

## **CEREBRAL MICROBLEEDS DURING TAVR: A PROSPECTIVE MRI COHORT**

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## **SUPPLEMENTAL MATERIAL**

	Study group (n=84)	Postprocedural ≥1 new CMB (n=19)	Postprocedural no new CMB (n=65)	P value (Postprocedural)
<b><u>VARC 2 criteria</u></b>	-	-	-	-
Device success n (%)	70 (84)	15 (79)	55 (85)	0.73
All Bleedings n (%)	23 (27)	7 (36)	16 (24)	0.31
Vascular Complications n (%)	10 (11)	2 (10)	8 (12)	0.83
CHF n (%)	2 (2)	0 (0)	2 (3)	0.43
Stage 2-3 AKI n (%)	13 (15)	3 (15)	10 (15)	0.86
New AF episode n (%)	4 (5)	1 (5)	3 (5)	0.90
Clinical TIA/Stroke n (%)	5 (5)	0 (0)	5 (7)	0.21
IntraHospital death n (%)	1 (1)	1 (1)	0 (0)	0.06
<b><u>TTE</u></b>	-	-	-	-
Aortic Regurgitation ≥2	9 (11)	4 (21)	5 (8)	0.09
Mean gradient mmHg mean ± SD	10.5 ± 4.6	11.2 ± 4.2	10.4 ± 4.9	0.82
Aortic valve area cm <sup>2</sup> mean ± SD	1.77 ± 0.58	1.76 ± 0.50	1.77 ± 0.60	0.97

**Supplemental Table 1. Early post-procedural outcome and new post-procedural CMB**

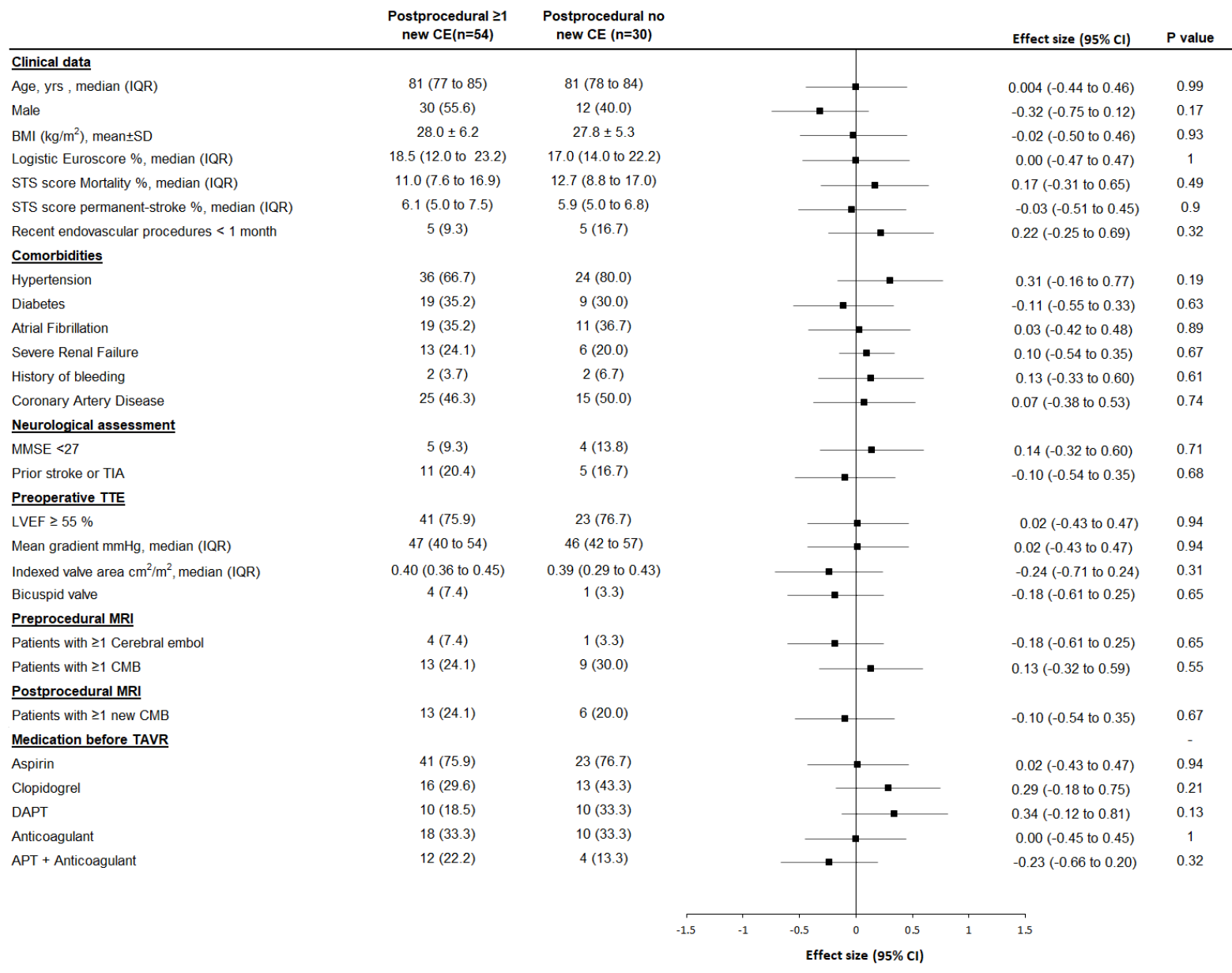
Early post-procedural outcomes at 30 days (VARC-2 criteria).

