimal device expansion (1). However, BAV has been shown to be associated with specific complications, including annular rupture, massive aortic regurgitation, destabilization of hemodynamic status related to rapid pacing, and possible cerebral embolization (2-5). Hence, avoiding BAV prior to TAVR is an attractive option that may also simplify the procedure. New-generation balloon-expandable THVs are associated with low-profile and orientable delivery systems that facilitate valve crossing. These systems have been associated with high TAVR success rates without prior dilatation of the native valve in observational studies and registries (6-9). However, such studies are prone to bias, and although the recent randomized DIRECT (The Predilatation in Transcatheter Aortic Valve Implantation Trial) study showed the feasibility of direct implantation of self-expandable THV (10), no randomized data are currently available concerning the safety and efficacy of this strategy using new-generation balloon-expandable THVs.

The aim of the present study was to demonstrate the noninferiority of TAVR without BAV to TAVR with prior BAV in terms of device success rate with the SAPIEN 3 balloon-expandable THV.

METHODS

STUDY DESIGN. DIRECTAVI (Direct Transcatheter Aortic Valve Implantation) was a prospective, randomized, single-center, open-label trial using the third-generation balloon-expandable Edwards SAPIEN 3 THV (Edwards Lifesciences, Irvine, California). We hypothesized that TAVR without prior BAV of the aortic valve (test arm; direct implantation group) would be noninferior to conventional practice using systematic prior valvuloplasty of the aortic valve (control arm; BAV group).

The study protocol was approved by an independent ethics committee before study initiation (Comité de Protection des Personnes Sud Méditerranée, Montpellier, France; ID RCB: 2015-A01823-46), and all patients provided oral and written informed consent providing information about the 2 compared strategies. An independent and out-of-region safety monitoring committee oversaw the study. The trial was conducted according to the World Medical Association's Declaration of Helsinki (NCT02729519).

PATIENT POPULATION. From May 2016 to May 2018, 236 consecutive patients undergoing TAVR via transfemoral or transcarotid approaches were enrolled in the study. Patients were confirmed to be eligible for TAVR by a multidisciplinary heart team including at least an interventional cardiologist, a cardiothoracic surgeon, and an anesthetist. The complete list of inclusion and exclusion criteria is provided in Online Table 1 and was previously published in the study design paper (11). All patients referred for TAVR at our center who met the inclusion criteria were included and randomized between the 2 strategies after checking of the eligibility criteria and collection of the informed consent. Random allocation sequences were computer generated by an independent statistician in a 1:1 ratio with permuted blocs of 4 and 6. The flowchart of the study is shown in **Figure 1**.

PROCEDURE. All TAVR procedures were performed using the Edwards SAPIEN 3 THV. For all patients, both vascular access and the aortic valve were evaluated before the procedure using multislice computed tomographic angiography of the entire aorta using vascular windows settings. The prosthesis size (23, 26, or 29 mm) and choice of vascular access were left to the discretion of the operating team. Transfemoral access was the first choice when possible. All TAVR procedures were performed in the same hybrid room (at Montpellier University Hospital) by 6 independent medical teams.

The procedure has been previously detailed (11). Briefly, most TAVRs were performed under general anesthesia using mild low-profile 14- to 16-F delivery systems and almost exclusive surgical vascular access with a pre-closing technique as previously described (12). For the control group, BAV was performed with a 20-, 23-, or 25-mm-diameter balloon according to the manufacturer's recommendations depending on the annular diameter measured using multislice computed tomographic angiography. To have homogeneous strategies in the pre-dilatation group, only balloons associated with the valve kit were allowed in the study. Clopidogrel 75 mg and aspirin 75 mg were administrated to all patients following TAVR, except those with indications for long-term anticoagulant therapy, who received only aspirin 75 mg in addition to anticoagulant therapy.

FOLLOW-UP. Baseline characteristics and clinical and procedural information were collected at the time of randomization (11). Patients were scheduled to

