

Prevalence of potentially reversible dementias and actual reversibility in a memory clinic cohort



Evidence

Études

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Abstract

Background: Although clinics for the evaluation of cognitive dysfunction have typically emphasized the detection and treatment of the reversible causes of dementia, it remains unclear whether the treatment of such causes results in reversal of the dementia. Therefore, the appropriate work-up for dementia is in dispute.

Methods: A chart review was performed with records from an urban tertiary care referral-based memory clinic. The records for 196 patients with dementia or suspected dementia, seen between October 1991 and December 1993, were examined to determine the prevalence of potentially reversible dementias and whether the cognitive dysfunction improved or resolved after treatment. Data abstracted from the medical charts included demographic information, medication use, presence of depression, and results of neuropsychological tests, blood work and neuroimaging. The clinical diagnosis, the response to treatment, if applicable, and the outcome (mean follow-up period 16 months) were analysed. The recommendations of the 1989 Canadian Consensus Conference on the Assessment of Dementia (CCCAD) on the use of CT were retrospectively applied in each case.

Results: Of the 196 patients, 45 (23.0%) had a potentially reversible condition identified by history, physical examination, blood testing or CT; in only 7 (3.6% of the total) did treatment result in improvement or resolution of the dementia. These 7 patients had higher results for the Mini-Mental State examination (mean result 26) and exhibited only mild cognitive deficits. Potentially reversible lesions were found in the CT scans of 6 (3.1%) patients: 4 had normal-pressure hydrocephalus and 2 had a brain tumour. If the CCCAD recommendations had been followed, CT would have been performed in 76 (38.8%) of the patients, and 1 of the 6 patients with a lesion would have been missed.

Interpretation: Both potential and actual reversibility of dementia was low in these memory clinic patients. The patients whose condition improved with intervention had early and milder cognitive deficits, which suggests that thorough evaluation of early memory loss is warranted.

Résumé

Contexte : Même si les cliniques d'évaluation des dysfonctionnements cognitifs ont toujours mis l'accent sur la détection et le traitement des causes réversibles de la démence, il reste à déterminer si le traitement de ces causes réussit à inverser la démence. C'est pourquoi l'examen qui convient pour déterminer s'il y a démence demeure une source de contestation.

Méthode : On a procédé à un examen rétrospectif des dossiers des patients d'une clinique urbaine de soins tertiaires où sont référés les patients pour des tests de mémoire. On a examiné les dossiers de 196 patients atteints de démence ou de démence soupçonnée reçus entre octobre 1991 et décembre 1993 pour déterminer la prévalence des démences qui pourraient être réversibles et si le dysfonctionnement cognitif s'est amélioré ou est disparu après le traitement. On a tiré des dossiers médicaux les données abrégées suivantes : renseignements dé-

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mographiques, utilisation de médicaments, présence de dépression et résultats de tests neuropsychologiques, d'analyse sanguine et de neuro-imagerie. Le diagnostic clinique, la réaction au traitement le cas échéant, et le résultat (suivi moyen de 16 mois) ont été analysés. Les recommandations de la Conférence canadienne pour un consensus sur l'évaluation de la démence (CCCED) portant sur l'utilisation de la tomodensitométrie ont été appliquées rétrospectivement à chaque cas.

Résultats : Sur les 196 patients, 45 (23,0 %) présentaient un état qui pourrait être réversible déterminé par les antécédents, l'examen médical, les analyses du sang ou la tomodensitométrie. Le traitement a atténué la démence ou l'a fait disparaître chez sept patients (3,6 % du total) seulement. Ces sept patients avaient obtenu des résultats plus élevés au mini-examen de l'état mental (résultat moyen de 26) et n'avaient que de faibles déficits de la cognition. La tomodensitométrie a révélé des lésions qui pourraient être réversibles chez six patients (3,1 %) : quatre avaient une hydrocéphalie à pression normale et deux avaient une tumeur au cerveau. Si l'on avait suivi les recommandations de la CCCED, on aurait soumis à une tomodensitométrie 76 (38,8 %) des patients et l'on aurait raté un des six patients atteints d'une lésion.

