Complete Summary

GUIDELINE TITLE

The utility of MRI in suspected MS: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society.

BIBLIOGRAPHIC SOURCE(S)

Frohman EM, Goodin DS, Calabresi PA, Corboy JR, Coyle PK, Filippi M, Frank JA, Galetta SL, Grossman RI, Hawker K, Kachuck NJ, Levin MC, Phillips JT, Racke MK, Rivera VM, Stuart WH. The utility of MRI in suspected MS: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2003 Sep 9;61(5):602-11. [47 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 23, 2007, Gadolinium-based Contrast Agents: The addition of a boxed warning and new warnings about the risk of nephrogenic systemic fibrosis (NSF) to the full prescribing information for all gadolinium-based contrast agents (GBCAs).

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Multiple sclerosis

GUIDELINE CATEGORY

Diagnosis
Education
Risk Assessment
Technology Assessment

CLINICAL SPECIALTY

Family Practice
Neurology
Radiology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To consider the evidence that magnetic resonance imaging (MRI) can prospectively predict the future conversion to clinically definite multiple sclerosis (CDMS) in patients presenting with a syndrome consistent with inflammatory demyelination
- To consider the evidence for the use of baseline and follow-up magnetic resonance imaging in the diagnosis of patients with suspected multiple sclerosis

TARGET POPULATION

- Patients with symptoms suggestive of multiple sclerosis (MS)
- Patients presenting with a syndrome consistent with inflammatory demyelination

INTERVENTIONS AND PRACTICES CONSIDERED

Magnetic resonance imaging (MRI)

MAJOR OUTCOMES CONSIDERED

Specificity, sensitivity, positive predictive value, and diagnostic accuracy of magnetic resonance imaging (MRI) in multiple sclerosis (MS)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A search was undertaken using the following terms: clinically isolated syndromes, multiple sclerosis, and magnetic resonance imaging. Guideline developers used the Medline database from 1966 to 2003. In addition, the reference lists of the articles identified were also reviewed to identify articles not found by the computer search. They reviewed the abstracts of these articles and further limited their assessment to English language studies that were prospective and utilized a well-defined gold standard for the development of clinically definite multiple sclerosis (CDMS).

Inclusion/Exclusion

The guideline developers only reviewed articles that studied at least 20 patients. There were 22 such studies identified. All of these articles considered the risk of developing clinically definite multiple sclerosis in patients with clinically isolated syndrome (CIS), based on the presence or absence of magnetic resonance imaging (MRI) lesions within the brain or spinal cord.

NUMBER OF SOURCE DOCUMENTS

46 articles were originally identified

22 studies met inclusion criteria

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Rating of Diagnostic Article

Class I: Evidence provided by a prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy. In addition, there must be adequate accounting for dropouts with numbers sufficiently low to have minimal potential for bias.

Class II: Evidence provided by a prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a

broad spectrum of persons with an established condition (by "gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation.

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls).

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Translation of Evidence to Recommendations

Level A rating requires at least one convincing Class I study or at least two consistent, convincing Class II studies.

Level B rating requires at least one convincing Class II study or at least three consistent Class III studies.

Level C rating requires at least two convincing and consistent Class III studies.

Rating of Recommendation

A = established as useful/predictive or not useful/predictive for the given condition in the specified population.

B = probably useful/predictive or not useful/predictive for the given condition in the specified population.

C = possibly useful/predictive or not useful/predictive for the given condition in the specified population.

U = data inadequate or conflicting. Given current knowledge, test/predictor is unproven.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines were reviewed for accuracy, quality, and thoroughness by the American Academy of Neurology (AAN) members, topic experts, and pertinent physician organizations.

Final guidelines were approved by the American Academy of Neurology Therapeutics and Technology Assessment Subcommittee on April 16, 2002, the American Academy of Neurology Practice Committee on April 2, 2003, and the American Academy of Neurology Board of Directors on June 22, 2003. They were published in *Neurology* 2003:61:602-611.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the strength of the recommendations (A, B, C, U) and classification of the evidence (Class I through Class IV) are provided at the end of the "Major Recommendations" field.

Recommendations

1. Magnetic resonance imaging (MRI) changes seen in multiple sclerosis (MS) are known to be nonspecific (refer to Table 2, entitled "Diagnostic Consideration in Patients with Suspected MS and/or MRI White Matter Abnormalities" in the original guideline document). Therefore, the information derived from imaging investigations must always be considered in the context of the specific clinical situation presented by an individual patient. As a result, the following recommendations are predicated on the exclusion, at baseline, of appropriate alternative conditions that can mimic MS or can mimic the radiographic findings seen in MS.
2. On the basis of consistent Class I, II, and III evidence, in patients with clinically isolated syndrome (CIS), the finding of three or more white matter lesions on a T2-weighted MRI scan is a very sensitive predictor (>80%) of the subsequent development of clinically definite MS (CDMS) within the next 7 to 10 years (***Type A recommendation***). It is possible that the presence of even a smaller number of white matter lesions (e.g., one to three) may be equally predictive of future MS although this relationship requires better clarification.