ABBREVIATIONS AND ACRONYMS

AVA = aortic valve area

BAV = balloon aortic valvuloplasty

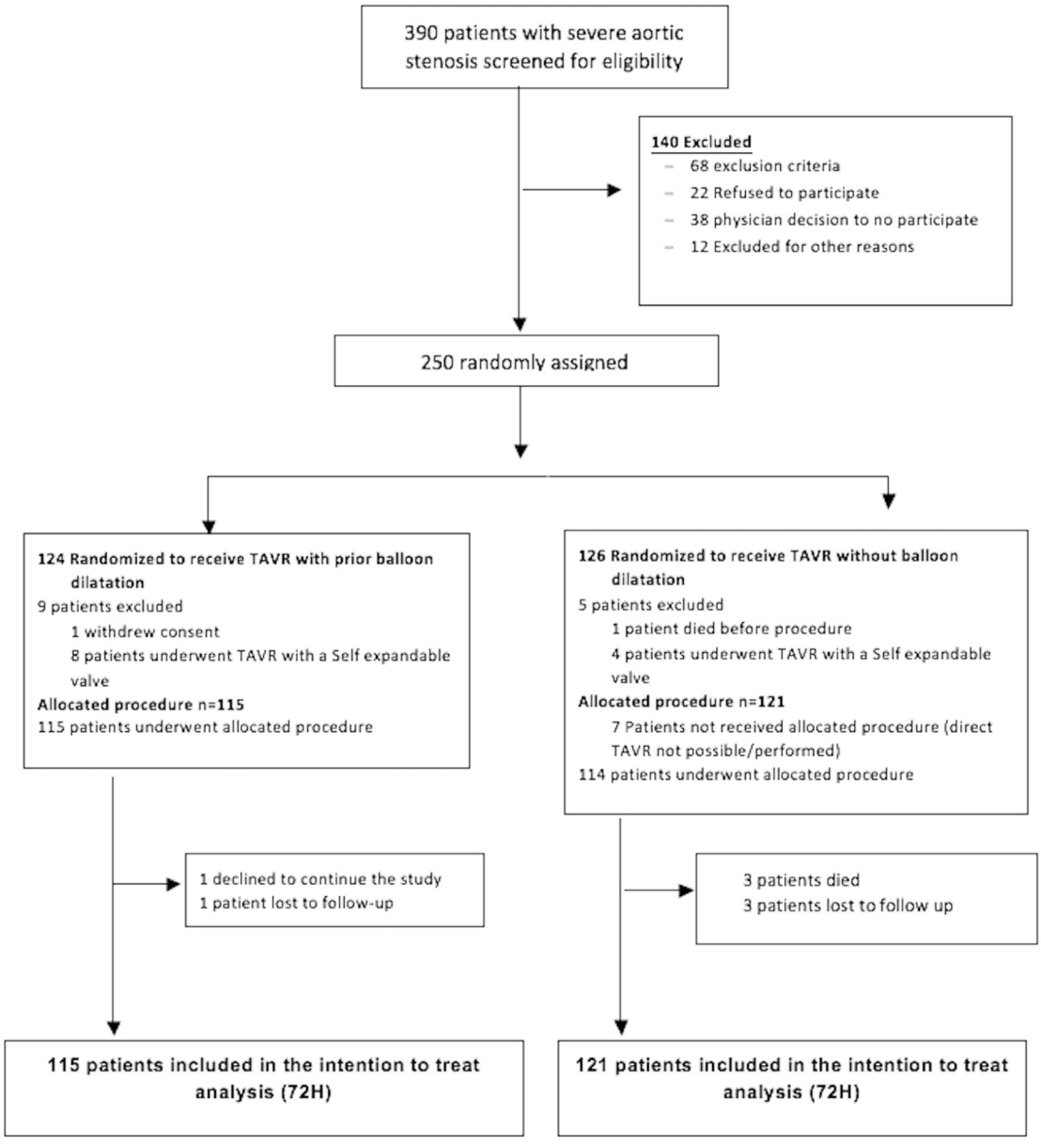
PPM = prosthesis-patient mismatch

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

VARC = Valve Academic Research Consortium

FIGURE 1 Flowchart of the DIRECTAVI Study



Three hundred ninety patients were screened, and 140 not meeting the inclusion criteria were excluded, related mainly to the use of a self-expandable transcatheter heart valve. Among the 240 patients randomly assigned, 16 patients were excluded because of protocol violation or death before transcatheter aortic valve replacement (TAVR).

undergo clinical evaluation at 72 h and at 1-month follow-up.

STUDY ENDPOINTS. The primary endpoint was the device success rate at 72 h post-TAVR according to the Valve Academic Research Consortium (VARC)-2 criteria (13). This composite endpoint was defined as: 1) absence of immediate procedural mortality (intra-procedural events resulting in immediate or subsequent death ≤72 h post-procedure [13]); 2) correct positioning of a single THV into the proper anatomic location; and 3) no moderate or severe prosthesis-patient mismatch (PPM), mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s, and no

