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Clinicians' perspective on key domains in ANCA-associated vasculitis: a Delphi exercise

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Abstract

Objective—The existing set of outcomes for ANCA-associated vasculitis (AAV) needs to incorporate views of outcome measure stakeholders to meet the current standards of outcome measurement proposed by the Outcome Measures in Rheumatology (OMERACT) initiative. This study identifies domains that clinical experts (one group of stakeholders) consider to be important to determining the impact of AAV using the International Classification of Functioning, Disability and Health (ICF), a framework that describes health along four components: body functions, body structures, activities and participation, and contextual factors.

Methods—An international group of clinicians with expertise in the clinical care of patients with vasculitis were identified through consultation with three major vasculitis societies. The relevant domains were determined using a three-round email-based Delphi questionnaire.

Results—Eighty-two clinicians were invited to participate in this study and forty-one responded. Nineteen domains were identified as important by > 80% of participants: 6 body functions (energy, seeing, hearing, pain, respiratory, and renal function), 7 body structures (peripheral nerves, eye, ear, nose, sinuses, lungs (and airways), and kidneys), 3 activities and participation (carrying out daily routine, remunerative employment, and recreation and leisure), and 3 environmental factors (medications, support and relationships, and health services, systems and policies).

Conclusions—Clinical experts focus on physiologic effects of AAV with less importance given to the effect of AAV on patients' activities and participation in life situations and the role of contextual factors. This study represents a step towards incorporating views of a range of stakeholders into disease assessment in AAV.

Vasculitis is a group of heterogeneous conditions characterized by inflammation of blood vessels. ANCA-associated vasculitis (AAV) is a sub-group of three vasculitides often associated with the presence of ANCA (anti-neutrophil cytoplasmic antibodies): granulomatosis with polyangiitis (GPA, Wegener's), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss). Clinical presentation of these conditions is variable, ranging from disease limited to ears, nose, and sinuses in some patients to life-threatening failure of kidneys, lungs, or heart in others. With the widespread use of effective therapies, the clinical course of AAV has changed from nearly universal early mortality to a chronic condition with a high level of morbidity and substantial economic burden (1, 2).

Assessment of the ability of new treatment regimens to change disease course and reduce the impact of the disease is critically important. Outcome Measures in Rheumatology (OMERACT) is an international organization that strives to identify outcome domains and develop optimal outcome measures for use in clinical trials through a systematic outcome measure development and validation process which was recently updated (3). A key aspect of the new OMERACT framework (called Filter 2.0 framework) is incorporating the views of relevant stakeholders, including patients, clinicians, researchers and policy makers (3).

The OMERACT Vasculitis Working Group focuses on outcome domains and instruments for different types of vasculitis (4). In 2010 OMERACT endorsed a core set of outcome measures for use in clinical trials of AAV (5). As this core set was developed before emergence of the current filter 2.0 framework, it now needs to be revised to meet the current standards of outcome measure development, particularly related to incorporating the views of relevant stakeholders. Several initiatives are ongoing by the Vasculitis Working Group to update and expand the outcome measurement in AAV, including a project to study AAV with respect to the World Health Organization's International Classification of Function, Disability and Health (ICF) (4, 6).

The ICF is a general health status framework based on the bio-psycho-social model of health and disease (7). The ICF views health as a broad concept that is described along 4 interacting "components": 1) body functions, 2) body structures, 3) activities and participation, and 4) contextual factors (personal and environmental) (7). The OMERACT initiative endorsed the ICF as a tool to identify and classify domains relevant to measurement of outcomes for a specific medical condition (3).

This study used the ICF to identify domains considered important to determining the impact of AAV by the vasculitis clinical expert, a group of key stakeholders in the area of outcome measurement in vasculitis.

Methods

This study utilized data obtained from an email-based 3-round Delphi exercise (8) that was created in accordance with a previously published ICF-based Delphi study conducted for other medical conditions (9).

The study was approved by the Research Ethics Board of the Ottawa Hospital (protocol number 20120829-01H).

Identification of study participants

Purposive snowball sampling technique (10) was used to identify potential participants. The leaders of three vasculitis groups (the Canadian Vasculitis Network, the European Vasculitis Society, and the Vasculitis Clinical Research Consortium) were contacted and asked to provide contact information for vasculitis experts who could be interested in participating in the study; the identified candidates were asked to provide contact information for additional potential participants, particularly from those specialties and geographic locations that were underrepresented in the accumulated cohort, until no additional contacts could be provided.

Identified clinicians were invited via email to participate in the study; the invitation included an “implied consent” form, which described the study and explained that participant’s response with a filled-out questionnaire (that was included with the email) constitutes their consent. Prospective participants were contacted for each of the 3 Delphi rounds irrespective of whether they chose to participate in any of the earlier rounds.

Identification of key domains

Each of the 3 rounds of Delphi questionnaire started with an overview of the study and the ICF framework and gave a brief explanation of each of the 4 ICF components.

