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Silent cerebral microbleeds during TAVR: Insight from a prospective study

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2 DROIT
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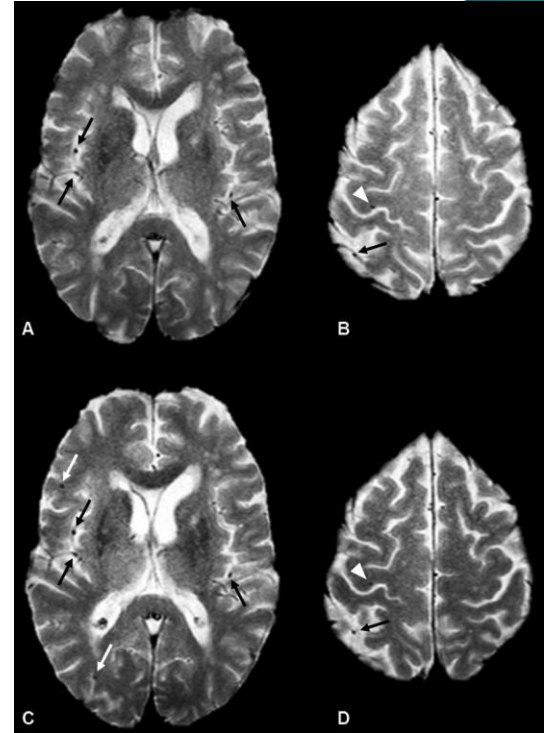


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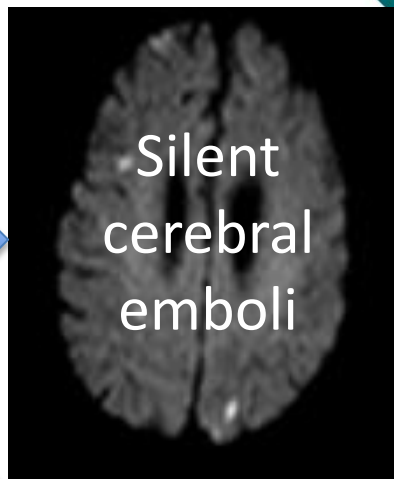
Cerebral microbleeds (CMB)

- Extravasations of blood components through fragile cerebral microvascular walls
- Markers of risk of stroke, dementia and cognitive impairment
- Endovascular procedures ?