3. The presence of two or more gadolinium (Gd)-enhancing lesions at baseline is highly predictive of the future development of clinically definite MS (***Type B recommendation***).
4. The appearance of new T2 lesions or new gadolinium enhancement 3 or more months after a clinically isolated demyelinating episode (and after a baseline MRI assessment) is highly predictive of the subsequent development of clinically definite MS in the near term (***Type A recommendation***).
5. The probability of making a diagnosis other than MS in patients with clinically isolated syndrome with any of the above MRI abnormalities is quite low, once alternative diagnoses that can mimic MS or can mimic the radiographic findings of MS have been excluded (***Type A recommendation***).
6. The MRI features helpful in the diagnosis of primary progressive MS (PPMS) cannot be determined from the existing evidence (***Type U recommendation***).

Definitions:

Rating of Recommendation

A = Established as useful/predictive or not useful/predictive for the given condition in the specified population.

B = Probably useful/predictive or not useful/predictive for the given condition in the specified population.

C = Possibly useful/predictive or not useful/predictive for the given condition in the specified population.

U = Data inadequate or conflicting. Given current knowledge, test/predictor is unproven

Rating of Diagnostic Article

Class I: Evidence provided by a prospective study in a broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy. In addition, there must be adequate accounting for dropouts with numbers sufficiently low to have minimal potential for bias.

Class II: Evidence provided by a prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation.

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls).

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- These guidelines may assist physicians in making appropriate clinical decisions regarding the clinical utility of magnetic resonance imaging (MRI) in suspected multiple sclerosis (MS).
- With MRI techniques, occult disease activity can be demonstrated in 50 to 80% of patients at the time of the first clinical presentation. Prospective studies have shown that the presence of such lesions predicts the future conversion to clinically definite MS (CDMS). Indeed, in a young to middle-aged adult with a clinically isolated syndrome (CIS), once alternative diagnoses are excluded at baseline, the finding of three or more white matter lesions on a T2-weighted MRI scan (especially if one of these lesions is located in the periventricular region) is a very sensitive predictor (>80%) of the subsequent development of clinically definite MS within the next 7 to 10 years. Moreover, the presence of two or more gadolinium (Gd)-enhancing lesions at baseline and the appearance of either new T2 lesions or new gadolinium enhancement on follow-up scans are also highly predictive of the subsequent development of clinically definite MS in the near term.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The guideline developers acknowledge inherent limitations of the literature. Any study of the predictive validity of magnetic resonance imaging (MRI) is dependant upon the gold standard used to establish the diagnosis of multiple sclerosis (MS). Generally, this standard is the development of clinically definite MS (CDMS) by some criteria, after some period of follow-up. Nevertheless, in a disease like MS (where the development of clinically definite MS can be delayed by decades from the onset of clinical symptoms)

such a design has serious limitations, especially when the follow-up is either too short or too variable. Most studies of the predictive validity of MRI in MS are confounded by this limitation.
- This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The American Academy of Neurology recognizes that specific patient-care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Frohman EM, Goodin DS, Calabresi PA, Corboy JR, Coyle PK, Filippi M, Frank JA, Galetta SL, Grossman RI, Hawker K, Kachuck NJ, Levin MC, Phillips JT, Racke MK, Rivera VM, Stuart WH. The utility of MRI in suspected MS: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2003 Sep 9;61(5):602-11. [47 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Sep 9

GUIDELINE DEVELOPER(S)

American Academy of Neurology - Medical Specialty Society
Child Neurology Society - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Neurology (AAN)

GUIDELINE COMMITTEE

Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology
Practice Committee of the Child Neurology Society

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Members of the Therapeutics and Technology Assessment Subcommittee: Douglas S. Goodin, MD (chair); Carmel Armon, MD; Elliot M. Frohman, MD, PhD; Robert S. Goldman, MD; David Hammond, MD; Chung Y. Hsu, MD, PhD; Andres M. Kanner, MD; David S. Lefkowitz, MD; Isaac E. Silverman, MD; Michael A. Sloan, MD; Yuen T. So, MD, PhD; Edgar J. Kenton III, MD; Wendy Edlund, AAN Staff Liaison

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the AAN Web site.

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 1080 Montreal Avenue, St. Paul, MN 55116.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- American Academy of Neurology (AAN) guideline summary for clinicians: the utility of MRI in suspected MS. St. Paul (MN): American Academy of Neurology, 2003 Sep. Electronic copies: Available from the AAN Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Electronic copies: Available from the American Academy of Neurology Web site.

PATIENT RESOURCES

The following is available:

- AAN guideline summary for patients and their families: diagnosis of MS using magnetic resonance imaging (MRI). St. Paul (MN): American Academy of Neurology, 2003 Sep. Electronic copies: Available from the American Academy of Neurology (AAN) Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on February 12, 2004. This summary was updated by ECRI Institute on May 17, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Gadolinium-based contrast agents. This summary was updated by ECRI Institute on June 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents.

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