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Quality of Life Issues in Vasculitis

Delesha Carpenter and Robert F. DeVellis
University of North Carolina at Chapel Hill
USA

1. Introduction

Over the past 40 years, the advent of more effective treatment regimens has transformed vasculitis from a frequently fatal, acute disease to a chronic condition with relapsing and remitting episodes with which patients can live for many years. Because vasculitis is now viewed as a chronic disease, the role of treatment has expanded from an almost exclusive focus on reducing mortality and inducing remission to include improving patient quality of life. In fact, most research studies with vasculitis patients, including clinical trials and observational studies, now measure patient quality of life to determine what factors hinder and facilitate optimal patient functioning and well-being.

The World Health Organization has defined quality of life as "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (WHO, 1997, p. 1). Implicit in this definition is the fact that many layers of influence, ranging from intrapersonal beliefs to environmental factors, affect quality of life. In chronic disease populations, researchers often focus on patient health-related quality of life (HRQOL). Although HRQOL is more narrowly focused than quality of life, it is a still a complex concept that refers to the overall perceived well-being of an individual as well as his/her ability to function in daily life (Hays et al., 1993). There are many definitions of HRQOL, but most scholars agree that HRQOL includes both multidimensional and subjective components (Cella, 1994). The multidimensional component refers to the many dimensions (e.g. physical, functional, emotional, financial, and social) on which chronic disease can affect the patient's health and functioning. The subjective component suggests that patients, rather than health care providers, for example, are in the best position to report their HRQOL.

Although the HRQOL literature has primarily described how vasculitis negatively impacts patients' physical and mental health, there is also some evidence that patients experience positive impacts. Moreover, in addition to directly affecting the patient, vasculitis also has the potential to influence patients' relationships with spouses, family members, and friends. Garnering a holistic understanding of how vasculitis affects patients and their social networks is of interest because individuals having a chronic disease often seek support from others to help cope with disease-related stressors, which can lead to improved physical and mental health (Pennix et al., 1996).

This chapter not only describes how vasculitis positively and negatively impacts patients' HRQOL, but also, the impacts of vasculitis on members of patients' social networks. We first focus on patient HRQOL issues, including an examination of how vasculitis affects patients

physically, functionally, psychologically, and financially. Next we describe how vasculitis impacts patients' social quality of life, including relationships with spouses, family, and friends. Last, we propose areas for future research and offer conclusions.

2. Patient quality of life issues

We identified 21 articles that have been published in English and primarily describe the HRQOL of vasculitis patients (Table 1). Taken together, these articles demonstrate that vasculitis negatively affects patients physically, functionally, psychologically, financially, and socially. Table 1 provides a brief overview of the articles, including the study design, subjects, and domains of quality of life assessed. In this section, we summarize the results of these studies by quality of life domain. Social quality of life is described in Section 3 "Impact on patients' relationships with social network members."

Study	**Design**	**Subjects**	**Domains of quality of life assessed**
Abdou et al., 2002	Cross-sectional	Granulomatosis with polyangiitis (GPA) (n= 701)	• Physical • Financial
Abularrage et al., 2008	Cross-sectional	Takayasu's arteritis (n= 158)	• Physical • Psychological • Functional • Financial • Social
Akar et al., 2008	Cross-sectional case-control	Takayasu's arteritis (n= 51)	• Physical • Functional • Psychological
Basu et al., 2010	Cross-sectional case-control	ANCA-associated vasculitis (n=74)	• Physical • Psychological
Bernabé et al., 2010	Cross-sectional	Behçet's disease (n= 362)	• Physical • Psychological
Boomsma et al., 2002	Cross-sectional case-control	Granulomatosis with polyangiitis (n =79)	• Functional • Psychological • Financial • Social
Carpenter et al., 2009	Cross-sectional	ANCA-associated vasculitis (n= 97)	• Physical • Functional • Psychological
Carpenter et al., 2011	Cross-sectional	Multiple vasculitis types (n=228)	• Physical • Functional • Psychological

