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Crossover balloon occlusion technique for access closure during transcatheter aortic valve implantation: a multicenter observational study

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The ProGlide system represents the most common approach to close the main access site during transcatheter aortic valve implantation (TAVI). A crossover balloon occlusion technique (CBOT) has been reported in small case-series to possibly provide a controlled, safe, and successful hemostasis during TAVI. We sought to investigate the comparative performance of a combined (CBOT + ProGlide) compared with a ProGlide only approach. Primary endpoint was VARC-3 type ≥ 2 bleeding. Secondary outcomes included red blood cells transfusion, vascular complications, acute kidney injury (AKI), length of hospital stay (LOS), and death. Our study retrospectively included 229 consecutive patients admitted to "Villa Verde" Clinic (Taranto, Italy) and "Mater Dei" Hospital (Bari, Italy) and treated with TAVI. The study population was divided based on the access closure strategy in two groups: the combined and the ProGlide suture only group. The CBOT + ProGlide treated group presented lower incidence of primary endpoint, as well as less red blood cells transfusions, AKI stages ≥ 2, and shorter LOS. After propensity-score matching, the CBOT + ProGlide group confirmed lower incidence of primary endpoint (2 (2.4%) vs. 10 (11.9%), $p = 0.016$), of AKI stage ≥ 2 (0 vs. 5 (6%), $p = 0.029$), and shorter LOS (6.9 ± 4.0 vs. 8.9 ± 6.1, $p = 0.015$); moreover, the multivariate logistic regression analysis confirmed the protective role of the combined approach against VARC-3 type ≥ 2 bleeding (CI 0.04–0.99; OR 0.2; $p = 0.05$). Data from this multicenter comparative study highlight that a routinary percutaneous closure of the main TAVI access with ProGlide coupled with CBOT is possible and safe. Moreover, this combined approach seems promising in terms of reduced bleeding, RBC transfusions, AKI incidence, and shortening of hospitalizations.

Aortic stenosis (AS) represents the most prevalent primary valve disease in Europe[1]. Over the past 15 years, the significant rise in the total number of aortic valve replacements (AVR) is partly due to the development of the transcatheter aortic valve implantation (TAVI) procedure. TAVI was firstly performed in patients with prohibitive surgical risk[2] but demonstrated afterward to be non-inferior to surgical AVR (SAVR) at 5 years follow-up also in high- and intermediate- surgical risk patients[3–5]. Moreover, at the same mid-term follow-up, the recent NOTION trial demonstrated comparable major clinical outcomes between TAVI and SAVR also in a low surgical risk population[6].

The transfemoral access is the current guidelines suggested approach for TAVI[7,8]. Transfemoral TAVI is nowadays feasible in more than 95% of patients thanks to improved expertise and technical progress[9]: (1)

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new generation of transcatheter heart valves (THVs) which have become smaller and more deliverable than previously; (2) new hydrophilic, small bore, expandable, and atraumatic sheaths[10]; (3) the widespread possibility to perform advanced peripheral transluminal angioplasty (PTA) in patients with peripheral artery disease (PAD). However, recent data suggest that major bleeding, major vascular complications, and need for transfusion still account for 4.6%, 5.6%, and 10% respectively[11–14] in transfemoral TAVI. Moreover, all these adverse events have been associated with worse short- and long-term clinical outcomes including all-cause mortality[15]. The pre-loading in the main femoral access site of a Perclose ProGlide (Abbott Vascular, CA) system, a suture-mediated closure device, remains the most common choice for vascular closure during TAVI. This approach may require the use of additional closure devices in up to 40% of patients and endovascular intervention in up to 5%[16].

The crossover balloon occlusion technique (CBOT), added to the pre-loading of a Perclose ProGlide (Abbott Vascular, CA) system, has been described in small case-series and proposed as a safe, successful, and more controlled access closure technique after TAVI[17] (Fig. 1). However, the performance of a routinary application of this technique has not been investigated. This study sought to compare the combined CBOT + ProGlide vs. the standard ProGlide only approach for the main access closure during TAVI in terms of technical success and clinical outcomes among which bleeding, need for red blood cells (RBCs) transfusions, major and minor vascular complications, acute kidney injury (AKI), death, and length of stay (LOS).