moderate or severe prosthetic valve regurgitation. Echocardiographic assessments used the VARC-2 recommendations. Aortic valve regurgitation was quantitatively assessed (mild, moderate, or severe). Aortic valve area (AVA) after TAVR was calculated using the continuity equation. AVA was indexed to body surface area, and PPM was defined as nonsignificant for indexed AVA >0.85 cm^2/m^2, moderate for indexed AVA ≥0.65 to ≤0.85 cm^2/m^2, and severe for indexed AVA <0.65 cm^2/m^2. For patients with body mass index ≥30 kg/m^2, moderate PPM was defined as indexed AVA ≤0.70 cm^2/m^2 and severe PPM as indexed AVA ≤0.60 cm^2/m^2. We also evaluated device success without including PPM in reference to the VARC-1 criteria (14). To determine the effect of crossover on the overall findings, we performed a per-protocol analysis of the primary endpoint, in which direct TAVR patients treated with pre-dilatation were in analyzed in the control (pre-dilatation) group. Secondary endpoints included procedural outcomes (length of procedure, radiation exposure, and contrast volume), post-dilatation rate, hospitalization length, and clinical events: all-cause mortality, stroke, major bleeding, acute kidney injury (stages 2 and 3), and pacemaker implantation at 1-month follow-up (VARC-2 criteria) (13).

SAMPLE SIZE. The study was designed to evaluate noninferiority. On the basis of recent studies and registries, we assumed a procedural success rate of 95% in the control group. Using a noninferiority threshold of 7%, power of 80%, and a 5% significance level, 240 patients would be necessary to demonstrate noninferiority of TAVR without pre-dilatation to conventional procedures. On the basis of previous nonrandomized studies and registries (6,9), in which the difference in device success between the 2 strategies ranged from 2% to 15%, this trial was scheduled to test for noninferiority with delta of 7% (6,9). All analyses were performed according to the intention-to-treat principle, with the inclusion of all randomized patients according to the original group allocation.

STATISTICAL ANALYSES. Patient characteristics are presented as proportions for categorical variables and as mean ± SD or median (interquartile range) for quantitative variables. Characteristics were compared between the test and control groups using Student's *t*-test or the Mann-Whiney *U* test for continuous variables and using the chi-square or Fisher exact test for categorical variables. Noninferiority was assessed using the 1-sided Farrington-Manning confidence limit for the risk method. For secondary endpoints, superiority analysis was used with the appropriate statistical test (the Wilcoxon-Mann-Whitney test for quantitative variables and the Fisher or chi-square test for qualitative variables). Statistical analyses were performed using SAS version 9.1 (SAS Institute, Cary, North Carolina).

TABLE 1 Baseline Characteristics of the Population

	Pre-Dilatation Group (n = 115)	Direct Implantation Group (n = 121)
Female	45 (39.1)	45 (37.2)
Age (yrs)	83 (79-87)	83 (78-87)
Body mass index (kg/m^2)	26 (24.3-29.2)	26.6 (24.5-29.6)
Diabetes mellitus	41 (35.7)	45 (37.2)
Previous PCI	48 (41.7)	53 (43.8)
Previous CABG	6 (5.2)	7 (5.8)
Previous BAV	10 (8.7)	12 (9.9)
Cerebrovascular disease	5 (4.4)	4 (3.3)
Peripheral vascular disease	13 (11.3)	12 (9.9)
COPD	8 (7.0)	20 (16.5)
Atrial fibrillation	31 (27.0)	48 (39.7)
Permanent pacemaker	15 (13.1)	14 (11.6)
Pulmonary hypertension	2 (1.7)	2 (1.7)
Creatinine (μmol/l)	102 (82.0-126.0)	104 (84-131)
Hypertension	81 (70.4)	74 (61.2)
EuroSCORE I	10 (7-14)	10 (7-14)
EuroSCORE II	3 (2-4)	2.3 (2-3.8)
NYHA functional class		
I and II	54 (47.0)	58 (47.9)
III and IV	61 (53.1)	63 (52.1)
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)	46 (40-55)	49.5 (40-58)

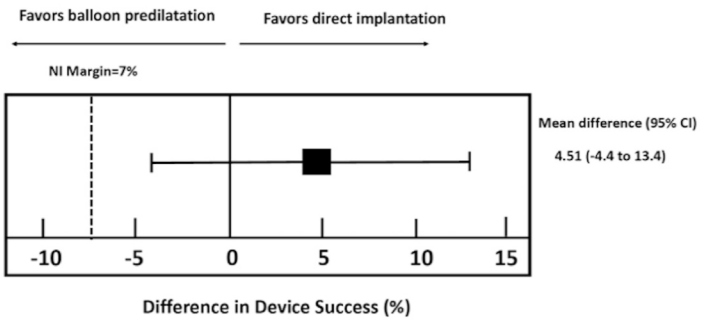
Values are n (%) or median (interquartile range).

BAV = balloon aortic valvuloplasty; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.

