Comparison of seven sets of criteria used for the diagnosis of vascular dementia

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Abstract

At least seven different sets of criteria are commonly used for the diagnosis of vascular dementia (VaD). These are the ischemic scales (IS) of Hachinski, Rosen and Loeb, the criteria from the DSM-III-R, those outlined by Erkinjuntti et al., the State of California Alzheimer's Disease Diagnostic and Treatment Centers (ADDTC) and the international workgroup of the American National Institute of Neurological Disorders and Stroke (NINDS) and the European 'Association Internationale pour la Recherche et l'Enseignement en Neurosciences'. To investigate the differences and similarities of these criteria, we applied them to a sample of 124 demented patients from the Maastricht Memory Clinic. Only 8 patients were diagnosed as having VaD by all criteria. Depending on which criteria were used, the frequencies of VaD and Alzheimer's disease (AD) ranged from 6 to 32%, and from 48 to 56%, respectively. The IS of Hachinski and Rosen resulted in the highest frequencies of VaD, whereas the criteria of Erkinjuntti and those from the ADDTC and the NINDS workgroup yielded the lowest. The number of patients with VaD was reduced substantially when neuroradiological data and the temporal relationship between stroke and dementia were taken into consideration. We conclude that the seven sets of criteria cannot be regarded as interchangeable. Differences in the criteria for VaD and AD may be an overlooked source of interstudy variance.

Key Words

Vascular dementia
Diagnostic criteria
Alzheimer's disease
Ischemic scales

Introduction

The differentiation between Alhzeimer's disease (AD) and vascular dementia (VaD) is important not only from a clinical viewpoint [1, 2], but also for epidemiological research [3]. At least seven instruments have been purposed for the diagnosis of VaD in the last 20 years, and all are currently used for clinical and research goals. The aim of the present

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study was to examine whether, and to what extent, the different criteria can be regarded as interchangeable. This has implications for the comparison of studies of VaD or AD carried out with the various criteria. Therefore, we applied the seven sets to a sample of demented patients visiting a university hospital, in order to compare the prevalence rates of VaD and AD as detected by each criterion and to obtain insight into the similarities and differences between the various criteria.

Patients and Methods

Patients

The data of patients with dementia [4, 5] who were consecutively referred to the Maastricht Memory Clinic were used for this study. The diagnostic procedure has been described elsewhere [6] and includes: a semistructured history provided by the patient and the caregiver, a standardized psychiatric interview, and internal, neurological examination and neuropsychological investigation, laboratory tests and a CT scan of the brain (in most cases using the Philips Tomoscan 310). A neurologist experienced in cerebrovascular pathology (J.L.) examined all CT scans for the presence of (lacunar or cortical) infarctions and leukoaraiosis, according to standardized criteria [7]. Only CT scans made during the assessment of dementia, and not those made earlier in the acute stage of a stroke, were used for this study.

Methods

Seven different sets of criteria for the diagnosis of VaD were studied. The criteria are shown in table 1.

The ischemic scale (IS) of Hachinski et al. (H-IS) [8] consists of 13 items related to the course, risk factors, behavioral features and neurological signs and symptoms. Rosen et al. [9] validated the H-IS by using the pathological data of 14 patients; in their version of the IS (r-IS), they omitted 5 of the original H-IS items that did not contribute to the clinical differentiation between AD and VaD. Loeb [10] and Gandolfo [11] validated the H-IS by using CT scan data from 101 patients with dementia and proposed their own version of the IS (L-IS).On the basis of these findings, the L-IS included only 4 of the original H-IS items and was expanded to include single or multiple low-density areas on CT scans [10, 11]. The criteria for VaD from the DSM-III-R [4], comprise, besides the presence of dementia: (1) the presence of a stepwise deteriorating course with a patchy distribution of deficits; (2) focal neurological signs and symptoms, and (3) evidence from history, physical examination or laboratory tests of significant cerebrovascular disease, judged to be etiologically related to the disturbance. In the DSM-IV criteria [5], which were not yet available at the time of this study, the first of these criteria is omitted. Erkinjuntti et al. [12, 13] defined VaD, multi-infarct type, as 'dementia evolving in connection with acute neurological symptoms or signs and/or findings on CT indicating multiple cortical and/or deep vascular lesions of the brain'. Recently, similar criteria for the diagnosis of VaD have been suggested by the State of California Alzheimer's Disease Diagnostic and Treatment Centers (ADDTC) [14] and by an international workgroup of the American National Institute of Neurological Disorders and Stroke (NINDS) and the European 'Association Internationale pour la Recherche et l'Enseignement en Neurosciences' (AIREN) [15]. In these recent proposals, less emphasis is put on course characteristics and behavioral features; neuroimaging evidence of an infarct (by CT or MRI) is necessary, and at least two ischemic strokes are required, or, in the case of one stroke, the evidence of a temporal relationship to the onset of dementia.

