AJR Supplemental Content

Supplemental content for Effect of GBCA Use on Detection and Diagnostic Performance of the Central Vein Sign: Evaluation Using a 3-T FLAIR* Sequence in Patients With Suspected Multiple Sclerosis

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doi.org/10.2214/AJR.22.27731
Published online: Aug. 17, 2022

The authors have supplied these materials to give readers additional information about the work.

Table S1. Comparison of symptom duration and clinical study measures between participants with and without MS based on 2017 McDonald criteria.

Characteristic	MS (n=13)	No MS (n=17)	p
Symptom duration (wks), median [IQR]	34 [505] (n=10)	57 [135] (n=12)	.82
T25FW, mean ± SD	4.9 ± 1.3	5.0 ± 1.6	.91
EDSS, mean ± SD	1.5 ± 1.2	1.0 ± 1.0	.33
9-HPT (sec), mean ± SD	21.8 ± 3.8	20.0 ± 6.4	.51
SDMT (number correct), mean ± SD	56.2 ± 8.9	54.1 ± 13.0	.59

Note: Symptom duration calculated at time of enrollment. Due to non-normality of distribution, the Mann-Whitney U test was used to determine the p value for symptom duration. All other p values in table were determined using t tests.

9-HPT= 9-hole peg test, EDSS = expanded disability status scale, SDMT= symbol digit modalities test, T25FW= timed 25-foot walk test.

Table S2. Number of CVS-positive WML and CVS-positivity rates based on postcontrast FLAIR* images, stratified by location and MS diagnoses.

Location	No. of CVS-Positive WML			CVS-Positivity Rate		
	MS	No MS	p	MS	No MS	p
Periventricular	42	6	<.001	74 (42/57)	46 (6/13)	.05
Juxtacortical	22	5	.004	51 (22/43)	33 (5/15)	.23
Subcortical or deep white matter	161	29	<.001	65 (161/249)	9 (29/341)	<.001
Infratentorial	4	0	.99	57 (4/7)	0 (0/3)	.2

Data expressed as counts for number of CVS-positive WML and as percentage with numerator (CVS-positive WML) and denominator (CVS-positive and CVS-negative WML) in parentheses for CVS-positivity rates. For number of CVS-positive WML, p values were calculated using a binomial model accounting for diagnosis of MS. For CVS-positivity rate, P values were calculated using the chi-square test for all locations except infratentorial, for which the Fisher's exact test was used due to small sample size.

CVS = central vein sign, WML = white matter lesion

Table S3. Distribution of CVS-positive WML by location and GBCA use.

Location	Precontrast (n=218)	Postcontrast (n=269)
Periventricular	41 (19)	48 (18)
Juxtacortical	24 (11)	27 (10)
Subcortical or deep white matter	148 (68)	190 (71)
Infratentorial	5 (2)	4 (1)

Data expressed as number of WML with percentage in parentheses.
CVS = central vein sign, GBCA = gadolinium-based contrast agent, WML = white matter lesion.

Table S4. Probability of detecting a CVS-positive WML, determined by a binomial model based on MS diagnosis using 2017 McDonald criteria at initial study visit and GBCA use.

Participant Group	Probability
MS, no GBCA	0.54
MS, GBCA	0.65
No MS, no GBCA	0.07
No MS, GBCA	0.11

CVS = central vein sign, GBCA = gadolinium-based contrast agent, MS = multiple sclerosis, WML = white mater lesion

Table S5. Clinical and imaging information for 17 participants who did not meet 2017 McDonald criteria for multiple sclerosis (MS) on initial study visit