AF: atrial fibrillation; AKI: acute kidney injury; CHF: congestive heart failure; CMB: Cerebral microbleed; TIA transient ischemic accident; TTE transthoracic echography.

	All (n=84)	Preprocedural ≥1 CE (n=5)	Preprocedural no CE (n=79)	P value
<b><u>Clinical data</u></b>	-	-	-	-
Age, yrs mean ± SD	80.6 ± 5.6	76.5 ± 5.6	80.9 ± 5.5	0.06
Male n (%)	42 (50)	3 (60)	39 (49)	0.64
BMI (kg/m <sup>2</sup> ) mean ± SD	27.9 ± 5.9	32.8 ± 11.1	27.6 ± 5.4	0.06
Logistic Euroscore % mean ± SD	20.0 ± 4.3	20.7 ± 7.2	20.0 ± 12.6	0.90
STS score Mortality % mean ± SD	12.3 ± 7.6	12.3 ± 5.7	12.4 ± 7.8	0.97
STS score permanent-stroke % mean ± SD	6.5 ± 2.4	7.9 ± 3.2	6.4 ± 2.4	0.17
Recent endovascular procedures < 1 month n (%)	10 (11)	4 (80)	6 (7)	<b>&lt;0.001</b>
<b><u>Comorbidities</u></b>	-	-	-	-
Hypertension n (%)	60 (71)	3 (60)	57 (72)	0.55
Diabetes n (%)	28 (33)	4 (80)	24 (30)	<b>0.02*</b>
Atrial Fibrillation n (%)	30 (35)	2 (40)	28 (35)	0.83
Severe Renal Failure n (%)	19 (22)	1 (20)	18 (22)	0.88
History of bleeding n (%)	4 (4)	0 (0)	4 (5)	0.60
Coronary Artery Disease n (%)	40 (47)	3 (60)	37 (46)	0.55
<b><u>Neurological assessment</u></b>	-	-	-	-
MMSE <27 n (%)	9 (11)	1 (20)	8 (10)	0.70
Prior stroke or TIA n (%)	16 (19)	3 (60)	13 (16)	<b>0.01</b>
<b><u>Preoperative TTE</u></b>	-	-	-	-
LVEF ≥ 55 n (%)	64 (76)	5 (100)	59 (74)	0.19
Mean gradient mmHg mean ± SD	48 ± 12	46.2 ± 15.3	48.4 ± 12.5	0.70
Indexed valve area cm <sup>2</sup> /m <sup>2</sup> mean ± SD	0.39 ± 0.10	0.43 ± 0.10	0.39 ± 0.04	0.50
Bicuspid valve n (%)	5 (6)	1 (20)	4 (5)	0.17
<b><u>Medication before TAVR</u></b>	-	-	-	-
Aspirin n (%)	64 (76)	2 (40)	62 (78)	0.05
Clopidogrel n (%)	29 (38)	3 (60)	26 (32)	0.21
DAPT n (%)	20 (23)	0 (0)	20 (25)	0.19
Anticoagulant n (%)	28 (33)	1 (20)	27 (34)	0.51
APT + Anticoagulant n (%)	16 (19)	0 (0)	16 (20)	0.26
<b><u>Preprocedural MRI</u></b>	-	-	-	-
Patients with Microbleeds (CMB) n (%)	22 (26)	2 (40)	20 (25)	0.46
Patients with Cerebral emboli n (%)	5 (5)	NA	NA	NA
<b><u>Postprocedural MRI</u></b>	-	-	-	-
Patients with ≥ New Microbleeds (CMB) n (%)	19 (22)	2 (40)	17 (22)	0.33
Patients with New Cerebral emboli n (%)	54 (64)	4 (80)	50 (63)	0.44