RESULTS

STUDY POPULATION. Between May 2016 and May 2018, a total of 236 patients were enrolled in the study, 115 patients in the BAV group and 121 in the direct implantation group (Figure 1). Baseline characteristics of the population are shown in Table 1. Transfemoral access was used for the majority of patients (n = 212 [89.8%]), while a transcarotid approach was chosen for cases of unsuitable iliofemoral anatomy (n = 24 [10.2%]). BAV was necessary in 7 patients (5.8%) allocated to direct implantation because of failure to cross the valve (n = 3) or a medical decision and anticipation of technical difficulties related to challenging anatomy with severe aortic stenosis and bulky calcification (n = 4). All

FIGURE 2 Primary Endpoint: Procedural Success at 72 h According to VARC-2 Criteria (Noninferiority Analysis)



No difference in device success rate was observed between the 2 strategies of pre-dilatation and direct implantation (noninferiority [NI] threshold of 7%; mean difference 4.5%; 95% confidence interval [CI]: −4.4% to 13.4%). Immediate device success was defined, according to the Valve Academic Research Consortium (VARC)-2 criteria, as the absence of immediate procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomic location, intended performance of the prosthetic heart valve (no prosthesis-patient mismatch and mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s), and no moderate or severe prosthetic valve regurgitation.

of these patients had tight stenoses with bulky calcifications, and 2 of them had bicuspid valves (Online Table 2).

PRIMARY ENDPOINT: DEVICE SUCCESS. Device success according to the VARC-2 criteria at 72-h follow-up was obtained for 184 patients (78.0%). The device success rate in the direct implantation group (n = 97 [80.2%]) was noninferior to that in the BAV group (n = 87 [75.7%]) (mean difference 4.5; 95% confidence interval: −4.4% to 13.4%; p = 0.02 for noninferiority) (**Figure 2**). The components of the primary endpoint (**Table 2, Central Illustration**) were not significantly different between the 2 groups. No severe aortic regurgitation or severe PPM was observed in the population, and all patients had correct positioning of a single valve. Excluding PPM evaluation and using the VARC-1 criteria, the device success rate at 72 h was 95.3% (n = 225), without a significant difference between the BAV and direct implantation groups: 94.7% (n = 109) and 95.9% (n = 116), respectively (mean difference −0.74; 95% confidence interval: −5.1% to 3.5%; p = 0.0008 for noninferiority).

In a per-protocol analysis of our primary endpoint, the 7 patients included in the direct implantation group treated with pre-dilation were analyzed in the control (BAV) group. Among these patients, 2 met the primary outcomes. In this analysis, the device success rate in the direct implantation group (n = 92 [80.7%]) was still noninferior to the device success rate in the BAV group (n = 92 [75.4%]) (mean difference 5.3; 95% confidence interval: −3.7% to 14.3%; p = 0.01 for noninferiority).

SECONDARY ENDPOINTS. No significant difference was observed for any endpoint, including mortality and post-dilatation rate (**Table 3**, Online Table 2). The most common event was pacemaker implantation. There was a trend toward lower rates of major vascular complications and acute renal failure in the direct implantation group. No life-threatening bleeding occurred in any group. No patient had severe aortic regurgitation at follow-up. Whereas there was a nonsignificant difference between the 2 groups, the 4 deaths occurred in the direct implantation group. Three deaths occurred during the procedure and 1 death at 29-day follow-up. Further description of the circumstances surrounding these deaths is provided in Online Table 3.

DISCUSSION

In this prospective, randomized study of an all-comers population of patients with severe aortic stenosis, we found that: 1) direct TAVR with new-generation balloon-expandable SAPIEN 3 valves is noninferior to conventional procedures using systematic BAV on standardized device success rate (VARC-2); 2) the safety of direct TAVR was similar to that of conventional procedures, without significant differences in procedural adverse events, particularly aortic regurgitation and pacemaker rate; 3) procedural times, contrast volume, and radiation doses were not statistically different between the 2 strategies; 4) overall use of post-dilatation was low and not higher in the direct strategy group; and 5) in a small number of patients with challenging anatomy, direct implantation was not possible.

DEVICE SUCCESS. Improved prosthesis expansion following balloon pre-dilatation during TAVR may in theory reduce the risk for underexpansion of the THV and the need for post-dilatation. However, the radial force provided by new-generation TAVR devices, particularly balloon-expandable valves, provided adequate expansion of the prosthesis in most cases (7,15,16). BAV may be helpful for annular sizing and to evaluate the risk for coronary occlusion in case of low sinus height, but with the use of multislice computed tomographic angiography for detailed assessment of the aortic native valve, optimal selection of patients is possible before the procedure, reducing the need for BAV during TAVR. The strategy of direct implantation has been suggested to facilitate the procedure with more stable position of the THV in the native

annulus during expansion of the device (17). Although recent reports have shown that direct valve implantation without BAV is feasible with a high success rate, these studies were mainly historical comparisons, and nonrandomized and upstream selection of patients with more favorable anatomy for direct implantation cannot be excluded (9,15,16). Recently, the randomized DIRECT study evaluated 171 patients who underwent TAVR with a different generation of the self-expandable CoreValve THV and showed that direct implantation was noninferior to pre-dilatation in terms of device success rate (10). To our knowledge, our study is the first prospective randomized trial powered to investigate the noninferiority of direct TAVR using a new generation of balloon-expandable valves and using the standardized international VARC-2 definition (13). Device success rates in our study were similar to those in the DIRECT trial, which supports the credibility of the results (10).