Methods
This multicenter case-control study, designed and written in accordance to the STROBE checklist[18] retrospectively included all consecutive patients who accessed the Cardiology Divisions of the "Villa Verde" Clinic (Taranto, Italy) and "Mater Dei" Hospital (Bari, Italy) with the diagnosis of severe AS and who underwent elective TAVI from September 2021 to May 2023. Both divisions are high-volume and high expertise centers according to the 2018 AATS/ACC/SCAI/STS Expert Consensus Systems of Care Document[19] since they have been involved in TAVI procedures for more than 10 years performing more than 100 TAVIs per year. Informed consent was obtained according to the study protocol. The study protocol was approved by the ethics committee of the participating centers (Territorial Ethics Committee of the "Azienda Ospedaliera Universitaria Consorziale Policlinico di Bari" – resolution dated March 6, 2024 protocol n. 0022011). All methods were performed in accordance with the relevant guidelines and regulations. In all patients the puncture of the main arterial access was executed under fluoroscopic guidance, based on the anatomical assessment of the arterial axis obtained from the pre-procedural TAVI-dedicated CT scan. Per internal protocol one of the two enrolling center adopts a default approach of combined (2 ProGlides + CBOT) hemostasis, while the other a 2 ProGlides technique. The internal protocol reflects a standardized local practice developed from institutional experience and consensus among TAVI operators within the heart team of each center. As stated before, in one of the two enrolling division this includes also the routine use of balloon-assisted hemostasis (2 ProGlides + CBOT); despite this technique is not mandated by current guidelines, it is widely adopted and was consistently applied to all eligible cases during the study period. Exclusion criteria were: need for surgical access, acute decompensated heart failure requiring urgent valvuloplasty before TAVI, PAD requiring propaedeutic PTA of the main access, severe tortuosity of ileo-femoral artery, enrollment in other clinical studies, planned occlusion method of the main access different from the default approach of the enrolling center. Demographic data, baseline clinical features, and hospital outcomes were gathered.

Primary endpoint was the incidence of Valve Academic Research Consortium-3 (VARC-3) type ≥ 2 bleedings. Secondary endpoints included RBCs transfusion, vascular complications, AKI, LOS, and death. Major vascular complications, minor vascular complications, and AKI were defined according the VARC-3 criteria[20]. Both Bleeding Academic Research Consortium (BARC) and VARC-3 criteria were used to define bleeding events[20,21].
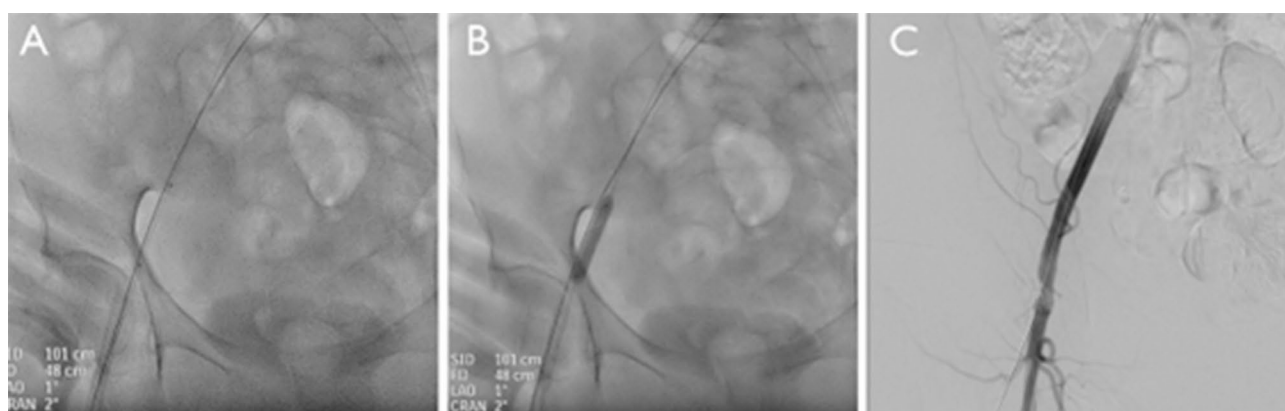

Fig. 1. Steb-by-step CBOT. **A** Before complete withdrawal of the TAVI delivery system, an appropriate sized balloon for PTA is placed in the external iliac artery, upstream of the main access site, over the 0.018" protection wire. **B** When TAVI sheath is retracted, the balloon is inflated to assure complete hemostasis during sheath removal. **C** The main arterial access is closed using the pre-implanted ProGlide, the balloon is deflated, and, if sufficient hemostasis is achieved, a final angiogram is performed to confirm the absence of vascular complications.

The sample size calculation was based on the expected incidence of the primary endpoint, which can reach up to 20% in high-risk populations[22]. To adopt a conservative approach, we assumed an event rate of 15% in the control group and 4% in the intervention group. Under these assumptions, with a two-sided alpha of 0.05 and a statistical power of 80%, a total sample size of 220 patients was calculated.