The first Delphi round was an open-ended questionnaire that asked participants to list up to 30 domains they considered relevant and important to patients with AAV for each ICF component. All domains identified by participants of round 1 of the Delphi were “linked” to the ICF according to previously-established ICF linkage rules (11, 12) by 2 investigators knowledgeable in the ICF (NM and AB). In brief, linking involves first identifying constructs contained in each of the participants’ responses, followed by linkage of each construct to the most precise ICF category using the ICF linkage rules (11, 12). One ICF category would represent one domain. As “personal factors” are currently not classified by the ICF, this study classified the identified “personal factors” following the general scheme proposed by Geyh et al. (13).

Rounds 2 and 3 of the Delphi exercise were designed to reduce the initial list of domains to those considered the most relevant and important. The second questionnaire round listed all domains identified by at least 20% of participants of round 1 and asked clinicians to select most important domains while taking into consideration results of the previous round (that were presented as percentage of participants who selected each of the listed domains). This process was repeated in the third round. Domains selected by at least 80% of clinicians in any of the Delphi rounds were accepted as critical to retain and were carried forward in subsequent rounds without further voting.

Results

Invitation to participate in the study was sent to 82 clinical experts in 24 countries and in 7 different clinical specialties routinely involved in the care of patients with AAV, including

rheumatologists [n=35], nephrologists [n=22], respirologists [n=8], internists [n=2], immunologists [n=1], and otorhinolaryngologists [n=11] as well as allied health professionals [n=3]. Overall 41 clinicians participated: 27 in round 1 of the Delphi exercise, 30 in round 2, and 36 in round 3 (Table 1). Twenty one clinicians participated in all 3 of the Delphi rounds, 10 participated in 2 of the 3 rounds, and 10 participated in 1 round.

The domains identified by participants of the first open-ended Delphi round were linked to 51 second-level categories in the ICF component “body functions”, 33 in “body structures”, 46 in “activities and participation”, 32 in “environmental factors” as well as 37 “personal factors”. Ten ICF categories (each representing one domain) were selected by >80% of participants at the first open-ended round of the Delphi questionnaire, an additional 7 categories were selected by >80% of participants at the second round, and 2 more were selected by 80% of participants at the third round (in addition to 4 subcategories of broader categories already selected at earlier stages) (Table 2). Overall, 19 domains were selected as important to determining impact of AAV by participating clinical experts: 6 body functions (energy, seeing, hearing, pain, respiratory, and renal function), 7 body structures (peripheral nerves, eye, ear (including specifically middle ear), nose (including specifically saddle nose and nasal crusting), sinuses, lungs (and specifically subglottic stenosis), and kidneys), 3 aspects of activities and participation (carrying out daily routine, remunerative employment, and recreation and leisure), and 3 environmental factors (medications (including specifically prednisone), support and relationships, and health services, systems and policies).

Discussion

This study identified domains considered important to determining the impact of AAV by clinical experts with the use of the ICF.

The current OMERACT Core Set of domains and outcome measures (which will be referred to as AAV Core Set 1.0 because it was developed in accordance with the previous OMERACT framework Filter 1.0 (14)) includes 3 measures of disease activity (3 versions of the Birmingham Vasculitis Activity Score), 1 measure of damage (Vasculitis Damage Index), 1 patient-reported outcome measure (Short Form 36 health Survey (SF-36)), and death (5). Following the development of the AAV Core Set 1.0, OMERACT approved Filter 2.0 framework that recommends (a) inclusion of a range of domains that address specific important “Areas” of outcome measurement: Pathophysiologic Manifestations, Life Impact, Resource Use, and Death, (b) consideration of the setting in which the clinical trial is to be conducted, and (c) identification of relevant contextual factors (3). When selecting the important domains and sub-domains, the OMERACT Filter 2.0 framework recommends involvement of all relevant stakeholders including patients and clinicians (3).

The OMERACT initiative endorsed the ICF as a tool to identify and classify domains relevant to measurement of outcomes for a specific medical condition (3). Categories belonging to the ICF components body functions and body structures would typically classify domains in the OMERACT area Pathophysiological Manifestations, categories within the ICF component activities and participation classify OMERACT area Life Impact,

and ICF contextual factors are a starting point to classify the context for outcome measurement (3).

Recently, the domains sampled by the existing AAV Core Set 1.0 were characterized by mapping of the contents of its constituent instruments to the ICF (6). This exercise revealed comprehensive coverage of the OMERACT area Pathophysiologic Manifestations but only limited coverage of Life Impact and lack of consideration of contextual factors. This pattern is similar with the results of this study, consistent with the fact that many of the clinical researchers who developed the currently-existing outcome measure instruments and who participated in selection of domains and instruments for inclusion into the current AAV Core Set 1.0 are also clinical experts like those participating in this study. As with all the OMERACT 1.0 core sets, the AAV Core Set 1.0 does not require sampling of ICF contextual factors, a step now required per OMERACT Filter 2.0. It is encouraging that the participants of this Delphi exercise identified 3 relevant environmental factors – the only 3 domains identified in this study that are not covered by the AAV Core Set 1.0: “products and substances for personal consumption (specifically medications)”, “support and relationships” and “health services, systems and policies”. Determining the precise way how contextual factors should be incorporated when interpreting outcomes of clinical studies is a current priority of the OMERACT initiative (3).