TABLE 2 Primary Endpoints at 72-h Follow-Up in the Total Population and According to Study Group

	Total Population (N = 236)	Pre-Dilatation Group (n = 115)	Direct Implantation Group (n = 121)	Absolute Difference
Device success at 72 h	184 (78)	87 (75.7)	97 (80.2)	4.5 (−4.4 to 13.4)
Procedural mortality	2 (0.8)	0 (0.0)	2 (1.7)	
Correct performance of the valve				
Moderate PPM	41 (17.4)	22 (19.1)	19 (15.7)	−3.4 (−13.1 to 6.2)
Severe PPM	0 (0.0)	0 (0.0)	0 (0.0)	
Aortic valve gradient >20 mm Hg or peak velocity > 3 m/s	3 (1.3)	2 (1.7)	1 (0.8)	−0.9 (−3.8 to 1.9)
Moderate AR	14 (5.9)	6 (5.2)	8 (6.6)	1.4 (−4.6 to 7.4)
Severe AR	0 (0.0)	0 (0.0)	0 (0.0)	
Second valve	0 (0.0)	0 (0.0)	0 (0.0)	
Secondary migration	0 (0.0)	0 (0.0)	0 (0.0)	
Improper positioning	0 (0.0)	0 (0.0)	0 (0.0)	

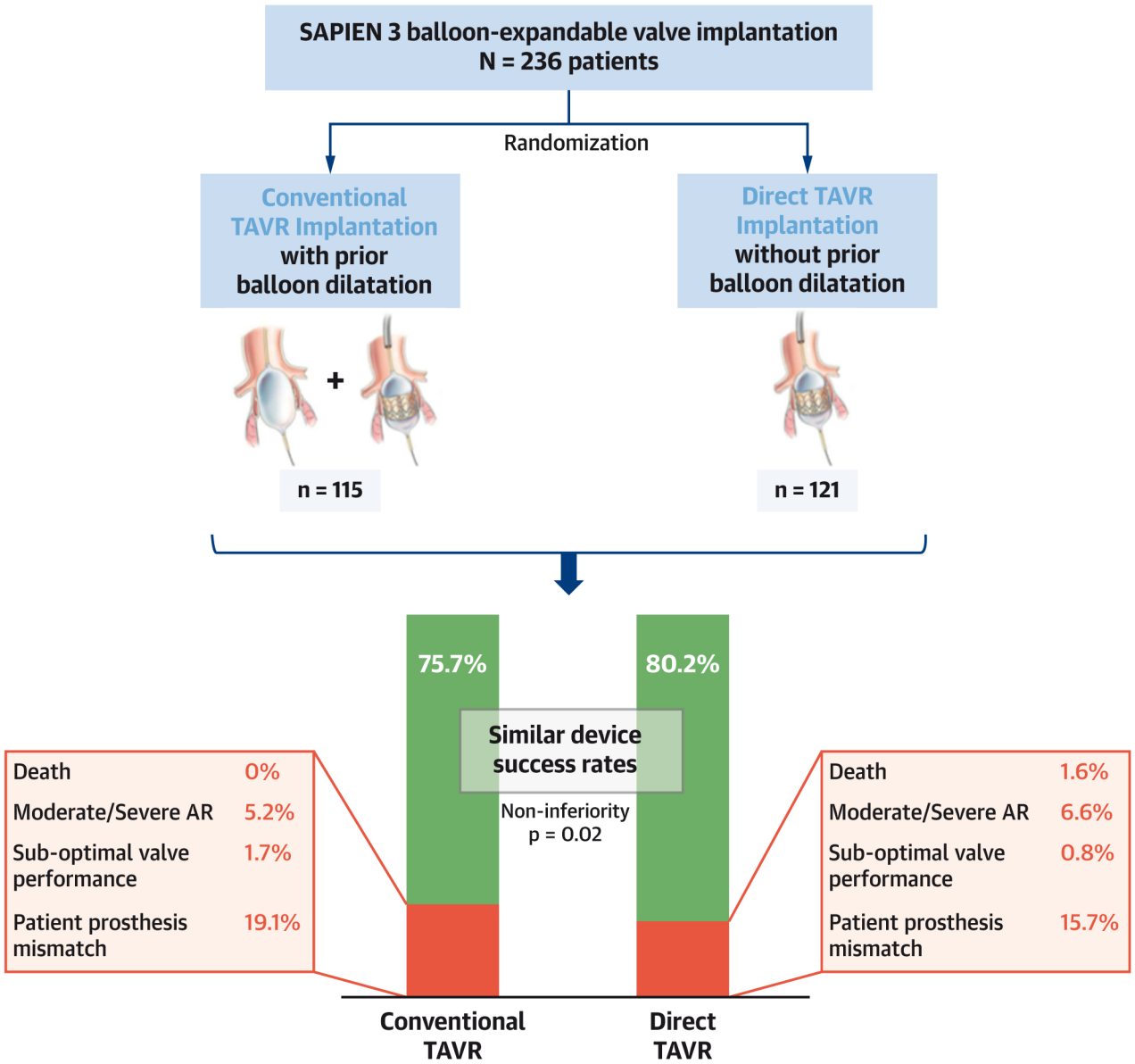
Values are n (%), unless otherwise indicated.
AR = aortic regurgitation; PPM = prosthesis-patient mismatch.