The study population was divided according to the vascular closure strategy in two groups: patients treated with both ProGlide and CBOT (CBOT group) and those only receiving the suture-based device (ProGlide group). Baseline characteristics, procedural features, and follow-up data were reported for the whole population and per group. All endpoints were assessed at the time of discharge or afterward. The Excel software (Microsoft Corporation, Redmond, Washington, USA) was used to build the database; statistical analysis was performed using both SPSS version 26 software (IBM, Inc., Armonk, NY) and R4.2.2 (R Foundation; Wirtschafts universitat Wien Welthandelsplatz, Vienna, Austria). Continuous variables are presented as means ± standard deviations (SD) and compared using paired Student's t-tests. Categorical variables are shown as numbers with percentages and compared using the chi-square analysis and Fisher's exact test for counts < 5.

For VARC-3 type ≥ 2 bleeding the association with baseline characteristics and procedural features has been tested with a univariate logistic regression analysis; odds ratios (ORs) were calculated with 95% confidence intervals (CIs). Each of the statistically significant ($p ≤ 0.05$) predictor of outcome was entered into a multivariable logistic regression model.

A propensity score (PS) analysis, performed with R4.2.2 (R Foundation; Wirtschafts universitat Wien Welthandelsplatz, Vienna, Austria) was also used to adjust for differences in patients' baseline and procedural characteristics. The following parameters were selected: age, sex, hemoglobin (Hb), creatinine (Cr), diabetes mellitus (DM), oral anticoagulation (OAC), double antiplatelet therapy (DAPT), and sheath size. These factors were chosen among those significantly different between the CBOT and ProGlide groups in our sample and/or significantly linked with VARC-3 type ≥ 2 bleeding in the multivariate logistic regression model and/or known to be predictors of bleeding from the literature. The 1:1 nearest neighbor matching without replacement method was used (standard deviation and caliper value were 0.1 and 0.2 respectively). Standardized differences were used to confirm negligible differences in the mean or prevalence of the selected covariates between treatment groups. For all tests significance was set for a 2-tailed value of $p ≤ 0.05$. The data that support the findings of this study are available from the corresponding author, MP, upon reasonable request.

Results

CBOT and ProGlide groups included 135 and 94 patients respectively. Table 1 depicts the baseline clinical characteristics of patients as a whole and by group. Mean age of the population was 81.8 ± 5.7 years, while aortic mean gradient was 47.1 ± 14.4 mmHg. Patients in the ProGlide group showed higher prevalence, though not statistically significant, of cardiac revascularization and DAPT. All other variables were comparable between groups. Tables 2 and 3 describe the procedural characteristics and main access related complications respectively. In the ProGlide group, the radial artery was prevalently used as secondary TAVI access. The differences in valve types between the two groups were reasonably mainly due to the corporate agreements of each institution. However, most procedures (71.2%) were performed with 14Fr sheath's size devices which were equally distributed between groups (supplementary Table 2). Minor access-related complications were significantly lower in CBOT group ($p = 0.029$), but major vascular complications did not differ between groups.

In hospital follow-up data are presented in Table 4: CBOT was associated with lower need for RBC transfusion ($p = 0.012$), fewer VARC-3 type ≥ 2 bleeding ($p = 0.010$), and shorter hospitalization ($p = 0.014$). Moreover, AKI resulted significantly lower in the CBOT treated group ($p = 0.033$), being the difference mainly driven by the AKI stages 2 and 3 ($p = 0.017$).

In the univariate logistic regression analysis (Table 5) only Hb, axillary arterial access, and CBOT were associated with VARC-3 type ≥ 2 bleeding. In the multivariate logistic regression analysis (Table 5) only Hb and CBOT showed a protective role against VARC-3 type ≥ 2 bleeding [$p = 0.003$ (95% C.I. 0.349–0.805) and $p = 0.045$ (95% C.I. 0.079–0.974) respectively].

After a PS-matching, a population of 168 patients was identified (baseline features are shown in supplementary Table 1). Standardized differences confirmed negligible differences in the mean or prevalence of the selected covariates (age, sex, DM, Hb, Cr, OAC, DAPT, and sheath size) between groups (supplementary Fig. 1).

Table 6 displays the main TAVI access-related complications and in-hospital follow-up data of the PS-matched population: a statistically significant difference between the two groups was confirmed in terms of VARC-3 type ≥ 2 bleeding and mean hospitalization. In addition, the adjusted analysis confirmed the higher prevalence of AKI stage ≥ 2 in the ProGlide treated group. The univariate logistic regression analysis (Table 7) showed that only Hb, Cr, and CBOT were significantly associated with VARC-3 type ≥ 2 bleeding. The multivariate logistic regression analysis proved that both Hb and CBOT had a protective role against VARC-3 type ≥ 2 bleeding in a PS-matched population, [$p = 0.003$ (95% C.I. 0.284–0.769) and $p = 0.050$ (95% C.I. 0.040–0.998) respectively], while Cr had a predictive role [$p = 0.011$ (95% C.I. 1.144–2.896)].