Interprétation : La réversibilité possible et réelle de la démence était faible chez ces patients dont la mémoire a été testée en clinique. Les patients dont l'état s'est amélioré après une intervention avaient des déficits précoces et moins marqués de la cognition, ce qui indique qu'une évaluation approfondie de la perte de mémoire précoce est justifiée.

Alzheimer's disease and the related dementias are a major public health concern and are becoming increasingly burdensome as the population ages.^{1,2} Their prevalence ranges from 2.4% to 11.1% in people over 65 years of age, rising to between 26% and 44% in people 85 years of age or older.^{1,3,4} The annual costs, direct and indirect, of Alzheimer's disease in Canada have been estimated to total \$3.9 billion.¹

Although there has been much interest in identifying other, potentially reversible causes of dementia, the utility of extensive laboratory evaluation has been debated.⁵⁻¹⁹ The prevalence of potentially reversible conditions ranges from 0% to 30%.¹² However, most studies describing the prevalence of potentially reversible dementias have not reported follow-up data on actual reversibility. Potentially reversible conditions include drug- and alcohol-induced dementias,^{6,9,12} acute confusional states and metabolic conditions (such as vitamin B₁₂ deficiency and hypothyroidism),^{12,20} and "pseudodementia" due to depression.²¹ Rarer structural brain lesions, such as subdural hematoma, normal-pressure hydrocephalus and brain tumours, are other potentially reversible causes of dementia.²²⁻²⁶ As a result, although there is general agreement on the value of a thorough history and physical examination, the utility of appropriate laboratory investigations, in particular neuroimaging, remains disputed.^{16-19,27-29}

The objectives of our study were to determine both the prevalence of potentially reversible dementia in an outpatient memory clinic population and the actual reversibility of the potentially reversible dementias.

Methods

A comprehensive chart review was carried out for 305 consecutive patients seen in the Memory Clinic of the Sir Mortimer B. Davis-Jewish General Hospital (a 620-bed teaching hospital affiliated with McGill University, Montreal) between October 1991 and December 1993. All patients, regardless of final diagnosis, were included in the study. This study was carried out as part of a research project on the early diagnosis of Alzheimer's disease, which was approved by the Jewish General Hospital Research and Ethics Committee.

Referrals to the Memory Clinic, received from family doctors, internists, neurologists and psychiatrists, are for patients with early or atypical memory loss. The standard Memory Clinic work-up includes a complete history, physical and neurological examinations, and extensive neuropsychological testing. The neuropsychological tests include the Wechsler Memory Scale-R (revised),³⁰ the modified Wechsler Adult Intelligence Scale,³¹ the Delayed Verbal Learning Test,³² the Boston Naming Test,^{33,34} the Hierarchic Dementia Scale,³⁵ the Mini-Mental State examination (MMSE),³⁶ the Trail-Making A test,³⁷ the Word Fluency test,³⁸ the Visual Perceptual Battery,³⁹ the Clock Drawing Test⁴⁰ and the Geriatric Depression Scale.⁴¹ Laboratory investigations include complete blood count, biochemistry tests (for sodium, potassium, chloride, bicarbonate, urea nitrogen, glucose, creatinine, bilirubin, alkaline phosphatase, calcium, aspartate aminotransferase and alanine aminotransferase), VDRL testing,



and determination of serum levels of thyroxine, thyrotropin, vitamin B₁₂ and folate. CT is requested for virtually all patients. A preliminary diagnosis is established at the time of the initial visit by a panel consisting of a neurologist, a geriatrician, a clinical psychologist and a geriatric nurse. The diagnosis is updated, when appropriate, during follow-up visits, on the basis of laboratory data and clinical developments. Patients are reassessed every 4 to 6 months.

Dementia is diagnosed on the basis of the standard criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA).⁴ Patients who meet none of these criteria are classified as not having dementia. Patients who meet some but not all of the criteria (for example, a convincing history of memory impairment with objective evidence of deterioration indicated by neuropsychological testing but no interference with usual activities) are classified as having suspected dementia.