SAFETY AND COMPLICATIONS. The main component of device failure in our study was PPM (17.4%), but notably, no severe PPM was observed. These results are in accordance with those of other recent studies with new-generation THVs (17,18). In an analysis of the randomized PARTNER (Placement of Aortic Transcatheter Valves) 2 study, Pibarot et al. (19) observed PPM in 43.8% of patients (severe in 13.6%) in the TAVR cohort. That recent studies have shown lower rates than earlier and large randomized studies (19,20) is probably due to advances in TAVR technology. No severe aortic regurgitation was reported, and moderate aortic regurgitation was rare. In observational studies (9,16), the rate of paravalvular regurgitation after device implantation has been reported to be lower with direct implantation than with prior BAV, an observation attributed to less accurate implantation in the aortic annulus in cases of fractured and separated commissures. Our randomized study did not confirm these results. One explanation may be that significant aortic regurgitation has become a rare event with increasing operator experience and the use of new-generation THVs. Furthermore, although a high correlation between the volume of calcification and the severity of paravalvular leaks has been previously demonstrated (21), the higher rate of aortic regurgitation associated with BAV may have been related to more complex anatomies selected for this strategy in the observational studies (22).

SECONDARY ENDPOINTS. In contrast to prior observational studies (6–9), our randomized comparison found no beneficial effect of direct implantation for duration of procedure, contrast volume, radiation doses, or hospitalization duration. In observational studies, implantation strategy is usually left to the operator's discretion, and patients were selected for suitability for direct implantation (less aortic calcification, favorable femoral and aortic anatomy), as previously shown in the SOURCE 3 registry (22). Contrast injection is not necessary during BAV, and radiation doses were probably related mostly to vascular approach difficulties or to the stability of the THV in the native annulus during deployment. Pacemaker implantation was relatively high (20%) in our study, but large indications of left bundle branch block >130 ms and old age in our population likely explain these results, which are similar to those observed in the DIRECT trial (10).

POST-DILATATION RATES. We found very limited need for post-dilatation, with rates consistent with those observed in prior observational studies and registries using balloon expandable THV (15,16,23). Similarly to device success rates, evaluation of post-dilatation rates may be biased in nonrandomized studies and registries, related to the selection of more favorable, less calcified anatomies with the direct strategy. Notably, the post-dilatation rates were similar in the 2 groups in our study, in contrast to the DIRECT trial (10), which showed a 2-fold increase in the need for post-dilatation in the direct implantation

CENTRAL ILLUSTRATION Study Design and Main Results



Leclercq, F. et al. J Am Coll Cardiol Intv. 2020;13(5):594–602.

Green bars represent device success rates in each group, and **red bars** represent the rate of implantation failure and its different components. AR = aortic regurgitation; TAVR = transcatheter aortic valve replacement.

group. As post-dilatation appears to be not necessary in most patients after balloon-expandable THV implantation, it might be used only for patients with greater degrees of calcification, as reported in the recent EASE-IT TF (Transfemoral Transcatheter Aortic Valve Implantation With or Without Predilation of the Aortic Valve) registry (24).