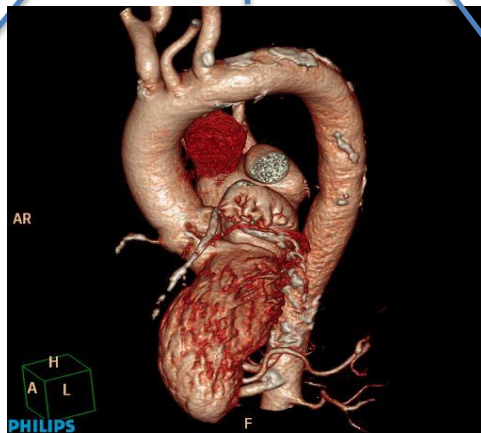


TAVR

- 3-5%
- x 3,5-10 mortality

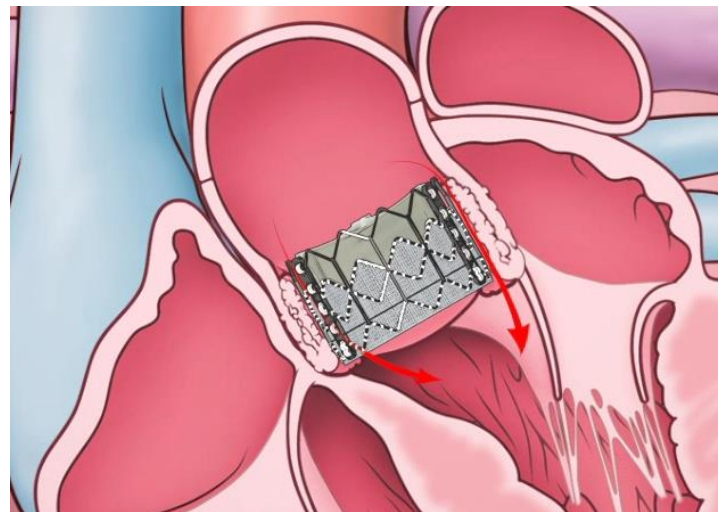
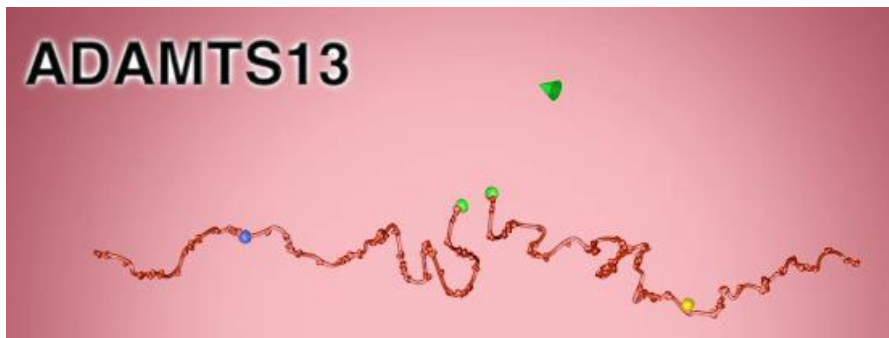


- ≈65%
- Long-term cognitive performance preserved



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- Acute changes of haemostasis parameters
- Correction of the acquired von Willebrand disease



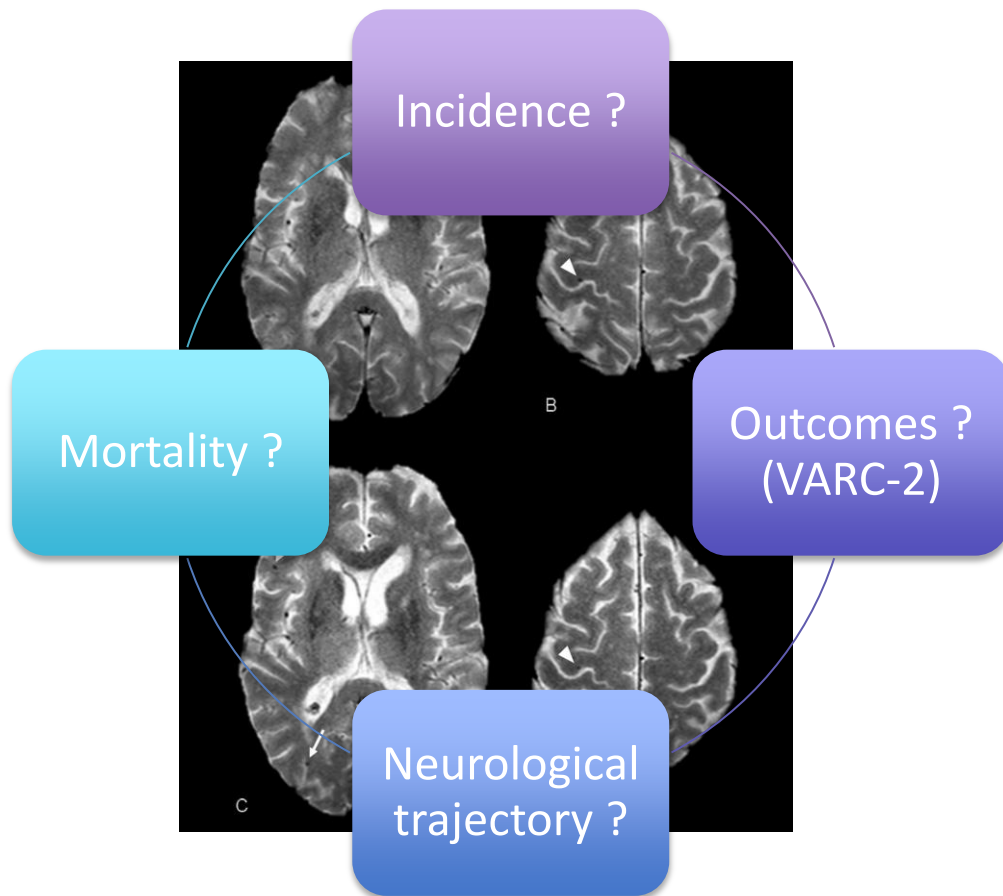
-Van Belle E, Rauch A, Vincentelli A, Jeanpierre E, Legendre P, Juthier F, et al. Von Willebrand factor as a biological sensor of blood flow to monitor percutaneous aortic valve interventions. *Circ Res.* 2015