Patient No.	Age (y)	Sex	Diagnosis at 12-Month Follow-up	Met DIS Criteria by MRI	Met DIT Criteria by MRI	Total WML	Total Evaluated WML[a] (Pre)	Total Evaluated WML[a] (Post)	CVS-Positivity Rate[b] (Pre)	CVS-Positivity Rate[b] (Post)
1	41	F	Paresthesias	Y	Y	128	55	46	0 (0/55)	5 (2/44)
2	55	F	Mixed connective tissue disease	Y	Y	102	31	22	7 (2/31)	0 (0/22)
3	19	F	Migraines, post-concussion syndrome	N	N	122	16	18	7 (1/14)	6 (1/17)
4	29	F	Radiologically isolated syndrome	Y	Y	41	12	16	46 (5/11)	75 (9/12)
5	48	F	Traumatic cervical myelopathy	Y	N	91	22	30	10 (2/21)	12 (3/25)
6	29	F	Radiologically isolated syndrome	Y	N	33	15	12	0 (0/15)	0 (0/12)
7	42	F	Clinically isolated syndrome	N	N	64	26	21	4 (1/23)	5 (1/20)
8	39	F	Migraines, post-concussion syndrome	N	N	20	6	4	33 (2/6)	75 (3/4)
9	49	F	Clinically isolated syndrome	Y	N	31	8	10	38 (3/8)	30 (3/10)
10	60	M	Transient ischemic attack, small vessel ischemic disease	N	N	63	11	14	0 (0/11)	23 (3/13)
11	35	F	Unknown	N	N	40	4	5	0 (0/4)	20 (1/5)
12	60	F	Non-specific white matter changes	N	N	7	3	3	67 (2/3)	67 (2/3)
13	49	F	Migraine	Y	N	221	86	111	3.5 (3/85)	5 (5/107)
14	57	F	Small-vessel ischemic disease	Y	N	102	46	28	0 (0/45)	8 (2/25)
15	58	F	Small-vessel ischemic disease	Y	N	87	34	39	15 (5/34)	13 (5/38)
16	45	F	Non-specific white matter changes	Y	N	38	10	12	0 (0/10)	0 (0/11)
17	59	F	Clinically isolated syndrome	Y	N	13	5	4	0 (0/5)	0 (0/4)

Date expressed as number of participants or WML, or as percentage with numerators and denominators in parentheses

[a]Based on NAIMS exclusion criteria

[b]Numerator represents number of CVS-positive lesions, and denominators represent number of CVS-positive and CVS-negative lesions. Discrepancies between total evaluated lesions and the denominator of the CVS-positivity rates is due to the presence of CVS-indeterminate lesions, which were analyzed separately.

DIS= dissemination in space, DIT= dissemination in time, F = female, M = male, NAIMS = North American Imaging in Multiple Sclerosis Cooperative, WML = white matter lesion

Table S6. Clinical and imaging information for 13 participants who met 2017 McDonald criteria for multiple sclerosis (MS) on initial study visit

Patient No.	Age (y)	Sex	Met DIS Criteria by MRI	Met DIT Criteria by MRI	Total WML	Total Evaluated WML[a] (Pre)	Total Evaluated WML[a] (Post)	CVS-Positivity Rate[b] (Pre)	CVS-Positivity Rate[b] (Post)
18	52	M	Y	Y	52	37	30	85 (29/34)	90 (27/30)
19[c]	25	F	Y	Y	27	8	7	43 (3/7)	43 (3/7)
20	32	F	Y	Y	49	20	25	80 (16/20)	87 (20/23)
21	39	F	Y	Y	35	14	14	25 (3/12)	60 (6/10)
22	64	F	Y	Y	20	5	9	40 (2/5)	67 (6/9)
23	43	F	Y	N	38	17	15	23 (3/13)	64 (9/14)
24	63	F	Y	Y	126	32	28	9 (3/32)	11 (3/28)
25	38	M	Y	Y	62	40	37	61 (19/31)	67 (22/33)
26	37	F	Y	N	192	81	100	38 (27/71)	52 (43/83)
27	46	M	Y	Y	69	12	15	78 (7/9)	79 (11/14)
28	36	M	Y	Y	89	57	43	67 (34/51)	84 (31/37)
29	38	M	Y	Y	136	74	69	69 (45/65)	70 (45/64)
30	54	M	Y	N	10	5	6	25 (1/4)	75 (3/4)

Date expressed as number of participants or WML, or as percentage with numerators and denominators in parentheses

