design of criteria for diagnosis

presentation:
1. criteria: different types and different functions
2. classification criteria: why and how
3. how it was done for systemic vasculitis and generalized autoimmune diseases
4. an example: Sjögren's syndrome
5. suggested approach for IC

Table 1. Types and purposes of criteria*

<table>
<thead>
<tr>
<th>Type</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification criteria</td>
<td>To separate those with a specific disease from those without the disease</td>
</tr>
<tr>
<td>Subclassification criteria</td>
<td>To separate diseases or subsets within a disease cluster</td>
</tr>
<tr>
<td>Prognostic criteria</td>
<td>To separate subjects with good or potentially favorable outcomes from those with bad outcomes</td>
</tr>
<tr>
<td>Status indexes</td>
<td>To assess present disease activity or accumulated damage from the disease</td>
</tr>
<tr>
<td>Activity indexes</td>
<td>To estimate current disease activity status</td>
</tr>
<tr>
<td>Damage indexes</td>
<td>(implies reversibility)</td>
</tr>
<tr>
<td>Outcome criteria</td>
<td>(implies irreversibility)</td>
</tr>
<tr>
<td></td>
<td>To estimate accumulated damage from the disease</td>
</tr>
<tr>
<td></td>
<td>To measure the overall impact of a disease and to serve as dependent variables for clinical studies</td>
</tr>
</tbody>
</table>


Figure 1. Classification criteria separate patients with the disease from the general population or from patients with potentially confusable conditions.
Classification criteria are needed if diseases have overlapping features

Clinical practice: diagnosis is necessary

High sensitivity → low specificity

Scientific studies

Scientific studies: definite disease

High specificity → low sensitivity

Do we need to invent the wheel?

Classification of systemic vasculitis and generalized autoimmune diseases

Examples:

Systemic vasculitis
- Wegener's granulomatosis
- Polyarteritis nodosa
- Microscopic polyangiitis
- Churg-Strauss syndrome
- Giant cell arteritis
- Takayasu disease
- Hypersensitivity vasculitis
- Henoch-Schönlein purpura

Generalized autoimmune diseases
- Systemic lupus erythematosus
- MCTD
- Systemic sclerosis
- CREST syndrome
- Sjögren's syndrome
- Antiphospholipid syndrome
- Subacute cutaneous LE
classification of systemic vasculitis and generalized autoimmune diseases

common features (and features in common with IC)

• causes unknown
• strong overlap between diseases in each group
• many different opinions on definition and classification
• diagnosis has implications for treatment

examples of diseases with classification rules:

systemic vasculitis
- Wegener's granulomatosis
- polyarteritis nodosa
- microscopic polyangiitis
- Churg-Strauss syndrome
- giant cell arteritis
- Takayasu disease
- hypersensitivity vasculitis
- Henoch-Schönlein purpura

generalized autoimmune diseases
- systemic lupus erythematosus
- MCTD
- systemic sclerosis
- CREST syndrome
- Sjögren's syndrome
- antiphospholipid syndrome
- subacute cutaneous LE

classification of systemic vasculitis and generalized autoimmune diseases

• classification rules have been broadly accepted

• classification rules:
  algorithms created with statistical methods based on the way how experts diagnose the disease and differentiate it from overlapping diseases

examples of classification methods:

1. "number of items present rule"

\[ Y = Z_1 + Z_2 + \ldots + Z_r \]

if any 1 or more* of a list of r items are present in a patient, then classify the patient as having the disease

* optimal cut-off points are selected with ROC-curves
classification methods

1. "number of items present rule"
   - pro
     - simple definitions (+/-) easy application
   - con
     - all items are given equal weight
     - all items must be dichotomous (+/-)
   - little insight into the characteristics of a classified patient group

useful for daily clinical practice? yes
useful for scientific studies? more or less

2. linear discriminant function
   \[ Y_L = a_0 + a_1 Z_1 + a_2 Z_2 + \ldots + a_r Z_r \]

   if \( Y_L > c \) then classify the patient as having the disease

   similar to method 1 if \( a_0 = 0 \) and \( a_x = 1 \)

3. multiple logistic regression
   \[ \ln \left( \frac{Pr(W=1)}{1-Pr(W=1)} \right) = b_0 + b_1 Z_1 + b_2 Z_2 + \ldots + b_r Z_r \]