FAILURE OF VALVE CROSSING. Failure to cross the valve in the direct implantation group was low in our study. An infrequent but possible need for bailout BAV when TAVR was initially planned without preimplantation BAV has been reported from an observational study (25). No crossing failure was reported in the DIRECT study (10), which was probably due to

TABLE 3 Secondary Outcomes in the Total Population and According to Study Group

	Total Population (N = 236)	Pre-Dilatation Group (n = 115)	Direct Implantation Group (n = 121)	p Value*
Procedural outcomes				
Need for post-dilatation	4 (1.7)	2 (1.7)	2 (1.7)	1.00
Contrast volume (ml)	79.01 ± 31.4	78.2 ± 29.3	79.7 ± 33.3	0.97
Procedure length (min)	53.06 ± 18.4	54.2 ± 18.2	52.0 ± 18.7	0.31
Radiation (cGy/cm^2)	3,907 ± 3,385	3,730 ± 3,487	4,073 ± 3,293	0.24
Hospitalization duration (days)	5.0 ± 2.7	5.2 ± 3.0	4.9 ± 2.2	0.90
1-month adverse events	60 (25.4)	29 (25.2)	31 (25.6)	0.94
All-cause mortality	4 (1.7)	0 (0.0)	4 (3.2)	0.24
Stroke	3 (1.3)	1 (0.9)	2 (1.7)	0.99
Major vascular complications	7 (3.0)	6 (5.2)	1 (0.8)	0.06
Major bleeding	8 (3.4)	3 (2.6)	5 (4.1)	0.70
Transfusion	4 (1.7)	2 (1.7)	2 (1.7)	1.00
Acute kidney injury	5 (2.1)	1 (0.9)	4 (3.3)	0.37
Pacemaker implantation	47 (19.90)	24 (20.90)	23 (19.01)	0.72
Heart failure	3 (1.3)	0 (0.0)	3 (2.5)	0.24
Aortic regurgitation				0.52
None (grade 0)	144 (61.5)†	75 (65.2)	69 (58.0)‡	
Mild (grade 1)	76 (32.5)	34 (29.5)	42 (35.3)	
Moderate (grade 2)	14 (6.0)	6 (5.2)	8 (6.6)	
Severe (grade 3)	0 (0.0)	0 (0.0)	0 (0.0)	

*Superiority analysis using the appropriate statistical test (the Wilcoxon-Mann-Whitney test for quantitative variables and the Fisher or chi-square test for qualitative variables).
†Data available for 234 patients. ‡Data available for 119 patients.

the exclusion of patients with complex anatomy, such as very calcified or bicuspid valves. Tight valve calcification or bicuspid valve but also aortic anatomy (i.e., horizontal arch and/or femoral tortuosity) may indicate crossing difficulties. Failure rates can be expected to decrease in the future as teams gather experience and device improve, facilitating valve crossings.

STUDY LIMITATIONS. One limitation of this analysis was the relatively small sample size. However, the statistical power was sufficient to demonstrate noninferiority, the primary objective. Another limitation was related to the use of post-dilatation without a formalized indication in the study protocol; post-dilatation was instead left to the discretion of the interventional cardiologist.

CONCLUSIONS

The DIRECTAVI trial, the first randomized study comparing direct implantation of a third-generation balloon-expandable THV against the routine use of prior BAV, found direct implantation to be noninferior in terms of device success rate. There was no difference in the rate of adverse events or post-dilatation. No significant difference between the 2 strategies was found regarding simplification of the procedure. BAV was required to cross the valve in a small number of patients, suggesting that selection on the basis of patient anatomy is necessary for the strategy.

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PERSPECTIVES

WHAT IS KNOWN? Randomized studies are lacking comparing TAVR without BAV against the conventional technique of TAVR with BAV.

WHAT IS NEW? Device success is noninferior between the 2 strategies using third-generation balloon-expandable THVs. However, the procedure is not simplified with direct implantation, which is associated with failure to cross the valve in a small number of patients.

WHAT IS NEXT? The efficacy and safety of direct implantation are demonstrated in this study using new-generation balloon-expandable THVs, but upstream selection of patients on the basis of valve and aortic anatomy is probably necessary for extension of this strategy.

REFERENCES

1. Vahanian A, Himbert D. Transcatheter aortic valve implantation: could it be done without prior balloon valvuloplasty? J Am Coll Cardiol Intv 2011;4:758-9.

2. Eltchaninoff H, Cribier A, Tron C, et al. Balloon aortic valvuloplasty in elderly patients at high risk for surgery, or inoperable: immediate and mid-term results. Eur Heart J 1995;16:1079-84.

3. Sack S, Kahlert P, Khandanpour S, et al. Revival of an old method with new techniques: balloon aortic valvuloplasty of the calcified aortic stenosis in the elderly. Clin Res Cardiol 2008;97:288-97.

4. Kahlert P, Al-Rashid F, Döttger P, et al. Cerebral embolization during transcatheter aortic valve implantation: a transcranial Doppler study. Circulation 2012;126:1245-55.

5. Nombela-Franco L, Webb J, de Jaegere PP, et al. Timing, predictive factors, and prognostic value of cerebrovascular events in a large cohort of patients undergoing transcatheter aortic valve implantation. Circulation 2012;126:3041-53.