Table 1. Summary of quality of life studies conducted with vasculitis patients

Study	Design	Subjects	Domains of quality of life assessed
Ertam et al., 2009	Cross-sectional case-control	Behçet's disease (n= 195)	• Physical • Functional • Psychological
Faurschou et al., 2010	Cross-sectional case-control	Granulomatosis with polyangiitis (n=68)	• Physical • Functional • Psychological
Hajj-Ali et al., 2011	Cross-sectional	Granulomatosis with polyangiitis	• Psychological
Hellmann et al., 2003	Cross-sectional	Giant cell arteritis (n= 145)	• Physical • Functional • Psychological
Herlyn et al., 1998	Longitudinal case-control	Multiple vasculitis types (n=303)	• Physical • Functional • Psychological
Hoffman et al., 1998	Cross-sectional	Granulomatosis with polyangiitis (n= 60)	• Physical • Functional • Psychological • Financial • Social
Koutantji et al., 2003	Cross-sectional	ANCA-associated vasculitis (n= 50)	• Physical • Functional • Psychological
Moses Alder et al., 2008	Cross-sectional case-control	Behçet's disease (n= 129)	• Physical • Functional
Mumcu et al., 2006	Cross-sectional case-control	Behçet's disease (n= 94)	• Physical • Functional • Psychological
Newall et al., 2005	Cross-sectional	ANCA-associated vasculitis (n= 30)	• Physical • Psychological
Reinhold-Keller et al., 2002	Cross-sectional	Granulomatosis with polyangiitis (n= 60)	• Physical • Functional • Psychological • Financial
Srouji et al., 2008	Cross-sectional	Churg-Strauss Syndrome (n= 25)	• Physical
Uguz et al., 2007	Cross-sectional	Behçet's disease (n= 50)	• Physical • Psychological • Social

Table 1. continued

2.1 Physical and functional quality of life

Of all the HRQOL domains, the physical domain has been best described for vasculitis populations. Physical quality of life can be directly affected by vasculitis symptoms, organ system damage, and treatment-related morbidities such as side effects and drug toxicity (Buhaescu et al., 2005; Exley & Bacon, 1996). Interestingly, physician-rated disease activity scores, such as the Birmingham Vasculitis Activity Score and the Vasculitis Damage Index (Flossmann et al., 2007), have been weakly correlated with patient HRQOL (Koutantji et al., 2003; Basu et al., 2010). This finding reinforces that quality of life cannot be reduced to biological effects of the disease and that accounting for other factors is important.

Physical HRQOL has commonly been assessed using scores from the four physical health subscales of the SF-36 (Ware & Kosinski, 2005). These include physical functioning, role limitations due to physical health, bodily pain, and general health. Although fatigue is sometimes categorized as a psychological quality of life issue, we include it here because it is a physical symptom of vasculitis that has been significantly correlated with the physical health component score (Ware & Kosinski, 2005). Thus, this section will describe fatigue, pain, and physical changes. Physical functioning and role limitations due to physical health are discussed in the functional quality of life section (Section 2.2).

2.1.1 Fatigue

Fatigue is a major problem affecting the quality of life of vasculitis patients. In studies using the SF-36, energy/vitality was one of the most consistently, negatively affected SF-36 subscales. Four studies have shown that over 75% of patients report problems with vasculitis-related fatigue (Abularrage et al., 2010; Bernabé et al., 2010; Hajj-Ali et al., 2011; Hoffman et al., 1998). More specifically, Basu and colleagues (2010) found that patients were more than twice as likely as controls to report mild/moderate and severe fatigue; and fatigue was a stronger predictor of worse physical health than disease activity.

Herlyn and colleagues (2010) found that fatigue and reduced energy levels were the most important patient-reported disease burden. One reason fatigue may be so important to vasculitis patients is that it can negatively impact other domains of quality of life by reducing the amount of energy patients have to engage in social activities and limiting patients' ability to fulfill important work- and home-related roles. Hajj-Ali and associates (2011) found that almost half of vasculitis patients believed that fatigue significantly limited their activities.