Discussion

The main findings of our study are the following: (1) in trans-femoral or trans-axillary TAVI procedures the main access percutaneous closure with ProGlide coupled with CBOT is possible and safe; (2) the unadjusted analysis suggests a possible association between the combined approach and a lower incidence of VARC-3 type ≥ 2 bleeding, RBC transfusions in the first post-procedural 72 h, and AKI; (3) the potential protection against VARC-3 type ≥ 2 bleeding of the combined approach was confirmed in the adjusted analysis; (4) the CBOT group displayed shorter time-to-discharge after TAVI.

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	Overall	(%)	CBOT	(%)	ProGlide	(%)	
	229	(100%)	135	(59%)	94	(41%)	P
Age (year)	81.8	±5.7	81.8	±5.8	81.8	±5.6	0.927
Female	121	(52.8)	75	(55.6)	46	(48.9)	0.324
Arterial Hypertension	200	(87.3)	121	(89.6)	79	(84.0)	0.211
Active Smoker	19	(8.3)	11	(8.1)	8	(8.5)	0.922
DM	77	(33.6)	44	(32.6)	33	(35.1)	0.692
AF	76	(33.2)	43	(31.9)	33	(35.1)	0.607
COPD	58	(35.3)	30	(22.2)	28	(29.8)	0.195
Prior Cardiac revascularization	46	(20.1)	22	(16.3)	24	(25.5)	0.086
Prior AMI	22	(9.6)	10	(7.4)	12	(12.8)	0.176
Prior PCI	40	(17.5)	19	(14.1)	21	(22.3)	0.105
Prior CABG	16	(7.0)	8	(5.9)	8	(8.5)	0.450
Prior TAVR	1	(0.4)	1	(0.7)	0	(0.0)	0.403
Prior SAVR	6	(2.6)	5	(3.7)	1	(1.1)	0.219
PAD	28	(12.2)	14	(10.4)	14	(14.9)	0.304
Hb (g/dL)	12.1	±1.7	12.2	±1.6	11.9	±1.8	0.213
Cr (mg/dL)	1.3	±1.3	1.3	±1.3	1.3	±1.1	0.683
EF (%)	55.7	±10.8	56.0	±9.9	54.5	±14.1	0.479
Aortic Mean Gradient (mmHg)	47.1	±14.4	47.7	±14.1	44.3	±15.4	0.259
Beta-blocker	140/228	(61.4)	79	(59)	61	(64.9)	0.365
OAC	77	(33.6)	41	(30.4)	36	(38.3)	0.212
ASA	140	(61.1)	82	(60.7)	58	(61.7)	0.883
Clopidogrel	42	(18.3)	20	(14.8)	22	(23.4)	0.098
Ticagrelor	3	(1.3)	1	(0.7)	2	(2.1)	0.364
DAPT	26	(11.4)	11	(8.1)	15	(16)	0.067

Table 1. Baseline characteristics of the overall population and by groups. *AF* atrial fibrillation, *AMI* acute myocardial infarction, *ASA* acetylsalicylic acid, *CABG* coronary artery bypass grafting, *COPD* chronic obstructive pulmonary disease, *Cr* creatinine, *DAPT* double antiplatelet therapy, *DM* diabetes mellitus, *EF* ejection fraction, *Hb* hemoglobin, *OAC* oral anticoagulant, *PAD* peripheral artery disease, *PCI* percutaneous coronary intervention, *SAVR* surgical aortic valve replacement, *TAVR* transcatheter aortic valve replacement.

	Overall	(%)	CBOT	(%)	ProGlide	(%)	
	229	(100%)	135	(59%)	94	(41%)	P
TAVR in SAVR	5	(2.2)	4	(3.0)	1	(1.1)	0.333
TAVR in TAVR	2	(0.9)	0	(0.0)	2	(2.1)	0.089
Sheath (Fr)	14.4	±0.6	14.4	±0.7	14.3	±0.5	0.301
TAVI access:							
TAVI access: femoral	226	(98.7)	134	(99.3)	92	(97.9)	0.364
TAVI access: axillary	3	(1.3)	1	(0.7)	2	(2.1)	0.367
2nd access: femoral	134	(58.5)	119	(88.1)	15	(16.0)	**<0.001**
2nd access: radial	95	(41.5)	16	(11.9)	79	(84.0)	**<0.001**
TAVI valve:							
Evolute	65	(28.4)	60	(44.4)	5	(5.3)	**<0.001**
R	57	(24.9)	52	(38.5)	5	(5.3)	**<0.001**
Pro +	8	(3.5)	8	(5.9)	0	(0)	**0.013**
Portico	140	(61.1)	67	(49.6)	73	(77.7)	**<0.001**
Navitor	21	(9.2)	8	(5.9)	13	(13.8)	**0.041**
Sapien 3	3	(1.3)	0	(0.0)	3	(3.2)	0.068

Table 2. Procedural features of the overall population and by groups.