**Supplemental Table 2. Risk factors for the presence of CE on preprocedural MRI**

APT: antiplatelet therapy; BMI: Body mass Index, CE: Cerebral emboli; CMB: Cerebral microbleed; DAPT: dual antiplatelet therapy; LVEF: left ventricular ejection fraction; MMSE: Mini-Mental State Examination; MRI: Magnetic Resonance Imaging; TIA: transient ischemic attack; TTE: transthoracic echography.



**Supplemental Table 3. Risk factors for the presence of new CE on post-procedural MRI**

APT: antiplatelet therapy; BMI: Body mass Index, CE: Cerebral embol; DAPT: dual antiplatelet therapy; LVEF: left ventricular ejection fraction; MMSE: Mini-Mental State Examination; TIA: transient ischemic attack; TTE: transthoracic echography.

	Index Event	N	Heart Valve disease	vWF defect*	Detailed data on vWF§	Detailed data On anticoagulation§	Pre-operative MRI	Post-operative MRI	Days between MRIs	Post-index event CMB rate	Pre-index event CMB rate	Localisation of CMB	Standardized Neurological evaluations
<b>Endocarditis</b>	-	-	-	-	-	-	-	-	-	-	-	-	-
Duval et al. 2010 <sup>31</sup>	Endocarditis	130	YES	†	NO	NO	1.5T	-	NA	57%	-	-	-
Goulenok et al. 2013 <sup>9</sup>	Endocarditis	30	YES	†	NO	NO	1.5T	-	NA	56%	-	-	-
lung et al. 2013 <sup>10</sup>	Endocarditis	120	YES	†	NO	NO	1.5T	-	NA	60%	-	-	-
Hess et al. 2013 <sup>32</sup>	Endocarditis	109	YES	†	NO	NO	1.5T	-	NA	57%	-	85% lobar	-
<b>Total:</b>	-	<b>389</b>	-	-	-	-	-	-	-	-	-	-	-
<b>Cardiovascular Interventions</b>	-	-	-	-	-	-	-	-	-	-	-	-	-
Sang-Beom Jeon et al. 2010 <sup>33</sup>	Cardiac valve Surgery CBP	19	YES	†	NO	NO	1.5T	1.5T	7 days	63%; 95%CI 38-83%	5% ; 95%CI 0.1-26%	46% lobar	-
Liebeskind et al. 2012 <sup>13</sup>	ECLS in Children	6	NO	‡	NO	NO	-	1.5T	NA	100%	-	Most lobar	-
Yoshioka et al. 2017 <sup>12</sup>	LVAD explantation	35	NO	‡	NO	Yes	-	3.0T	NA	<b>97%</b>	-	-	-
Patel et al. 2019 <sup>11</sup>	Cardiac Surgery CBP	75	YES	†	NO	NO	1.5T	1.5T	7 weeks	76%	<b>36%</b>	70% lobar	YES
Van Belle et al. 2022	TAVR	<b>84</b>	<b>YES</b>	†	<b>Yes</b>	<b>Yes</b>	<b>1.5T</b>	<b>1.5T</b>	<b>3 days</b>	<b>23%; 95%CI 14-33%</b>	<b>26%, 95%CI=17-37%</b>	<b>69% lobar</b>	<b>YES</b>
<b>Total:</b>	-	<b>219</b>	-	-	-	-	-	-	-	-	-	-	-

**Supplemental Table 4. Summary of studies describing cerebral microbleeds in acute cardiac scenarios**

- : no data

CBP: cardiopulmonary bypass; CMB: Cerebral microbleed; CBP: Cardiopulmonary bypass; ECLS: extra-corporeal life support; LVAD: left ventricular assist device, MRI; Magnetic resonance imaging; NA: non applicable, T: Tesla (MRI); VWF: von Willebrand Factor.

\*: according to published literature<sup>20,22,45</sup> all these clinical scenarios are known to be associated with at least moderate VWF multimer defect:

- † Moderate to severe VWF multimer defect is known to be present in patients with severe aortic stenosis and severe regurgitant valve disease<sup>20,22</sup>

- ‡ Severe to profound VWF multimer defect is known to be present in patients with assist device (ECLS or LVAD)<sup>45</sup>

§ : To describe whether these data were provided as part of the study.