-Van Belle E, Rauch A, Vincent F, Robin E, Kibler M, Labreuche J, et al. Von Willebrand Factor Multimers during Transcatheter Aortic-Valve Replacement. *N Engl J Med.* 2016

Cerebral microbleeds (CMB)



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Methods



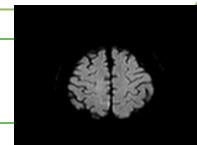
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1

- Patients referred for TAVR procedure

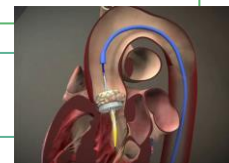
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- Pre-procedural cerebral MRI : cerebral microbleeds ?



3

- Neurological assessment (baseline): NIHSS score, modified Rankin score, EQ-5D scale, MMSE score
- Analysis of High Molecular Weight(HMW)-multimers of VWF

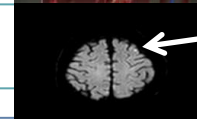


3

- TAVR procedure

4

- Analysis of High Molecular Weight(HMW)-multimers of VWF
- Post-procedural cerebral MRI : new cerebral microbleeds ?



5

- Intrahospital outcomes : VARC-2 criteria

6

- Neurological assessment (6 months): NIHSS score, modified Rankin score, EQ-5D scale, MMSE score, QVFS questionnaire