	Overall	(%)	CBOT	(%)	ProGlide	(%)	
	229	(100%)	135	(59%)	94	(41%)	P
Need for surgical closure	2	(0.9)	0	(0.0)	2	(2.1)	0.089
Perforation	8	(3.5)	2	(1.5)	6	(6.4)	**0.047**
Femoral artery occlusion	2	(0.9)	1	(0.7)	1	(1.1)	0.796
Pseudo-aneurysm	1	(0.4)	1	(0.7)	0	(0.0)	0.403
Retroperitoneal hematoma	1	(0.4)	0	(0.0)	1	(1.1)	0.230
Minor vasc. complications	11	(4.8)	3	(2.2)	8	(8.5)	**0.029**
Major vasc. complications	2	(0.9)	0	(0.0)	2	(2.1)	0.089

Table 3. Main TAVI access-related complications of the overall population and by groups.

	Overall	(%)	CBOT	(%)	ProGlide	(%)	
	229	(100%)	135	(59%)	94	(41%)	P
Cr after TAVI (higher value during first week)	1.4	± 1.2	1.3	± 0.6	1.6	± 1.6	**0.016**
AKI	40/225	(17.8)	18	(13.3)	22	(24.4)	**0.033**
AKI stage 1	33/225	(14.7)	17	(12.6)	16	(17.8)	0.281
AKI stages ≥ 2	7/225	(3.1)	1	(0.7)	6	(6.7)	**0.017**
Need for RBC transfusion (1–3 days after TAVI)	21	(9.2)	7	(5.2)	14	(14.9)	**0.012**
BARC type ≥ 3a bleeding	28	(12.2)	14	(10.4)	14	(14.9)	0.304
VARC-3 type ≥ 2 bleeding	19	(7.4)	5	(3.7)	12	(12.8)	**0.010**
Permanent PM implantation	53	(23.1)	28	(20.7)	25	(26.6)	0.301
Stroke/TIA	2	(0.9)	1	(0.7)	1	(1.1)	0.796
Death	3	(1.3)	2	(1.5)	1	(1.1)	0.785
Mean Hospitalization (TAVI to discharge) (days)	7.8	± 5.6	7.0	± 5.2	8.9	± 6.0	**0.014**
Pt. discharged ≤ 72 h after TAVI (n)	32/226	(14.2)	27	(20.3)	5	(5.4)	**0.002**

Table 4. In hospital follow-up of the overall population and by groups. *AKI* acute kidney injury, *BARC* Bleeding Academic Research Consortium, *Cr* creatinine, *PM* pacemaker, *RBC* red blood cell, *TIA* transient ischemic attack, *VARC* Valve Academic Research Consortium.

	Univariate logistic regression analysis				Multivariate logistic regression analysis			
	95% C.I.		OR	*p*	95% C.I.		OR	*p*
Age	0.897	1.059	0.975	0.546	–			
Arterial Hypertension	0.237	5.053	1.095	0.908	–			
DM	0.385	3.049	1.083	0.880	–			
PAD	0.062	3.858	0.49	0.498	–			
Prior PCI	0.494	4.879	1.504	0.496	–			
OAC	0.519	3.889	1.420	0.495	–			
DAPT	0.470	6.591	1.761	0.401	–			
Cr	0.933	1.521	1.192	0.160	–			
Hb	0.325	0.735	0.498	**0.001**	0.349	0.805	0.530	**0.003**
Main TAVI access: axillary artery	2.411	328.285	28.1333	**0.008**	1.486	289.795	20.749	**0.024**
Sheath size	0.462	1.457	0.82	0.499	–			
CBOT	0.089	0.773	0.263	**0.015**	0.079	0.974	0.277	**0.045**
					–			

Table 5. Association between VARC-3 type ≥ 2 bleeding and baseline/procedural features. *CBOT* crossover balloon occlusion technique, *Cr* creatinine, *DAPT* double antiplatelet therapy, *DM* diabetes mellitus, *Hb* hemoglobin, *OAC* oral anticoagulant, *PAD* peripheral artery disease, *PCI* percutaneous coronary intervention, *PM* pacemaker.