Patients who meet the full criteria for dementia are further categorized by cause, after investigation. Vascular dementia or mixed dementia (Alzheimer's disease and vascular dementia) are diagnosed in the clinical context of a history of hypertension and previous cerebrovascular accidents, a high Hachinski score, and corroborative evidence from CT, MRI or single-photon emission CT (SPECT). Probable and possible Alzheimer's disease are diagnosed on the basis of the NINCDS-ADRDA criteria.⁴

Other possible causes of dementia are identified from the history (e.g., alcohol abuse, medications, depression, head trauma or chronic psychiatric disorder) and the physical examination (e.g., progressive supranuclear palsy, Parkinson's disease or focal neurological signs). Metabolic causes of dementia are evaluated on the basis of routine blood work. Subdural hematoma, brain tumour and normal-pressure hydrocephalus, if suspected from the history and results of the physical exam, are evaluated by CT, as well as nuclear cisternography in cases of normal-pressure hydrocephalus. For the purposes of this study, potentially reversible causes of dementia included hypothyroidism, vitamin B₁₂ deficiency, depression, alcohol abuse, medication, tertiary syphilis, normal-pressure hydrocephalus, brain tumour and subdural hematoma. Vascular dementia was not considered reversible.

Variables extracted from the charts included age at first presentation to the Memory Clinic, sex and level of education attained. The preliminary and final diagnoses were recorded, and the length of follow-up was noted. Medications were recorded, as were the physicians' impressions regarding whether the medications were interfering with cognition. The results of the MMSE and the Hachinski scores from the initial visit were noted. The results of CT

were recorded, and each case was analysed with respect to the CCCAD recommendations for the use of CT.³

In cases where a potentially reversible condition was identified, the type and duration of treatment were noted. Response to therapy is determined by the Memory Clinic team at follow-up from a clinical assessment, interviews with caregivers and repeat neuropsychological testing. Cognitive impairment is judged as reversed, improved, unchanged or worse. The outcome is registered as reversed if the results of repeat neuropsychological testing and the clinical assessment are completely normal. The outcome is classified as improved on the basis of the subjective impression of the patient and the family, the clinician's global rating of patient function and objective improvement indicated by improvement in neuropsychological test results of either greater than one standard deviation (one *z*-score of the clinic's neurologically impaired individuals) on 2 or more neuropsychological measures or greater than 2 standard deviations on the MMSE or a single neuropsychological measure.

Patients were excluded from our analyses if they did not have any dementia, if they had not undergone CT or if they had not been followed for at least 4 months.

Results

The records for a total of 305 patients were reviewed. Of these, 196 had definite or suspected dementia, had undergone CT and had been followed for a period of at least 4 months at the time we completed our study. Of the remaining 109 patients, 52 did not have dementia, 44 had not been followed (7 refused, 13 were awaiting follow-up at the time of study completion, and 24 were not followed after the initial diagnosis) and 13 had not undergone CT. Of these 13, 6 had refused, 3 had advanced Alzheimer's dementia, and 4 were awaiting CT at the time of study completion.

Among the 196 patients remaining in the study cohort, the average age was 74.6 (range 49–92) years. The group consisted of 87 men (44.4%) and 109 women (55.6%). In 77 (39.3%) of the subjects the highest education level achieved was elementary school or less, 68 (34.7%) had completed high school, 22 (11.2%) had completed college or vocational school, and 29 (14.8%) had obtained a university degree. There was no baseline difference in age, sex, education or MMSE score between patients who were followed for at least 4 months and those who were not. There was also no difference between patients who underwent CT and those who did not in terms of age, sex and education. However, the patients who did not undergo CT had a statistically significantly higher baseline MMSE score than those who had undergone CT (25.2 v. 23.4) ($F_{(1)} 4.2, p = 0.041$).

Forty-five (23.0%) of the 196 patients had one or more potentially reversible causes of dementia. There was improvement (4 patients) or complete reversal (3 patients) of the cognitive impairment in a total of 7 patients (Fig. 1). Four of the 7 had suspected, not definite, dementia. The mean baseline MMSE score of the 7 patients with favourable outcomes was 26 (range 19–30, standard deviation 4), which indicated mild impairment.