Soon after the workup, all relevant clinical data of each patient were entered in the database of the Maastricht Memory Clinic. These included, among others, all items from the H-IS, the number, type and localization of the strokes, relevant CT scan data, existence of a temporal relationship with the onset of dementia and clinical features of Binswanger's disease as defined in the ADDTC report (urinary incontinence, vascular risk factors and extensive white-matter changes on CT scans) [14]. Thus, although many of the patients had been assessed before, the more recent criteria were published, the different sets of criteria could be applied in retrospect. The only unavailable data pertained to the DSM-III-R criterion for VaD, of a 'patchy distribution of deficits'. This aspect was ignored because it was felt that it could not be easily used in practice. Cut-off scores for VaD and AD were used as described in the original publications. Four diagnostic categories were used: (1) VaD, including 'multi-infarct dementia' scores above the cut-off values of the ISs [8–10], 'multi-infarct dementia' by the DSM criteria, [4], VaD multi-infarct type [12], and 'probable VaD' [14, 15]; (2) mixed dementia, an intermediate category for patients with IS scores between the cut-off values for VaD and AD, probable and hemodynamic-type VaD [12] and possible VaD [14, 15]; (3) AD, including the patients who formed the 'counterpart' of VaD, i.e. ful-

Table 1. The items of seven sets of criteria for the diagnosis of VaD

	H-IS 1975	R-IS 1980	L-IS 1982	DSM 1980/87	ERK 1986	ADDTC 1992	NINDS 1993
Dementia	+	+	+	+	+	+	+[1]
Abrupt onset	2	2	2	−	+	−	±[2]
Stepwise deterioration	1	1	−	+	−	−	−
Fluctuation	2	−	−	−	−	−	−
Nocturnal confusion	1	−	−	−	−	−	−
Preserved personality	1	−	−	+	−	−	−
Depression	1	−	−	−	−	−	−
Somatic complaints	1	1	−	−	−	−	−
Emotional lability	1	1	−	−	−	−	−
Hypertension	1	1	−	−	−	−	−
History of strokes	2	2	1	+	−	+	+
Signs of atherosclerosis	1	−	−	−	−	−	−
Focal neurological symptoms	2	2	2	+	+	+	+
Focal neurological signs	2	2	2	+	+	+	+
Low-density area on CT scan	−	−	2/3[3]	±	+	+	+
Multiple strokes	−	−	−	±	+	+[4]	±[2]
Temporal relation	−	−	−	−	+[5]	+[6]	−

ERK = Criteria of Erkinjuntti et al.; + = obligatory; ± = ambiguous.

1 Definition of dementia slightly different; neuropsychological testing obligatory.

2 Either multiple strokes or 1 single stroke with abrupt onset of dementia.

3 Either isolated (2 points) or multiple (3 points) hypodense areas on CT scan.

4 At least 1 infarct outside the cerebellum.

5 In absence of a temporal relation: probable VaD.

6 In case of a single stroke.

filling regular research criteria for AD [16], using the corresponding criteria to exclude VaD, and (4) unclassifiable, a category formed by the patients who could not be classified in any of the above categories.

The agreement between the different sets of criteria was assessed by calculating the κ statistics. κ is the rate of observed agreement between a single pair of sets adjusted for the proportion of the agreement that can be expected to occur by chance.

Results

One hundred and twenty-four patients were included in this study. The mean age of the patients was 70.1 ± 8.8 years. In 25 patients, the examination yielded a cause other than a cerebrovascular or primary degenerative cause (e.g. Parkinson's disease, frontal lobe dementia or alcohol abuse), leaving 109 patients for further differentiation between VaD and AD. These patients were mildly or moderately demented, as reflected by a mean score of 17.9 ± 5.8 on the Mini Mental State Examination [17].