This study has limitations. Possible bias was introduced by restricting the participants to those who read and write English; however, it was not felt feasible to translate the Delphi questionnaires into different languages for the purpose of increasing geographic scope. Furthermore, the ICF classification is currently only available in English. The over-representation of English-speaking countries was likely further enhanced by the sampling frame that started with members of North American and European vasculitis societies. The particular sampling frame was chosen in an attempt to maximize response rate of prospective participants, in view of anticipated high respondent burden (because of large number of ongoing vasculitis-related studies) amongst the vasculitis experts. Although the resulting response rate was still relatively low (50% overall), reassuringly, it is consistent with the reported rates for email-based questionnaires of 30–40% (15, 16).

This study has important strengths. The use of the ICF as a generic framework to capture clinicians’ views of the most important domains of AAV provides structure to the results and allows comparison across different settings and different conditions (6). There is considerable geographic breadth within the study population; clinical experts from 18 countries across 5 continents were included, allowing for inclusion of specialists practicing within different medical systems and different economies. Furthermore, clinicians from several different subspecialties routinely involved in the care of AAV were included, minimizing potential bias from clinicians only identifying aspects of AAV related to their specific area of expertise.

In conclusion, the ICF proved to be useful as a framework for detailed description of domains relevant and important to determining the impact of AAV from the point of view of clinical experts. Several domains that are not sampled by the current OMERACT Core Set of outcome measures for AAV, all representing contextual factors, were identified as

important by the participating clinical experts. Further exploration of the ICF for vasculitis is planned to complement these results, including through a study of patients' perspectives. These results and the planned new studies will deepen the understanding of this group of complex diseases, facilitate the current effort to revise the current AAV Core Set 1.0 to meet the requirements of the new OMERACT Filter 2.0 framework, and ultimately positively impact clinical care and outcomes for patients with these serious and complex diseases.

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Table 1
Demographic characteristics of potential participants and participants of each of the 3 Dephi rounds

Characteristic	Clinicians Contacted (n=82)	Round 1 (n=27)	Round 2 (n= 30)	Round 3 (n= 36)
Geographic location				
North America	28	8	9	13
Canada	5	3	4	4
Mexico	3			2
United States	20	5	5	7
Central and South America	12	3	3	3
Argentina	2			
Brazil	1	1	1	1
Chile	4	2	1	1
Colombia	1			
Ecuador	1			
Guatemala	1		1	1
Peru	2			
Europe	20	10	13	14
Denmark	2	1	1	1
France	1			
Germany	1		1	1
Iceland	1			1
Italy	1			1
Netherlands	1			1
Spain	2	2	2	2
Sweden	2	1	1	
United Kingdom	9	6	8	7
Asia	15	4	3	4
China	1			
Japan	6	1	1	2
Turkey	8	3	2	2

Characteristic	Clinicians Contacted (n=82)	Round 1 (n=27)	Round 2 (n= 30)	Round 3 (n= 36)
Australia	6	1	1	1
New Zealand	1	1	1	1
Clinical specialty				
Rheumatologist	35	14	15	22
Nephrologist	22	3	3	2
Respirologist	8	1	3	3
Otorhinolaryngologist	11	5	5	5
Immunologist	1	1	1	1
Internist	2	2	2	2
Allied health professional	3	1	1	1

Table 2

Key ICF categories (representing domains) identified by at least 80% of participants

ICF category code	ICF category description	Round 1 [*]	Round 2	Round 3
Body Functions				
B1300	Energy level	44%	93%	**
B210	Seeing functions	81%		
B230	Hearing functions	89%		
B280	Sensation of pain	63%	90%	
B440	Respiratory functions	93%		
B610	Urinary excretory functions	96%		
Body Structures				
S198	Structure of the nervous system, other specified (peripheral nerves)	81%		
S2	The eye and related structures	70%	90%	
S2	The ear and related structures	52%	83%	
→ S250 [#]	→ Structure of middle ear	41%	67%	81%
S310	Structure of nose	93%		
	→ Saddle nose deformity	93%		
	→ Nasal crusting	22%	60%	86%
NC [^]	Structure of sinuses	52%	87%	
S4301	Structure of lungs	81%		
→ S4300 [#]	→ Subglottic stenosis	48%	77%	83%
S6100	Structure of kidneys	81%		
Activities and Participation				
D230	Carrying out daily routine	44%	67%	81%
D850	Remunerative employment	74%	73%	83%
D920	Recreation and leisure	85%		
Environmental Factors				
E110	Products and substances for personal consumptions (drugs (their side effects))	30%	90%	
→ E110	→ Products and substances for personal consumptions (prednisone (side effects))	26%	67%	86%
E3	Support and relationships	93%		
E580	Health services, systems and policies	74%	80%	

* Numbers in cells represent % of participants who identified the specified category for each Delphi round.

** Categories identified by >80% of participants at any of the Delphi rounds are “accepted” into the final list and are not voted on in subsequent rounds (thus designated with a “ ” mark).

[#] Categories following → are subsets of the categories in the previous row. →NC (for “not covered”) represents the category currently not classified by the ICF.