2.1.2 Pain

The results regarding pain have not been as consistently negative as those for fatigue. Although most studies have found that vasculitis patients report more bodily pain than national norms or healthy controls, two studies report results to the contrary. Specifically, Carpenter and colleagues (2009) and Faurschou and associates (2010) documented that bodily pain was not significantly different for vasculitis patients when compared with national norms or age and sex-matched controls, respectively. However, Carpenter et al. (2011) found that bodily pain was worse for relapsing patients than for those in remission. Thus, mixed results may partially be due to the proportion of patients in relapse versus remission in any given sample; the Faurschou et al. (2010) sample included only patients with inactive vasculitis. Also, both studies consisted primarily of Granulomatosis with polyangiitis (GPA; formerly Wegener's) patients, and pain may be a greater issue for other types of vasculitis.

Kountantji and associates (2003) have conducted more thorough analyses of how pain affects GPA patients. They found that patients in greater pain reported significantly worse

quality of life when compared to patients who reported little or no pain. Also, patients in greater pain experienced more problems with depression, fatigue, and sleep. Moreover, patients with significant pain had more severe role limitations due to physical health than patients in less pain. Moses Alder and colleagues (2008) also found that Behçet's (BD) patients with arthritis reported more pain than patients without arthritis.

2.1.3 Physical changes

In addition to fatigue and pain, vasculitis symptoms and organ damage can negatively impact patient quality of life. Hearing loss, headaches, shortness of breath, and comprised kidney function are some examples of how vasculitis affects patients physically (Langford, 2005; Seo et al., 2005). In some cases, vasculitis can directly alter a patient's physical appearance by causing weight loss or nasal bridge collapse, otherwise known as saddle nose deformity. Patients may also experience skin problems, such as ulcers or purpura (i.e. a rash of purple spots). Readers who are interested in learning more about vasculitis and organ system damage are referred to articles by Seo and colleagues (2005) and Langford (2005).

Vasculitis medications can also cause changes to a patient's physical appearance. For example, patients who are treated with steroids often report weight gain and a condition called moon face, where the face swells into a rounded shape. Patients treated with immunosuppressive medications also report hair loss, hair growth, acne, and mouth sores. Although side effects like these are physical in nature, they can also take a toll on patients psychologically by adversely affecting their self-esteem. Thus, it is important to account for physical changes due to the disease itself as well as treatment-related effects when considering physical quality of life for vasculitis patients.

2.2 Functional quality of life

Functional quality of life is intimately related with physical quality of life and is commonly considered part of the physical domain. In this chapter, we dedicate a separate section to functional quality of life to specifically focus on how vasculitis affects patients' ability to engage in activities of daily living, such as bathing and completing household chores. Most studies have captured functional quality of life issues with the physical functioning subscale of the SF-36 (Ware & Kosinski, 2005). The physical functioning scale contains 10 items that ask how limited patients are in conducting a range of physical activities, from bending and kneeling to running and lifting heavy objects.

Overall, research using the SF-36 has shown that vasculitis patients have worse physical functioning when compared with healthy controls or national norms. In two cases, physical functioning was the most negatively affected of the eight SF-36 dimensions (Herlyn et al., 1998; Koutantji et al., 2005). Furthermore, the physical changes associated with vasculitis, including pain and fatigue, often led to increased role limitations. For example, patients often have to cut down the amount of time they spend on work or have to exert extra effort to engage in activities of daily living.

Other studies have provided more detail about the extent to which vasculitis negatively impacts patients' ability to engage in activities of daily living. For example, Hoffman and colleagues (1998) found that 56% of Granulomatosis with polyangiitis (GPA) patients reported moderately or severely compromised activities of daily living. Similarly, two-thirds of GPA patients reported that vasculitis had negatively affected their ability to perform everyday activities, with many patients noting that the disease had a stronger impact on their physical functioning at the time of diagnosis (Boomsma et al., 2002). Moreover, daily

activities, like being able to shower, shave, chew, and walk without difficulty or losing balance, were all ranked among the top ten most important quality of life issues for patients living with giant cell arteritis (Hellmann et al., 2003), while patients with Behçet's disease noted negative changes to their ability to engage in usual activities and mobility (Ertam et al., 2010). Additionally, patients who were unemployed (Reinhold Keller et al., 2002), had active disease (Mumcu et al., 2006; Ertam et al., 2009), or were in more pain (Koutantji et al., 2003) were more likely to report greater physical role limitations.