Thirty-nine had VaD according to at least one set of criteria, whereas only 8 patients were diagnosed as having VaD by all sets of criteria. Seventy-five patients had AD diagnosed by at least one set of criteria, whereas 51 patients were diagnosed as such by all sets. Table 2 shows the numbers of patients diagnosed according to each criterion.

Table 2. Frequencies of VaD and AD among 124 patients with dementia, using different sets of criteria

Category	Criterion	n	%
H-IS (1975) [18]			
VaD	score ≥ 7	32	26
Mixed	score > 4 and < 7	10	8
AD	NINCDS-ADRDA and H-IS score ≤ 4	65	52
Unclassifiable		2	2
R-IS (1980)			
VaD	score ≥ 4	36	29
Mixed	score of 3	6	5
AD	NINCDS-ADRDA and L-IS score ≤ 2	64	52
Unclassifiable		3	2
L-IS (1982)			
VaD	score ≥ 5	23	19
Mixed	score of 3 or 4	12	10
AD	NINCDS-ADRDA and L-IS score ≤ 2	70	56
Unclassifiable		4	3
DSM-III-R (1980/1987)			
VaD	MID	15	12
Mixed	not covered by DSM criteria	0	0
AD	primary degenerative dementia	59	48
Unclassifiable		35	28
Erkinjuntti's criteria (1986)			
VaD	MID	14	11
Mixed	PVD and hemodynamic-type dementia	26	21
AD	NINCDS-ADRDA with exclusion of MID	61	49
Unclassifiable		8	6
ADDTC criteria (1992)			
VaD	probable IVD	156	12
Mixed	possible IVD	9	7
AD	NINCDS-ADRDA with exclusion of IVD	66	54
Unclassifiable		19	15
NINDS/AIREN (1993)			
VaD	probable	8	6
Mixed	possible	32	26
AD	NINCDS-ADRDA with exclusion of VaD by NINDS criteria	63	50
Unclassifiable		6	5

MID = Multi-infarct dementia; PVD = probable VaD [12]; IVD = ischemic VaD [14]; NINCDS-ADRDA: criteria for AD by NINCDS-ADRDA work group [16]; unclassifiable = not classifibable as either VaD, AD or mixed dementia.

Table 3. Agreement (κ values) between the different sets of criteria for the diagnosis of VaD and AD

	H-IS	R-IS	L-IS	DSM-III	ERK	ADDTC
Criteria for VaD						
R-IS	0.87	–	–	–	–	–
L-IS	0.74	0.70	–	–	–	–
DSM-III	0.50	0.49	0.56	–	–	–
ERK	0.37	0.36	0.58	0.40	–	–
ADDTC	0.40	0.39	0.62	0.46	0.88	–
NINDS	0.32	0.28	0.46	0.38	0.60	0.57
Criteria for AD						
R-IS	0.91	–	–	–	–	–
L-IS	0.83	0.81	–	–	–	–
DSM-III	0.66	0.68	0.68	–	–	–
ERK	0.78	0.79	0.83	0.56	–	–
ADDTC	0.65	0.64	0.82	0.85	0.66	–
NINDS	0.81	0.83	0.79	0.52	0.96	0.62

ERK = Criteria of Erinjuntti et al. κ statistics, interpretation of the level of agreement: 0.0–0.2, slight; 0.2–0.4, fair; 0.4–0.6, moderate; 0.6–0.8, substantial, and 0.8–1.0, almost perfect [19].

The R-IS and H-IS resulted in the highest number of patients with VaD (36 and 32, i.e. 29 and 26%, respectively), whereas only 8 (6%) of the subjects were diagnosed as having VaD when the NINDS criteria were used. The number of patients diagnosed as having AD varied between 59 (48%) using the DSM criteria and 70 (56%) using the L-IS. Between 0 and 26% of the patients were diagnosed as suffering from mixed dementia, using the DSM criteria and those of the NINDS, respectively. The proportion of patients who could not be classified ranged from 32% (using the DSM criteria) to 2% (using the H-IS).