	PS-matched population	(%)	CBOT	(%)	ProGlide	(%)	
	168	(100%)	84	(50%)	84	(50%)	p
Need for surgical closure	1	(0.6)	0	(0.0)	1	(1.2)	0.316
Perforation	6	(3.6)	2	(2.4)	4	(4.8)	0.406
Femoral artery occlusion	1	(0.6)	1	(1.2)	0	(0.0)	0.500
Pseudo-aneurysm	1	(0.6)	1	(1.2)	0	(0.0)	0.500
Retroperitoneal hematoma	0	(0.0)	0	(0.0)	0	(0.0)	-
Minor vasc. complications	8	(4.8)	3	(3.6)	5	(6.0)	0.469
Major vasc. complications	2	(1.2)	0	(0.0)	2	(2.4)	0.249
Cr after TAVI (higher value during first week)	1.3	± 0.9	1.4	± 0.7	1.7	± 1.7	0.138
AKI	33	(19.6)	14	(16.7)	19	(22.6)	0.332
AKI stage 1	28	(16.7)	14	(16.7)	14	(16.7)	1.000
AKI stages ≥ 2	5	(3.0)	0	(0.0)	5	(6.0)	**0.029**
Need for RBC transfusion (1–3 days after TAVI)	16	(9.5)	5	(6.0)	11	(13.1)	0.115
BARC type ≥ 3a bleeding	20	(11.9)	9	(10.7)	11	(13.1)	0.634
VARC-3 type ≥ 2 bleeding	12	(7.1)	2	(2.4)	10	(11.9)	**0.016**
Permanent PM implantation	41	(24.4)	18	(21.4)	23	(27.4)	0.369
Stroke/TIA	2	(1.2)	1	(1.2)	1	(1.2)	1.000
Death	1	(0.6)	1	(1.2)	0	(0.0)	0.500
Mean Hospitalization (TAVI to discharge) (days)	7.9	± 5.2	6.9	± 4.0	8.9	± 6.1	**0.015**
Pt. discharged ≤72 h after TAVI (n)	24	(14.4)	19	(22.9)	5	(6.0)	**0.002**

Table 6. Main TAVI access-related complications and in hospital follow-up of the PS-Matched population. *AKI* acute kidney injury, *BARC* Bleeding Academic Research Consortium, *Cr* creatinine, *PM* pacemaker, *RBC* red blood cell, *TIA* transient ischemic attack, *VARC* Valve Academic Research Consortium.

	Univariate logistic regression analysis				Multivariate logistic regression analysis		
	95% C.I.		OR	p	95% C.I.	OR	P
Age	0.906	1.110	1.003	0.953	–		
Arterial Hypertension	< 0.001	–	–	0.998	–		
DM	0.398	4.328	1.312	0.656	–		
PAD	< 0.001	-	-	0.998	–		
Prior PCI	0.617	7.767	2.190	0.225	–		
OAC	0.225	2.698	0.779	0.693	–		
DAPT	0.278	6.663	1.360	0.705	–		
Cr	1.065	2.257	1.550	**0.002**	1.144	2.896	1.820	**0.011**
Hb	0.307	0.792	0.494	**0.003**	0.284	0.769	0.467	**0.003**
Main TAVI access: axillary artery	0.825	240.809	14.091	0.068	–		
Sheath size	0.226	2.247	0.712	0.563	–		
CBOT	0.038	0.851	0.180	**0.03**	0.040	0.998	0.200	**0.050**

Table 7. Association between VARC-3 type ≥ 2 bleeding and baseline/procedural features of the PS-matched population. *CBOT* crossover balloon occlusion technique, *Cr* creatinine, *DAPT* double antiplatelet therapy, *DM* diabetes mellitus, *Hb* hemoglobin, *OAC* oral anticoagulant, *PAD* peripheral artery disease, *PCI* percutaneous coronary intervention, *PM* pacemaker.

The study explores the use of CBOT as endoclamping technique in addition to ProGlide for the main arterial access closure after TAVI (Fig. 2). To the best of authors knowledge, this is the first real-world comparison of the CBOT performance vs. the standard closure using the ProGlide device.