[a]Based on NAIMS exclusion criteria

[b]Numerator represents number of CVS-positive lesions, and denominators represent number of CVS-positive and CVS-negative lesions. Discrepancies between total evaluated lesions and the denominator of the CVS-positivity rates is due to the presence of CVS-indeterminate lesions, which were analyzed separately

[c]Only patient in table without diagnosis of MS at 12-month follow-up; had diagnosis of postinfectious encephalomyelitis at 12-month follow-up

DIS= dissemination in space, DIT= dissemination in time, F = female, M = male, NAIMS = North American Imaging in Multiple Sclerosis Cooperative, WML = white matter lesion

Figure S1—Patient-by-patient comparison of CVS-positivity rate between precontrast (black boxes) and postcontrast (gray circles) FLAIR* images based on 12-month follow-up diagnoses, classifying participants with follow-up diagnosis of radiologically isolated syndrome or clinically isolated syndrome as having MS; thin diagonal lines connect precontrast and postcontrast values for individual participants, and thick horizontal lines denote median percentage across participants for precontrast and postcontrast images. Median CVS-positivity rate was higher on postcontrast than precontrast images for participants with MS (67% [IQR, 57%] vs 38% [IQR, 52%], p=.03), although was not significantly different between postcontrast and preconstrast images for those without MS (12% [IQR, 28%] vs 7% [IQR, 24%], p=.08). Likelihood of having at least one CVS-positive lesion was significantly higher for participants with than without MS [odds ratio (OR), 14.0 [95% CI: 10.2–19.4]; p<.001). Likelihood of having at least one CVS-positive lesion was significantly higher for postcontrast than precontrast FLAIR* images (OR, 1.5 [95% CI: 1.2–2.0]; p<.001). CVS = central vein sign, MS= multiple sclerosis, WML = white matter lesion

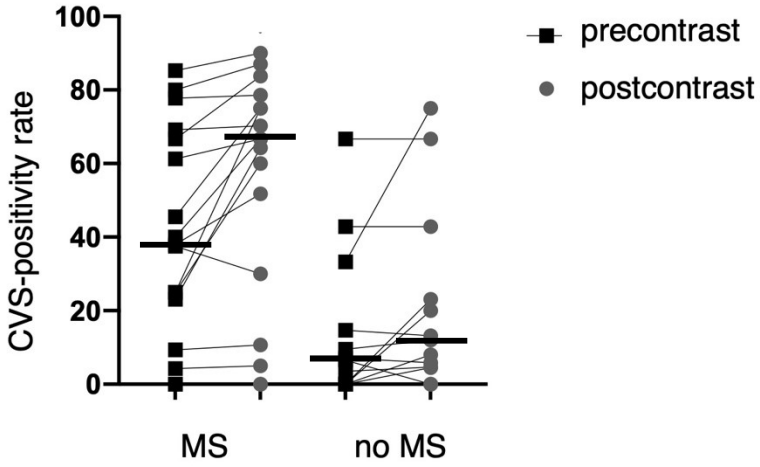

Figure S2—Patient-by-patient comparison of CVS-positivity rate between precontrast (black boxes) and postcontrast (gray circles) FLAIR* images based on 12-month follow-up diagnoses and excluding participants with follow-up diagnosis of radiologically isolated syndrome or clinically isolated syndrome; thin diagonal lines connect precontrast and postcontrast values for individual participants, and thick horizontal lines denote median percentage across participants for precontrast and postcontrast images. Median CVS-positivity rate was higher on postcontrast than precontrast images for participants with MS (69% [IQR, 21%] vs 51% [IQR, 51%], p=.002) although was not significantly different between postcontrast and preconstrast images for those without MS (12% [IQR, 28%] vs 7% [IQR, 24%], p=.08). Likelihood of having at least one CVS-positive lesion was significantly higher for participants with than without MS [odds ratio (OR), 20.0 [95% CI: 13.2–28.1]; p<.001). Likelihood of having at least one CVS-positive lesion was significantly higher for postcontrast than precontrast FLAIR* images (OR, 1.6 [95% CI: 1.2–2.0]; p=.002). CVS = central vein sign, MS= multiple sclerosis, WML = white matter lesion