7

- Mid-term survival at 12 months

Methods



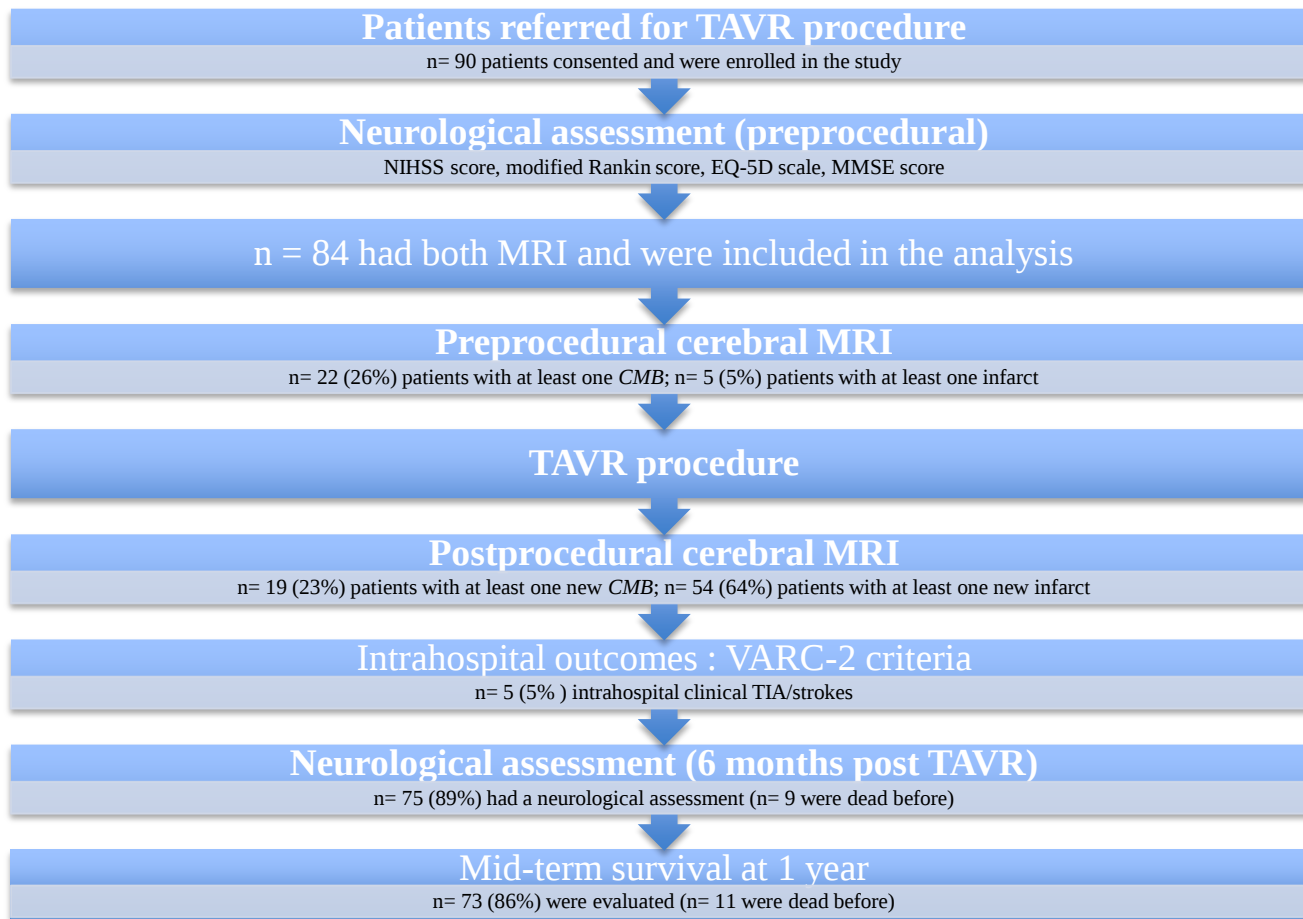
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- **Primary endpoint** : appearance and **incidence** of new cerebral microbleeds on the post-procedural cerebral MRI.
- **Secondary endpoints** : presence of microbleed on the preprocedural MRI and cerebral emboli (CE) at preprocedural or post-procedural MRI.
- **Analyses** :
 - Identification of predictive factors of primary and secondary endpoints.
 - Evaluation of their impact on early outcomes VARC-2
 - Impact on the neurological functions examined at 6 months
 - Impact on the global mortality at 1 year follow-up.