   \( Pr(W=1) \) is the estimated probability that the subject has the disease

4. classification tree
   is constructed by repeated splits of groups into 2 descendant subgroups
classification methods

4. classification tree

- **pro**
  - items may be polychotomous or continuous
  - nonparametric: no reference to a model for the relationship between classification items and disease status
  - high information content - classified groups of subjects in studies may be referred to the exact classifying subgroup of the tree

useful for daily clinical practice? more or less excellent

Ann Rheum Dis 1990;33:1137-44

classification methods

4. classification tree

classification

SS patients* 64
no SS patients* 2

rank order
0.0 (0/18) 10 is best

No SS 0
SS 18

0.97 (64/66)

* diagnosis according to the expert clinicians

Arthritis Rheum 1990;33:1137-44

"number of criteria present rule" (1)

2 subjective items

4 objective items

rules for classification

exclusion criteria

Ann Rheum Dis 2002;61:554-8

"number of criteria present rule" (2)

Ann Rheum Dis 2002;61:554-8

Joop P van de Merwe - Design of Criteria for Diagnosis - ESSIC Meeting - Copenhagen 4 June 2004
classification criteria

Classification criteria often serve as diagnostic criteria. This is particularly true when the sensitivity and specificity of classification criteria are both close to 100%. In this case, classification criteria could be used as diagnostic criteria. This is rather unusual at the beginning of the disease, when the typical signs and symptoms are often lacking or are not entirely expressed. Classification criteria are therefore not perfect for use in diagnosis and a certain proportion of patients may be misclassified, particularly in the early stages of the disorder. Thus, classification cannot be considered the medical standard for a diagnosis and the expert doctor is the only person who can establish a definitive diagnosis for any individual patient. However, classification criteria for disease syndromes can be used to ensure the standardisation of the diagnosis in patients taking part in clinical studies, and to facilitate the analysis of results and the comparison of patients between institutions.

5 suggested approach in a multicentre study

1. collect what information (symptoms and signs) is used/needed - by experts - to diagnose IC and differentiate IC from confusable diseases (for both women and men)

2. collection of data from patients with IC and patients with confusable diseases (controls) to define classification criteria for IC

3. validation with new patient groups

suggested approach in a multicentre study

1. collect what information (symptoms and signs) is used/needed - by experts - to diagnose IC and differentiate IC from confusable diseases (for both women and men)

2. collection of data from patients with IC and patients with confusable diseases (controls) to define classification criteria for IC

The same database can be used to create "number of items present rule" for clinical diagnoses and a "classification tree" for scientific studies.

how it was done in Sjögren’s syndrome

The European Study Group on Classification for Sjögren’s Syndrome started in 1988 and published in:

1989 selection of questions and tests
1993 preliminary criteria
1996 validation in a prospective multicentre study
2002 revision by the American-European Consensus Group
suggested approach in a multicentre study

1. collect what information (symptoms and signs) is used/needed - by experts - to diagnose IC and differentiate IC from confusable diseases (for both women and men)
2. collection of data from patients with IC and patients with confusable diseases (controls) to define classification criteria for IC

For 1 a lot of work has already been done in Copenhagen 2003!


summary & conclusions (1)

1. the first thing we need is classification criteria based on - diagnoses (by experts) - items used (by experts) for diagnosis and exclusion of confusable diseases (later: prognostic, status and outcome criteria)
2. extensive knowledge is available on the use of classification criteria with systemic vasculitis and generalized autoimmune diseases

summary & conclusions (2)

3. classification methods with the same patient data several rules can be obtained
   optimal rules:
   for clinical practice: "number of items rule" (easy to memorize and easy to use)
   for scientific studies: classification tree (exact description of patient population)
   but both can be used in either situation

summary & conclusions (3)

4. classification criteria are conceptually the same as diagnostic criteria (both aimed at a correct diagnosis)
5. classification criteria are not perfect and a proportion of patients may be misclassified (the expert's diagnosis is perfect by definition)
6. sensitivity and specificity are interchangeable properties of decision making processes; cut-off point can be chosen to obtain a high sensitivity or a high specificity, depending on clinical or scientific applications, respectively
7. if classification criteria have a high sensitivity and a high specificity they can be used as diagnostic criteria in clinical situations

do we need to reinvent the wheel?