Updating OMERACT Core Set of Domains for ANCA-Associated Vasculitis: Patient Perspective Using the International Classification of Function, Disability and Health

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Running head: Patient perspective on AAV

ABSTRACT

Objective: Aspects of ANCA-associated vasculitis (AAV) prioritized by patients with AAV were described using the International Classification of Function, Disability, and Health. Methods: Items identified during 14 individual interviews were incorporated into ICF-based questionnaire administered to participants of 2 vasculitis patient symposia, 36 in UK and 63 in USA. Results: Categories identified as at least “moderately relevant” by ≥ 5% of subjects included 44 body functions, 14 body structures, 35 activities and participation, 31 environmental factors, and 38 personal factors. Conclusion: Identified categories differ from those captured by the current OMERACT core set and those prioritized by vasculitis experts.

INTRODUCTION

The vasculitides are a group of heterogeneous conditions characterized by inflammation of blood vessels. ANCA-associated vasculitis (AAV) are small vessel vasculitides that include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). AAV can affect practically any organ system, with manifestations ranging from disease limited to ears, nose, and sinuses to life-threatening failure of kidneys, lungs, or heart.

Outcome Measures in Rheumatology (OMERACT) is an international organization that strives to develop data-driven, optimal outcome measures for use in clinical trials (1). In 2010 OMERACT endorsed a Core Set of Outcome Measures for ANCA-Associated Vasculitis (2). Subsequently, a framework was developed for selection of areas and domains that should be assessed in clinical trials, referred to as the OMERACT Filter 2.0 framework (1,3); it calls for inclusion of a range of stakeholders, especially patients, into the process of outcome measure development.

The OMERACT Vasculitis Working Group has conducted several projects aimed at updating and expanding the existing expert-driven OMERACT Core Set for AAV(4,5), including this project which utilizes the International Classification of Function, Disability and Health (ICF). The ICF is a general health status framework (6) that views health as a broad concept shaped by the relationship between various ICF components: impairments of body functions and body structures, limitations of activities, restrictions of participation and the influence of environmental and personal contextual factors (6). ICF also offers a classification system to describe functioning and health using categories organized into a four-level hierarchically nested structure (6). The OMERACT initiative endorsed ICF as a tool to identify and classify (sub)-domains relevant to measurement of outcomes for a specific medical condition (1).

This manuscript describes the ICF-based analysis of aspects of health prioritized by patients with AAV.

METHODS

The study consisted of two parts, both overseen by a steering committee comprised of content experts, methodologists, including qualitative experts, and patients with AAV. The research received approval from the Ottawa Hospital's Research Ethics Board (protocol # 20120604-01H and 20150189-01H), and all participating patients gave informed consent.

The first, qualitative, part of the study, consisted of a series of individual semi-structured interviews conducted with English-speaking adult patients with AAV at the Ottawa Hospital in Ottawa, Canada and the Nuffield Orthopaedic Centre in Oxford, United Kingdom (UK). A purposive sampling strategy was used to select interviews for this study and aimed at including patients with each of the 3 types of AAV, with different severities, and at different stages of disease (7); interviews were performed until saturation of the identified concepts was reached (8).

Interviews were audio recorded, professionally transcribed, and all basic concepts were "linked" to the most precise ICF category according to previously established ICF linking rules by Cieza et al (9,10), and then summarized on the 2nd ICF level, as we described previously (11). As personal factors are currently not classified by the ICF, the general scheme proposed by Geyh et al (12) was followed. It divides the personal factors into 3 broad groups: 1) "facts" about the individual's position in the physical, social, and temporal context, 2) "experience" of the concept in question (feelings, thoughts, beliefs and motives,) and 3) "patterns" of experience and behaviour including personality traits and habits.

In the second part of the study, categories identified through the qualitative analysis were incorporated into an ICF-based questionnaire that was administered to participants of 2 vasculitis patient symposia: International Vasculitis and ANCA Workshop in London, UK, April 18, 2015 and the Vasculitis Foundation symposium in Jacksonville FL, USA, June 19-21, 2015. Participants rated the relevance of each listed category on a standardized ordinal scale associated with the ICF classification (6). The physiologic

effects of vasculitis and its effects on patients' activities were rated on a 5-level scale from 0 to 4 with the following categories: "no effect," "mild," "moderate," "severe," and "complete impairment." The relevance of environmental and personal factors was rated on a 9-level scale from -4 ("extreme negative effect on health"), through the same gradations to 0 ("no effect"), and then to +4 ("extreme positive effect"). Factors that have at least "moderate" effect for at least 5% of respondents were selected, as suggested previously (13).

RESULTS

Fourteen individual interviews (10 from Ottawa, Canada and 4 from Oxford, UK) were available for the qualitative portion of the study. Participants identified a wide range of important aspects of AAV that were linked to 159 ICF categories.