Table 1 outlines the potentially reversible causes of dementia identified in the 45 patients and records the patients' outcome. Of the 3 patients whose cognitive impairment was completely reversed, 2 were treated for depression and 1 discontinued using a medication (lorazepam). Of the 4 patients whose cognitive impairment improved, 1 received treatment for hypothyroidism, 1 dis-

continued using a medication (bentropine), 1 received a shunt for normal-pressure hydrocephalus, and 1 underwent resection of a brain tumour.

Of the 196 CT scans obtained, potentially reversible lesions were found in 6 (3.1%). Four of the scans were interpreted as indicating normal-pressure hydrocephalus, and 2 scans revealed brain tumours. With neurosurgical treatment, the level of dementia declined in 2 patients, remained unchanged in 2 and continued to increase in 2. None of these patients experienced complete resolution of their cognitive dysfunction (Table 1).

Five of the six patients with potentially reversible lesions indicated by CT would have met at least one CCCAD criterion for CT. The patient who did not meet any of these criteria had a glioma; the mental status did

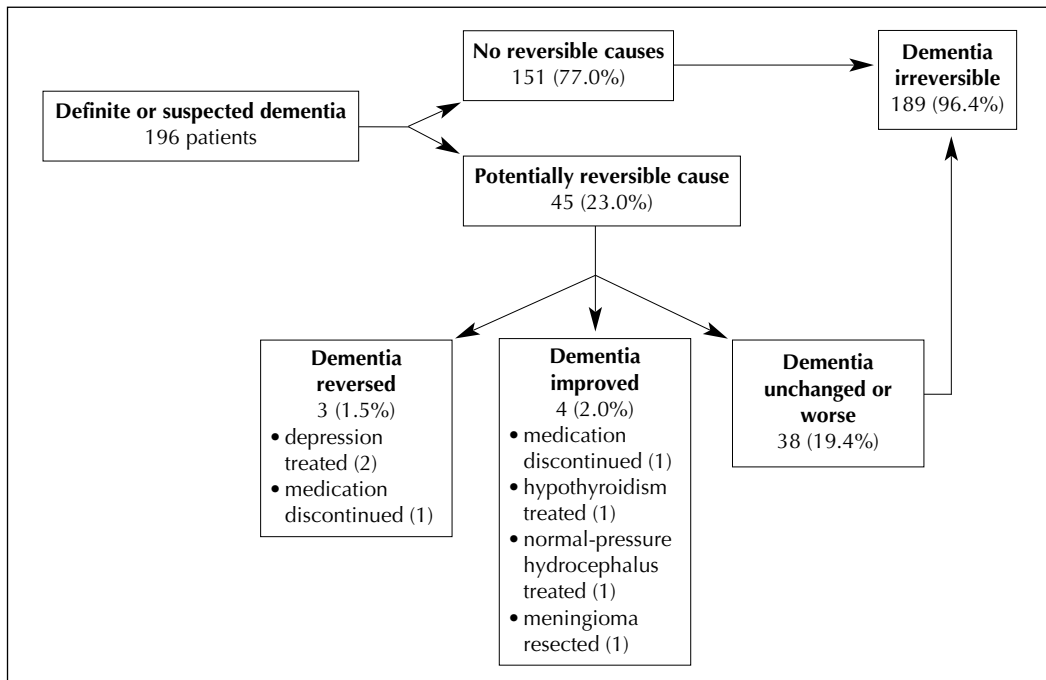


Fig. 1: Outcome for 196 patients with definite or suspected dementia seen in a memory disorders clinic between October 1991 and December 1993.

Table 1: Outcome after treatment in 45 patients with potentially reversible dementia*

Potentially reversible condition	No. (and %) of patients	Outcome; no. of patients			
		Dementia reversed	Dementia improved	Dementia unchanged	Dementia worse
Hypothyroidism	2 (4)	0	1	1	0
Vitamin B ₁₂ deficiency	8 (18)	0	0	2	6
Depression	23 (51)	2	0	11	10
Alcohol abuse	1 (2)	0	0	1	0
Medication	10 (22)	1	1	7	1
Normal-pressure hydrocephalus	4 (9)	0	1	2	1
Brain tumour	2 (4)	0	1	0	1
Total	50† —	3	4	24	19

*Note: No patients had syphilis or subdural hematoma.

†Five of the patients had 2 different potentially reversible conditions. Each is thus represented twice.



not improve despite neurosurgical intervention, and the patient died within a year.