We purposely restricted the analysis to patients admitted after September 2021 because TAVI represents a rapidly evolving field due to the quick improvement of operators' expertise and of technological progresses. We thus focused on recent bioprosthetic devices with reduced sheath size and high deliverability; as a proof, most of the procedures were performed with 14 Fr devices which represent the best technology currently available[10,23,24]. However, even if a dramatic reduction in vascular complications and bleeding rates has been observed with newer generation devices[25], to date the incidence of major bleeding during TAVI is still reported to be 4.3–11.3%, and its management remains difficult[11,12,14,26]. Major bleeding, major vascular complications, and transfusions unfavorably impact on patients' short- and long-term clinical outcomes, including all-cause
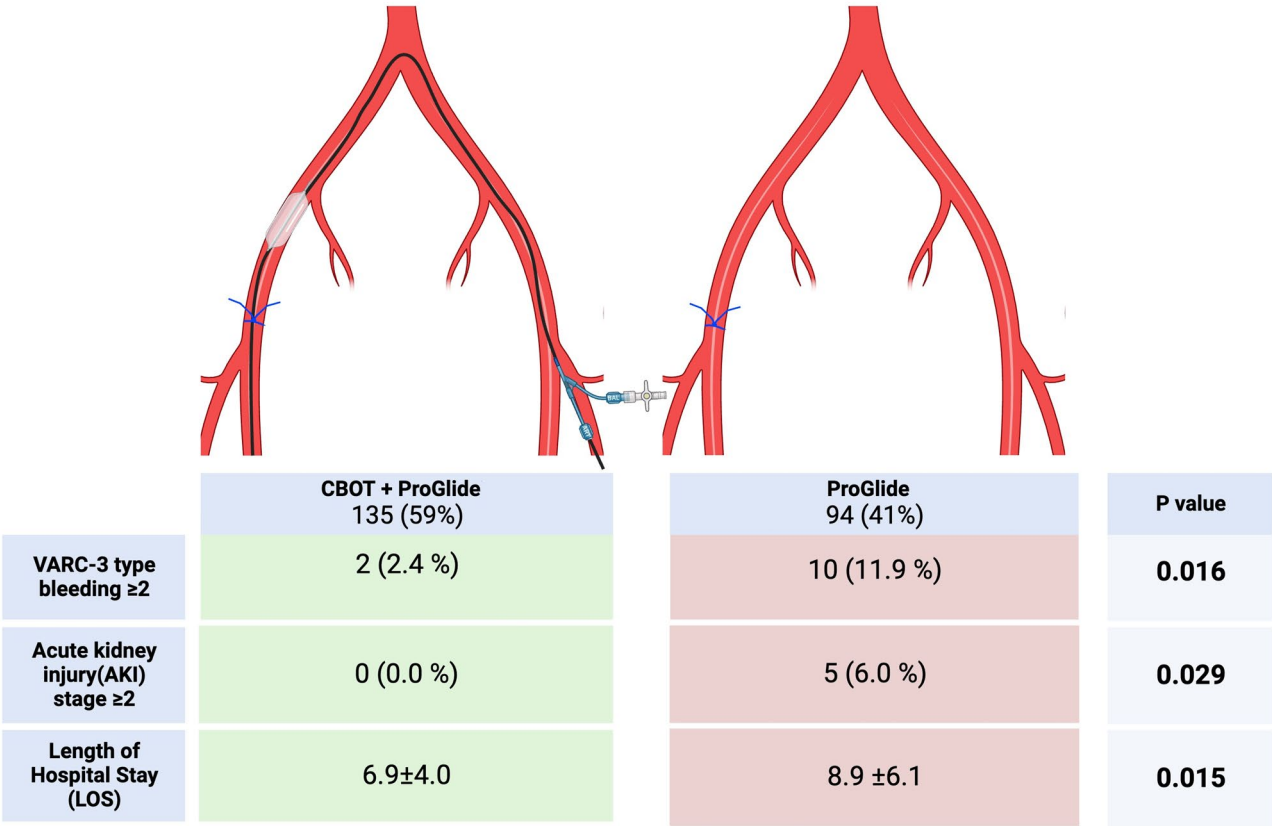
	CBOT + ProGlide 135 (59%)	ProGlide 94 (41%)	P value
VARC-3 type bleeding ≥2	2 (2.4 %)	10 (11.9 %)	0.016
Acute kidney injury(AKI) stage ≥2	0 (0.0 %)	5 (6.0 %)	0.029
Length of Hospital Stay (LOS)	6.9±4.0	8.9 ±6.1	0.015

Fig. 2. The crossover balloon occlusion technique (CBOT), in which a balloon is placed in the external iliac artery, upstream of the main TAVI access site, over the 0.018" protection wire, assures complete hemostasis during sheath removal and access closure with the pre-implanted ProGlide. In this multicenter comparative study, 229 consecutive patients treated with TAVI were divided based on the main access closure strategy in two groups: the combined (CBOT + ProGlide) and the ProGlide suture only group. The CBOT + ProGlide treated group presented lower incidence of minor vascular complications, red blood cells transfusions, Valve Academic Research Consortium-3 (VARC-3) type ≥ 2 bleeding and acute kidney injury stages ≥ 2, and reduced LOS. Even after a propensity score matching, the combined approach was associated with fewer major bleedings (CI 0.04–0.99; OR 0.2; p = 0.05). Prospective, pragmatic, randomized trials would be valuable to possibly confirm the clinical benefit of this endoclamping technique.