The underpinning qualitative findings were incorporated into a questionnaire administered to approximately 100 participants at each of the 2 vasculitis patient symposia described above; 51 and 74 patients from the UK and USA returned the questionnaire, and 36 and 63 (respectively) had AAV and were included in this analysis. Participants' demographic and clinical characteristics are summarized in **Supplementary Table 1**; the respondents' disease spectrum was representative of a general population of patients with AAV.

All of the categories presented in the questionnaire were rated as at least "moderately relevant" by at least 5% of subjects. This includes 44 second-level categories in the ICF component body functions, 14 in body structures, 35 in activities and participation, 31 in environmental factors, and 38 in personal factors. A subset of the most relevant categories, ranked as at least "moderately relevant" by at least 30% of participants, is summarized in **Tables 1-3**.

A greater proportion of participants from the USA compared to the UK reported financial situation and healthcare system issues, such as access to medications, as relevant to their health (38% and 60% versus 19% and 44%, respectively). Similarly, more American participants reported positive effects of having vasculitis (personal factors -> experience of vasculitis), including increased appreciation of life, increased sensitivity to other people's misfortunes, and increasing activities related to helping others (72%, 73%, and 64% versus 42%, 36%, and 39%, respectively). In contrast, the effect of the vasculitis on patients' ability to travel (activities and participation -> recreation and leisurely activities) was reported as at least moderately relevant by 61% of participants from the UK compared to 29% of Americans.

Similar analyses by type of AAV demonstrated expected trends: more respondents with EGPA reporting effect of their disease on the heart and lungs and a prominent impact of air quality (consistent with asthma being a central feature of the disease); subjects with MPA had the most difficulty with blood pressure and kidneys. Furthermore, subjects with MPA seemed to be most affected by the various aspects of their psychosocial functions, including mental functions (motivation, appetite, concentration, and emotions); domestic, community, and social life (activities and participation), and interpersonal interactions and relationships (environmental factors.)

DISCUSSION

In this analysis mainly limited by the narrow geographic sampling, the ICF was a useful framework for describing aspects of AAV relevant to patients. Comparisons of prioritized items by country of residence and by diagnosis revealed that while the majority of differences between the 3 different forms of AAV were in keeping with the expected differences in the frequencies of specific organ involvement, most variability between the 2 participating countries was seen in the importance of various contextual factors. As the role of contextual factors in interpreting outcome measures continues to be clarified (14),

considering some key contextual factors will deepen the ability to fully assess the impact of AAV and other diseases.

An earlier ICF-based analysis of the current OMERACT Core Set for AAV (11) revealed that it does not measure the whole spectrum of limitations in activities and participation prioritized by patients in this study, and covers only a small number of environmental and personal factors, likely because contextual factors have only recently become recognized as relevant for interpreting the measured outcomes (14). The areas under-sampled by the core set were also found to be less important to vasculitis clinical experts in a recent ICF-based analysis (15); this is not surprising, given that the composite tools that constitute the current OMERACT Core Set for AAV were designed by the same clinical experts. Notably, the few contextual factors that clinicians did identify as important differ from those prioritized by patients: clinicians focus on hard "objective" factors such as demographics, comorbidities, availability of health services, and social support (15), while the range of factors identified by patients is much broader and dominated by the more subjective factors such as attitudes of other people and patients' own reactions and thoughts. In contrast, several of the more severe disease manifestations of AAV, such as lung and kidney involvement, visual impairment, and hearing loss, that are prioritized by the majority of vasculitis clinical experts (15) were rated as at least "moderately relevant" by <50% of patient participants, likely reflecting the frequency of these manifestations in the cohort. Along with similar findings in other studies (16), the observed differences in perspectives of patients and clinicians support OMERACT's recommendation to include perspectives of different stakeholders, including patients, into the process of development of core sets of domains and outcome measures (1). To comply with these standards, the OMERACT Vasculitis Working Group is working to update the current OMERACT core set for AAV.