In 12 (6.1%) of the cases the CT results led to a change in the initial diagnosis, to normal-pressure hydrocephalus in 1 patient, to a brain tumour in 2 and to an infarct in 9. However, in none of the patients with an initial diagnosis of probable Alzheimer's disease on clinical grounds was a potentially reversible lesion subsequently found by CT.

Interpretation

The prevalence of potentially reversible dementias in the population attending our outpatient Memory Clinic was 23.0%, which is within the range previously reported.¹² Unfortunately, potential reversibility does not translate into actual clinical change after treatment in most cases, as shown by our results and results reported elsewhere.^{6,42,43} In the present study only 3.6% of all patients who underwent investigation and follow-up for dementia and suspected dementia showed any improvement in cognitive function with treatment of the potentially reversible cause. Of the blood tests that constitute the typical work-up for dementia, the only one for which replacement therapy led to documented improvement in cognitive status was the thyroid profile. Vitamin B₁₂ replacement did not result in improvement in any patient in this study. The complete blood count and the biochemistry and VDRL tests were also noncontributory. History-taking revealed depression or overmedication in 33 patients (16.8%), of whom only 4 experienced improvement in cognition with intervention.

Neuroimaging studies are the most expensive and thus the most controversial procedures recommended in the routine evaluation of patients with suspected dementia. The practice of scanning all such patients is not clinically indicated, given that the prevalence of potentially reversible lesions detected by CT is very low. Furthermore, as we have shown, actual reversibility is even lower. A recent prospective memory clinic study reached similar conclusions.⁴⁴ The need for consensus criteria in the evaluation of patients with dementia has been widely recognized.²⁸ With the aging of the population, the prevalence of dementia is rising rapidly. Given that most patients with dementia are not referred to a memory disorders clinic, the results of this study provide further reassurance that not all such patients need neuroimaging.

However, it is important to note that the 7 patients in whom cognitive impairment declined or was reversed had mild dysfunction; 4 of them did not meet the full criteria for dementia and were considered to have suspected dementia. These findings underscore the importance of investigating for reversible conditions in patients presenting with early dementia or even with mild

cognitive impairment, as suggested by recent reviews.^{5,45} Further research is necessary to characterize patients with objective deterioration of cognitive function who do not meet the formal criteria for dementia.

On the basis of the CCCAD guidelines, we did not consider vascular dementia as potentially reversible, even though it could be argued that controlling risk factors might halt or slow the progression of disease. These same risk factors should, in any case, be controlled in most patients with dementia. CT can contribute to more accurate clinical diagnosis and in fact resulted in a change in diagnosis in 12 patients, 9 of whom had vascular changes that corresponded with the clinical presentation. A recent study has suggested that the presence of cerebrovascular disease may play an important role in determining the presence and severity of the clinical presentation of Alzheimer's disease.⁴⁶

In total, 109 patients were excluded from the study. Of these, 52 did not satisfy criteria for dementia or suspected dementia, and thus should not have received a dementia work-up in any case. The patients who were not followed did not differ from those who were in terms of any of the baseline characteristics. Similarly, not all of the patients at the Memory Clinic underwent CT. Those who did not undergo neuroimaging were similar to those who did, except that they scored higher on the MMSE.

We conclude that, among patients with dementia presenting to a memory disorder clinic in a teaching hospital, both potential and actual reversibility of the condition are low.

There is a relatively low cost and some benefit to taking a complete history and performing a physical examination in patients with memory loss.⁴⁷ Furthermore, the need for an accurate clinical diagnosis is important in terms of comprehensive patient management. The emergence of medications that may slow the progression of Alzheimer's disease underscores the importance of accurate diagnosis.⁴⁸⁻⁵⁰ However, the expectations of both patients and families about the possibility of clinical improvement should not be falsely elevated when a potentially reversible cause is found.

Within the limitations of a descriptive retrospective study, our data highlight the importance of recognizing and diagnosing cognitive impairment at an early stage. In our cohort, the patients whose condition improved with intervention were those with early or mild cognitive dysfunction. This finding suggests that thorough and early evaluation of memory disorders is warranted.

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