Methods



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Results: baseline



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	All (n=84)	Preprocedural ≥ 1 CMB (n=22)	Preprocedural no CMB (n=62)	P value (Preprocedural)	Postprocedural ≥ 1 new CMB (n=19)	Postprocedural no new CMB (n=65)	P value (Postprocedural)
Clinical data	-	-	-	-	-	-	-
Age, yrs mean $\pm$ SD	80.6 $\pm$ 5.6	80.0 $\pm$ 5.9	80.9 $\pm$ 5.5	0.51	79.1 $\pm$ 5.2	81.2 $\pm$ 5.3	0.35
Male n (%)	42 (50)	11 (50)	31 (50)	1	12 (63)	30 (46)	0.19
BMI (kg/m ²) mean $\pm$ SD	27.9 $\pm$ 5.9	27.6 $\pm$ 6.9	28.0 $\pm$ 5.5	0.78	27.9 $\pm$ 6.1	27.7 $\pm$ 5.2	0.88
Logistic Euroscore % mean $\pm$ SD	20.0 $\pm$ 4.3	19.4 $\pm$ 4.7	20.2 $\pm$ 3.6	0.80	19.0 $\pm$ 5.3	20.2 $\pm$ 3.9	0.72
STS score Mortality % mean $\pm$ SD	12.3 $\pm$ 7.6	12.1 $\pm$ 5.3	12.6 $\pm$ 8.5	0.80	12.8 $\pm$ 4.9	12.1 $\pm$ 8.1	0.11
STS score permanent-stroke % mean $\pm$ SD	6.5 $\pm$ 2.4	7.3 $\pm$ 2.0	6.2 $\pm$ 2.5	0.07	5.7 $\pm$ 1.7	6.7 $\pm$ 2.5	0.13
Recent endovascular procedures < 1 month n (%)	10 (11)	2 (9)	8 (12)	0.63	3 (15)	7 (10)	0.77
Comorbidities	-	-	-	-	-	-	-
Hypertension n (%)	60 (71)	21 (95)	39 (62)	0.003 #	16 (84)	44 (67)	0.16
Diabetes n (%)	28 (33)	11 (50)	17 (27)	0.05	8 (42)	20 (30)	0.35
Atrial Fibrillation n (%)	30 (35)	11 (50)	19 (30)	0.10	9 (47)	21 (32)	0.22
Severe Renal Failure n (%)	19 (22)	7 (32)	12 (19)	0.23	3 (15)	16 (24)	0.41
History of bleeding n (%)	4 (4)	2 (9)	2 (3)	0.26	3 (15)	1 (1)	0.01*
Coronary Artery Disease n (%)	40 (47)	10 (45)	30 (48)	0.81	12 (63)	28 (43)	0.12
Neurological assessment	-	-	-	-	-	-	-
MMSE <27 n (%)	12 (14)	5 (23)	7 (11)	0.18	5 (26)	7 (10)	0.08
Prior stroke or TIA n (%)	16 (19)	7 (32)	8 (13)	0.04 #	3 (15)	13 (20)	0.68
Preoperative TTE	-	-	-	-	-	-	-
LVEF $\geq$ 55 n (%)	64 (76)	18 (81)	46 (74)	0.35	14 (73)	50 (76)	0.77
Mean gradient mmHg mean $\pm$ SD	48 $\pm$ 12	49 $\pm$ 12	47 $\pm$ 12	0.65	51 $\pm$ 16	47 $\pm$ 11	0.25
Indexed valve area cm ² /m ² mean $\pm$ SD	0.39 $\pm$ 0.10	0.39 $\pm$ 0.13	0.40 $\pm$ 0.10	0.90	0.37 $\pm$ 0.12	0.40 $\pm$ 0.10	0.33
Preprocedural MRI	-	-	-	-	-	-	-
Microbleeds (CMB) n (%)	22 (26)	NA	NA	NA	7 (36)	15 (23)	0.23
Cerebral emboli n (%)	5 (5)	2 (9)	3 (5)	0.46	1 (5)	4 (6)	0.88
Postprocedural MRI	-	-	-	-	-	-	-
Microbleeds (CMB) n (%)	19 (22)	7 (31)	12 (19)	0.23	NA	NA	NA
Cerebral emboli n (%)	54 (64)	12 (54)	42 (67)	0.26	9 (47)	45 (69)	0.08
Medication before TAVR	-	-	-	-	-	-	-
Aspirin n (%)	64 (76)	16 (73)	48 (77)	0.65	12 (63)	52 (80)	0.12
Clopidogrel n (%)	29 (38)	7 (32)	22 (35)	0.75	8 (42)	21 (32)	0.42
DAPT n (%)	20 (23)	3 (14)	17 (27)	0.19	5 (26)	15 (23)	0.77
Anticoagulant n (%)	28 (33)	8 (36)	17 (27)	0.43	9 (47)	19 (29)	0.16
APT + Anticoagulant n (%)	16 (19)	5 (23)	11 (18)	0.60	6 (31)	10 (15)	0.11

Results: procedure and outcomes



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	All (n=84)	Postprocedural ≥1 new CMB (n=19)	Postprocedural no new CMB (n=65)	P value (Postprocedural)
<i>Procedural data</i>	-	-	-	-
Fluo tim, sec mean ± SD	1530 ± 580	1770 ± 691	1460 ± 536	0.04*
N>2 postdilation n (%)	15 (17)	5 (26)	10 (15)	0.03*
UFH only n (%)	24 (28)	7 (36)	17 (26)	0.36
UFH + Protamine n (%)	23 (27)	2 (10)	21 (32)	0.04
Bivalirudine n (%)	37 (44)	10 (52)	27 (41)	0.39