death[11–13,15]. In this study, the incidence of major vascular complications in the overall population was 0.9%, which confirms the high-level expertise of the two high volume enrolling centers. Minor vascular complications and RBC transfusions occurred in 4.8% and 9.2% of patients, respectively. Notably, although the two groups differed in the prosthetic valves used, the size of the delivery systems, which is a known predictor of vascular complications and bleeding[27], was comparable between groups with slight advantage in terms of lower profile observed in the ProGlide treated population (supplementary Table 2).

Interestingly, in the present study most of the transfusions were unrelated to vascular complications (major vascular complications and VARC-3 type ≥ 2 bleeding were 0.9% and 7.4% respectively). As a consequence, the main advantage of CBOT seems to come from the complete occlusion of the artery during the access closure which provides a clean tightening of the pre-implanted ProGlides and an effective temporary hemostasis in cases of ProGlide failure, thus allowing the operator to safely deliver an additional closure device system. Moreover, routinary use of the endoclamping technique can favor the quick management of any complications occurring after the removal of the prosthetic delivery system. These advantages seem to result in reduced bleedings and fewer post-operative transfusions. Notably, the balloon inflation may also eventually reduce the arterial stenosis related to the ProGlide sutures.

Intraoperative bleeding is one of the most consistent contributing factors for AKI development[28,29]. In turn, a recent meta-analysis suggested that even AKI stage 1 negatively impacts on both the one year and three year survival rates after TAVI[30]. Yan-biao Liao et al. demonstrated that significant bleedings and number of RBC transfusions predict in a directly proportional manner the incidence of AKI and long term mortality, mainly due to structural and functional alterations in the preserved RBCs and the buildup of pro-inflammatory mediators[31]. Moreover, a 1.8-fold increased risk of AKI was also associated to anemia after TAVI[32]. In agreement with the

above cited literature, the lower incidence of AKI in the CBOT treated population may reasonably occur as the result of less transfusions and major bleedings observed in this group.

However, because of the non-randomized nature of enrolment, our findings must be interpreted with caution. Purposively, PS matching was used to partly overcome disparities in the baseline clinical profile of the two patients' groups. The adjusted analysis confirmed the protective role of CBOT against VARC-3 type > 2 bleeding and the correlation between this technique and lower mean hospitalization time. Moreover, a slight tendency to higher incidence of AKI was observed in the ProGlide group after PS-matching, mainly driven by stage 2 and 3 AKI.

Conclusively, these findings represent the first report on a relatively large population of a possible protective effect against bleeding of a routine endoclamping technique adjunctive to conventional sutures. On the other hand, this technique carries an increase in procedural time and costs due to the need for additional devices; future investigations will clarify if the hypothesized reduction in vascular complications and in consequent additional unplanned interventions may ultimately offset in terms of clinical and economic net benefit the above-mentioned drawbacks.

Some limitations of the present study should be acknowledged. Firstly, sample size, despite larger than previous reports, is in absolute terms small. Second, this was a non-randomized study and, even if PS-matching was used to adjusting for potential confounding variables, it was not able to correct for the unmeasured variables. Third, the choice of prostheses was left to the discretion of operators in each institution, and not all of the devices currently in use were included in this study. Finally, patients with severe PAD or significant tortuosity of the iliofemoral axes were excluded from the analysis; thus, the routine application of CBOT was not assessed in these cases.

Furthermore, despite the favorable interplay between novel devices and trans-axillary access, TAVI represents a challenging procedure requiring careful patient selection and management[28]. –[29] As a result, our findings should be regarded only as hypotheses generating and would require and, to authors opinion, deserve further confirmation from a large randomized trial[30].

Conclusions

This multicenter comparative study highlights that in patients undergoing trans-femoral or trans-axillary TAVI a routinary percutaneous access closure with ProGlide paired with supplementary CBOT is possible and safe. Moreover, our data suggest that CBOT effectively contributed in reducing in-hospital major bleedings, RBC transfusions, AKI, and hospitalization time in patients undergoing TAVI. Prospective, pragmatic, randomized trials would be valuable to possibly confirm the clinical benefit of this endoclamping technique.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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GN, MP and RT wrote the main manuscript text; GN and GN prepared tables; GN and PLN did statistical analysis; All authors reviewed the manuscript.

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Declarations

Competing interests

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Additional information

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