6. Grube E, Naber C, Abizaid A, et al. Feasibility of transcatheter aortic valve implantation without balloon pre-dilation: a pilot study. J Am Coll Cardiol Intv 2011;4:751-7.

7. Fiorina C, Maffeo D, Curello S, et al. Direct transcatheter aortic valve implantation with self-expandable bioprosthesis: feasibility and safety. Cardiovasc Revasc Med 2014;15:200-3.

8. Möllmann H, Kim WK, Kempfert J, et al. Transfemoral aortic valve implantation of Edwards SAPIEN XT without predilatation is feasible. Clin Cardiol 2014;37:667-71.

9. Deharo P, Resseguier N, Koning R, et al. Impact of direct transcatheter aortic valve replacement without balloon aortic valvuloplasty on procedural and clinical outcomes insights from the FRANCE TAVI registry. J Am Coll Cardiol Intv 2018;11:1956-65.

10. Toutouzas K, Benetos G, Voudris V, et al. Predilatation versus no pre-dilatation for implantation of a self-expanding valve in all comers undergoing TAVR: the DIRECT trial. J Am Coll Cardiol Intv 2019;12:767-77.

11. Leclercq F, Robert P, Labour J, et al. Prior balloon valvuloplasty versus DIRECT transcatheter aortic valve implantation (DIRECTAVI): study protocol for a randomized controlled trial. Trials 2017;18:303-12.

12. Du Cailar C, Gandet T, Du Cailar M, Albat B. A simple sheath removal after open trans-femoral catheterization procedure: the ZIP technique. Eur J Cardiothorac Surg 2014;45:746-8.

13. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Am Coll Cardiol 2012;60:1438-54.

14. Leon MB, Piazza N, Nikolsky E, et al. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. Eur Heart J 2011;32:205-17.

15. Liao YB, Meng Y, Zhao ZG, et al. Meta-analysis of the effectiveness and safety of transcatheter aortic valve Implantation without balloon predilation. Am J Cardiol 2016;117:1629-35.

16. Auffret V, Regueiro A, Campelo-Parada F, et al. Feasibility, safety, and efficacy of transcatheter aortic valve replacement without balloon predilation: a systematic review and meta-analysis. Catheter Cardiovasc Interv 2017;90:839-50.

17. Herrmann HC, Daneshvar SA, Fonarow GC, et al. Prosthesis-patient mismatch in patients undergoing transcatheter aortic valve replacement from the STS/ACC TVT Registry. J Am Coll Cardiol 2018;72:2701-11.

18. Miyasaka M, Tada N, Taguri M, et al., for the OCEAN-TAVI Investigators. Incidence, predictors, and clinical impact of prosthesis-patient mismatch following transcatheter aortic valve replacement in Asian patients: the OCEAN-TAVI registry. J Am Coll Cardiol Intv 2018;11:771-80.

19. Pibarot P, Weissman NJ, Stewart WJ, et al. Incidence and sequelae of prosthesis-patient mismatch in transcatheter versus surgical valve replacement in high-risk patients with severe aortic stenosis: a PARTNER trial cohort analysis. J Am Coll Cardiol 2014;64:1323-34.

20. Little SH, Oh JK, Gillam L, et al. Self-expanding transcatheter aortic valve replacement versus surgical valve replacement in patients at high risk for surgery: a study of echocardiographic change and risk prediction. Circ Cardiovasc Interv 2016;9:e003426.

21. Khalique OK, Hahn RT, Gada H, et al. Quantity and location of aortic valve complex calcification predicts severity and location of paravalvular regurgitation and frequency of post-dilation after balloon-expandable transcatheter aortic valve replacement. J Am Coll Cardiol Intv 2014;7:885-94.

22. Wendler O, Schymik G, Treede H, et al. SOURCE 3 registry: design and 30-day results of the European post approval registry of the latest generation of the SAPIEN 3 transcatheter heart valve. Circulation 2017;135:1123-32.

23. Wang N, Lal S. Post-dilation in transcatheter aortic valve replacement: a systematic review and meta-analysis. J Interv Cardiol 2017;30:204-11.

24. Butter C, Okamoto M, Schymik G, et al. Degree of valve calcification in patients undergoing transfemoral transcatheter aortic valve implantation with and without balloon aortic valvuloplasty: findings from the multicenter EASE-IT TF registry. Catheter Cardiovasc Interv 2019;94:469-78.

25. Chan PH, Mario CD, Moat N, et al. Transcatheter aortic valve implantation without balloon predilatation: not always feasible. Catheter Cardiovasc Interv 2013;82:328-32.

KEY WORDS balloon aortic valvuloplasty, device success, direct implantation, randomized clinical trial, transcatheter aortic valve replacement