In table 3, the κ values for VaD and AD between all possible combinations for criteria are shown. On the average, the agreement was substantial for AD (κ = 0.75) but only moderate for VaD (κ = 0.52), whereas only fair agreement existed for mixed dementia (κ = 0.32). Concerning the diagnosis of VaD, substantial or even almost perfect agreement existed between the criteria of the ADDTC, Erkinjuntti et al. 13] and the NINDS, as well as between the ISs. In general, there was only fair to slight agreement between the ISs and the modern criteria (ADDTC, Erkinjuntti and NINDS).

The lowest agreement for the diagnosis of VaD occurred between the H-IS and the R-IS on the one hand, and the criteria fo the ADDTC, Erkinjuntti et al. and the NINDS on the other. For instance, 32 patients had an H-IS score indicative of VaD, but no more than 8 would have been diagnosed as such according to the NINDS criteria. Common reasons for this disagreement were the following: 4 of the 32 patients diagnosed as having VaD by the H-IS criteria demonstrated slight unexplained focal signs and/or symptoms (e.g. one-sided palmomental reflex), whereas the fifth patient demonstrated a fluctuating course and scored on the one-point behavioral items of the H-IS, leading to a high H-IS score; however, they also had an insidious onset of dementia with neither a clinical history of

stroke nor hypodense areas on the CT scan and were thus diagnosed as having AD using the NINDS criteria for the exclusion of VaD; 9 other patients with VaD according to the H-IS were classified as having possible dementia by the NINDS criteria – 3 patients with Binswanger's disease without multiple strokes and 6 with evidence of only 1 stroke without a clear temporal connection with dementia. Six patients identified with the H-IS as having VaD could not be classified by the ADDTC or the NINDS criteria: 3 patients were said to have become demented acutely instead of insidiously (thus not fulfilling criteria for AD); there was also no evidence of stroke in the history, the physical examination or on the CT scan (thus not fulfilling the criteria for possible or probable VaD). Three other patients became demented after having a single stroke clinically, without any demonstrable hypodense areas on the CT scan. The ADDTC and the NINDS criteria do not cover these two situations, but Erkinjuntti's criteria would have classified them as mixed dementia.

Discussion

The present study shows that application of the seven sets of criteria for the diagnosis of VaD (or for the exclusion of vascular factors for AD) led to differences in the frequency of AD and VaD that cannot be neglected. For example, applying the R-IS resulted in more than twice as many patients with VaD as when the DSM-III-R criteria were applied. The more recent criteria showed substantial agreement with each other as did the ischemic scales. Otherwise, the sets of criteria cannot be interchanged without due consideration. In the 'clear-cut' patients, i.e. in those who demonstrated clear evidence of multiple strokes in their histories, clinical examinations and CT scans, different criteria led to similar diagnoses. The criteria diverged when information from one category did not confirm the other, e.g. evidence of stroke in a CT scan without focal neurological symptoms or vice versa. The present study shows that if the temporal connection or neuroimaging data are taken into account, the diagnostic outcome is influenced considerably. The choice of a particular set of criteria appears more critical in demonstrating a vascular etiology for the diagnosis of VaD than in making such an etiology unlikely for the diagnosis of AD.

The controversy as to whether VaD is overdiagnosed [20] or underdiagnosed [21] may be related to differences in the criteria used, which is possibly an overlooked source of interstudy outcome variance; e.g. in a recent epidemiological study in Sweden, differences in diagnostic criteria were found to lead to a great variation in the prevalence of VaD [3]. Likewise, ischemic infarcts have been described as varying from 20 to 90% of the patients with VaD and from 0 to 37% of the patients with AD [7, 22–24]. Depending on which criterion was used, ischemic infarcts on CT scans were found in our study in 45–100% of the patients diagnosed as having VaD, and in 0–13% of the patients with AD.

In the absence of neuropathological data, no definite conclusion can be drawn as to which criterion is superior. For the diagnosis of VaD, the more strict criteria of Erkinjuntti, the ADDTC and the NINDS seem preferable because they lead to more homogeneous patient groups. All versions of the IS can be regarded as clinically useful tools for the exclusion of a vascular etiology in the diagnosis of AD.

Conclusion

Results of studies which use different criteria for the diagnosis or the exclusion of VaD must be compared with caution. Given the impact of temporal connection and neurodiological data, the more recent criteria of the ADDTC, the NINDS and Erkinjuntti can presently be regarded as the choice criteria, although they still await further validation by pathological studies.

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