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ICF CODE[#]	ICF Category description	% ranking category as ≥moderately impaired
	BODY FUNCTIONS	
b1	**Mental Functions**	
b130	Energy and drive	
b1300	Energy	87%
b1301	Motivation (wanting to do things)	59%
b1302	Appetite	47%
b134	Sleep (quality and quantity)	68%
b147	Agitation, feeling "jittery"	31%
b152	Emotions such as feeling down or depressed, anxious, frustrated	46%
b180	Body image (one's satisfaction with their look)	42%
b2	**Sensory Functions, Pain, Voice and Speech**	
b230	Hearing	40%
b240	Sensations related to the ears - ringing, irritation, pressure	38%
b279	Numbness, decreased sensation (peripheral sensory neuropathy)	47%
b280	Pain	80%
b4	**Cardiovascular, hematological, immunological, respiratory systems**	
b420	Blood pressure	35%
b435	Functions of immune system: protection against infections, hypersensitivity reactions (e.g. allergies)	50%
b440	Lung function (breathing, results of lung function tests)	50%
b455	Exercise tolerance	67%
b460	Shortness of breath, wheezing, chest tightness / other sensations associated with lungs or heart	56%
b5	**Digestive, metabolic, and endocrine functions**	
b530	Weight issues (weight loss or gain)	64%
b535	Sensations related to digestive system: nausea, feeling bloated, heartburn, abdominal cramps	40%
b550	Fever, chills, sweats	46%
	Other body functions	
b310	Ability to speak, quality of voice	30%
b610	Functions of kidney and bladder (making urine, peeing)	37%
b710	Joint functions (moving joints etc.)	44%
b840	Sensation related to the skin: itching, burning, and tingling	34%
	BODY STRUCTURES	
s310	Nose	55%
nc-bs*	Sinuses	59%
s430	Lungs and airways (breathing tubes)	53%
s6100	Kidneys and urinary bladder	37%
s7701	Joints (includes arthritis)	42%
s810	Skin - rashes, scarring, thinning and breaking down	34%
	ACTIVITIES AND PARTICIPATION	
d4	**Mobility**	
d430	Lifting and carrying objects	37%
d450	Walking	42%
d4551	Climbing (e.g. stairs)	52%
	Other activities and participation	
d920	Recreation and leisurely activities	65%

[#]ICF code is a numeric identifier that uniquely identifies each ICF category; it starts with a letter that denotes the ICF component (b: body functions; s: body structures; d: activities and participation) and is followed by numbers that specify progressively more detailed categories; for example, category b1300

(energy) is a sub-category of the broader category b130 (energy and drive). *Not covered – body structures; category not covered by the current ICF classification.

Table 2: International Classification of Function (ICF) Environmental Factors identified as at least moderately relevant by at least 30% of participants

ICF Code[#]	ICF Category description	% ranking category as ≥ moderately relevant
e1	**Products and technology**	
e1101	Medications	75%
	> Unwanted side effects of medications	64%
	>Unwanted side effects of prednisone specifically	73%
e130	Products and technology for education (books, computer hardware and software, internet)	42%
e1650	Financial assets (money), tangible assets (houses, land, owned goods and technology), other assets	31%
e3	**Support and relationships**	
e310	Immediate family	79%
e320	Friends	72%
e325	Acquaintances, peers, colleagues, neighbours, community members	51%
e350	Health professionals	82%
nc-cf*	Support from others in a similar situation – e.g. other patients with vasculitis, patients with other chronic conditions, support groups	63%
eE4	**Attitudes (of family members, friends, colleagues, health professionals, etc.)**	
e410	Attitudes of immediate family members	73%
e420	Attitudes of friends	61%
e425	Attitudes of acquaintances, peers, colleagues, neighbours and community members	47%
e450	Attitudes of health professionals	73%
	Other factors that may affect health	
e260	Air quality	32%
e580	Health-related services, systems and policies including access to medical services and medications, health insurance	55%
nc-cf*	Information about disease and drugs, either provided by health care providers or researched in journals, books, or internet	71%
nc-cf *	Living arrangement - private house or apartment, amount of external noise, proximity to traffic, to parks or exercise facilities, etc.	50%
nc-cf *	Stress - physical or psychological stress from any source	49%
nc-cf *	Clinical research in teaching hospitals	33%

[#]ICF code is a numeric identifier that uniquely identifies each ICF category; it starts with a letter that denotes the ICF component (e for environmental factors) and is followed by numbers that specify progressively more detailed categories; for example, category e310 (family members) is a sub-category of the broader category e3 (support and relationships). *Not covered – contextual factors; category not covered by the current ICF classification.

Table 3: International Classification of Function (ICF) Personal Factors identified as at least moderately relevant by at least 30% of participants

ICF Code	ICF Category description	% ranking category as ≥ moderately relevant
p1	**Facts about individual and his/her personal life**	
	Demographic characteristics	
	Marital status	40%
	Health literacy - one's ability to understand the nature of vasculitis and prescribed treatments	76%
	Occupation - job or profession	37%
	Personal history and biography	
	Personal and family circumstances - specific events in one's personal life	37%
	Roles and responsibilities in one's family (dependants to look after, etc.)	40%
	Financial situation	48%
p2	**One's experience of vasculitis**	
	General well-being (how well do you feel overall compared to how you were before the diagnosis of vasculitis)	67%
	Mental / psychological well-being	35%
	Feelings / emotions / mood related to vasculitis or its treatments	68%
	Thoughts and beliefs related to vasculitis or its treatments	93%
	Change of potential and goals	61%
p3	**Personality, habits and patterns of behavior**	
	Personality	73%
	Habits	81%
	Lifestyle, interests and hobbies before diagnosis	68%
	Health-related habits (tendency to look after oneself, compliance with treatments, interest in own health)	72%
	Adaptation to chronic illness	75%