	All (n=84)	Preprocedural ≥1 CMB (n=22)	Preprocedural no CMB (n=62)	P value (preprocedural)	Postprocedural ≥1 new CMB (n=19)	Postprocedural no new CMB (n=65)	P value (Postprocedural)
<i>VARC 2 criteria</i>	-	-	-	-	-	-	-
Device success n (%)	70 (84)	19 (86)	51 (82)	0.75	15 (79)	55 (85)	0.73
Aortic Regurgitation ≥2	9 (11)	2 (9.1)	7 (11.3)	0.99	4 (21)	5 (8)	0.15
Mean gradient mmHg mean ± SD	10.5 ± 4.6	10.1 ± 5.2	10.6 ± 4.6	0.73	11.2 ± 4.2	10.4 ± 4.9	0.82
All Bleedings n (%)	23 (27)	6 (27)	17 (27)	0.98	7 (36)	16 (24)	0.31
Vascular Complications n (%)	10 (11)	5 (23)	5 (8)	0.06	2 (10)	8 (12)	0.83
CHF n (%)	2 (2)	1 (1)	1 (0)	0.43	0 (0)	2 (3)	0.43
Stage 2-3 AKI n (%)	13 (15)	5 (22)	8 (12)	0.27	3 (15)	10 (15)	0.86
<i>Other variables</i>	-	-	-	-	-	-	-
New AF episode n (%)	5 (5)	2 (1)	3 (1)	0.46	1 (0)	4 (6)	0.88
Clinical TIA/Stroke n (%)	5 (5)	2 (1)	3 (1)	0.46	0 (0)	5 (7)	0.21
IntraHospital death n (%)	1 (1)	1 (1)	0 (0)	0.09	1 (1)	0 (0)	0.06



Results: predictive factors of CMB

- a prolonged procedure(RR=1.21 [1.01-1.170] for every increased 5 min of fluoroscopy time, p=0.04)
- post-procedural acquired-VWD(RR 1.42 [1.08-1.89] for every lower “0.1 unit” of the HMW-multimer-ratio, p=0.004)
- →were associated with the occurrence of new post-procedural microbleed(s).

Results: neurological exam



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	All (n=84)	Preprocedural ≥ 1 CMB (n=22)	Preprocedural no CMB (n=62)	P value (preprocedural)
<i>Neurological examination (preprocedural)</i>	-	-	-	-
Modified Rankin scale >1 n (%)	6 (7)	2 (9)	4 (6)	0.67
NIHss score >1 n (%)	8 (9)	3 (13)	5 (8)	0.44
EQ-5D score mean $\pm$ SD	42 $\pm$ 12	42 $\pm$ 18	42 $\pm$ 11	0.85
MMSE score mean $\pm$ SD	28 $\pm$ 2	26 $\pm$ 3	28 $\pm$ 1	0.01 #
<i>Clinical events at 6 months</i>	-	-	-	-
Death n (%)	9 (10)	2 (1)	7 (11)	0.77
MACCE n (%)	5 (5)	1 (1)	4 (6)	0.74
		Postprocedural ≥ 1 CMB (n=34)	Postprocedural no CMB (n=50)	P value
<i>Neurological examination at 6 months</i>	-	-	-	-
QVFS questionnaire n (%)	5 (5)	3 (8)	2 (4)	0.35
Modified Rankin scale >1 n (%)	18 (21)	12 (35)	6 (12)	0.008*
NIHss score >1 n (%)	4 (4)	3 (8)	1 (2)	0.14
EQ-5D score mean $\pm$ SD	61 $\pm$ 12	62 $\pm$ 13	60 $\pm$ 12	0.52
MMSE score mean $\pm$ SD	27 $\pm$ 2	27 $\pm$ 3	28 $\pm$ 2	0.11
<i>Clinical events at 6 months</i>	-	-	-	-
Death n (%)	9 (10)	5 (14)	4 (8)	0.32
MACCE n (%)	5 (5)	3 (8)	2 (4)	0.35



Conclusions

- Occurrence of new microbleeds as measured 3 days after the procedure is high ($\approx 20\%$)
- Presence of microbleeds as detected after the procedure is impacting the 6-month neurological outcome
- Procedural management and persistence of acquired-VWD are predictors of the occurrence of microbleeds.
- Importance of preprocedural Cerebral MRI: 6% of patients had at least one cerebral emboli