2.3 Psychological quality of life

Most of the studies listed in Table 1 used the SF-36 (Ware & Kosinski, 2005) to measure psychological quality of life. The SF-36 contains four subscales, including social functioning, energy/vitality, role limitations due to emotional health, and mental health, which load on a summary mental health component score. Overall, SF-36 results reveal that vasculitis patients experience compromised psychological health. A more in-depth discussion of psychological aspects of vasculitis appears in an editorial by Koutantji and colleagues (2000). We save the discussion of social functioning issues until Section 3, which summarizes the impact of vasculitis on patients' relationships with social network members.

2.3.1 Depression and anxiety

It is common for patients living with chronic disease to experience feelings of depression and anxiety. Because depression is associated with many other negative sequelae, including worse treatment adherence (DiMatteo et al., 2000), it is important to assess the mental health of vasculitis patients. An examination of the mental health subscale results from studies that used the SF-36 shows that mental health is generally lower for vasculitis patients than either healthy controls or the general U.S. population. There are some exceptions to this as a few studies have found that vasculitis patients did not differ significantly from controls in terms of mental health (Basu et al., 2010; Koutantji et al., 2003). These mixed results may be due to differences in study populations. Because few studies have provided a more detailed description of depression and anxiety in vasculitis populations, little is known about what factors may moderate depression or which patients are most at risk. As we will describe below, preliminary results indicate that depression and anxiety are serious issues for patients that warrant further examination.

Depression and anxiety are problems for vasculitis patients regardless of the type of vasculitis with which they have been diagnosed. To illustrate, Hajj-Ali and colleagues (2011) discovered that the prevalence of depression in GPA patients was much higher than the general population; 23.6% and 7.6%, respectively. Other studies have documented that between 33% and 43% of GPA patients report disease-related depression, with 7% to 14% reporting depression associated with suicidal thoughts (Hoffman et al., 1998; Boomsma et al., 2002). Similarly, Bernabé and colleagues (2010) found that 60% of Behcet's patients noted problems with depression and anxiety, and Koutantji and associates (2003) documented that fully 43% of patients reported increased anxiety and 25.5% experienced increased depressive symptoms.

2.3.2 Other psychological impacts

Unfortunately, other than depression and anxiety, there is not much published information about how vasculitis impacts patients psychologically. In fact, some of the other

psychological variables examined are conceptually related to depression and anxiety (e.g., happiness and stress, respectively) but are sufficiently distinct to warrant a separate discussion. Regarding happiness, 32% of GPA patients were unhappy because of their vasculitis (Boomsma et al., 2002), while 52% of Takayasu's arteritis (TA) patients reported being less happy overall (Abularrage et al., 2008). One study has documented that over half of GPA patients reported problems with stress (Abdou et al., 2002), suggesting that further examination of stress and vasculitis is justified. In addition, although positive effects of vasculitis are reported less frequently than negative effects, there appears to be a subset of patients who describe beneficial changes that result from a vasculitis diagnosis. Because vasculitis exacts a negative toll physically, functionally, and financially, the majority of these positive effects are seen in the psychological and social domains. For example, Abularrage and colleagues (2008) have found that 11% of TA patients reported an improvement in overall happiness and 12% reported an improvement in overall mood. No analysis was presented of differences between patients reporting positive effects versus those who reported negative or no effects; thus, we do not know whether other factors moderated the effect of vasculitis on patients' psychological responses.

We have unpublished qualitative survey data from a sample of 232 patients that offers some preliminary evidence as to why some patients report positive changes to their mood. In our study, patients commonly discussed how they reevaluated their lives and priorities after receiving a vasculitis diagnosis. Patients who recovered from a particularly bad relapse often described how they now appreciated every day and considered each moment precious. This reevaluation led patients to feel calmer and to not become stressed by minor inconveniences that used to bother them. Improvements in relationships with family members were also commonly reported, which may decrease patients' psychological distress.

2.4 Financial quality of life

Very few studies have explored the economic burden of vasculitis. Using hospital records from 1986-1990, Cotch (2000) estimated that the costs of vasculitis-related hospitalizations alone were $150 million per year in the United States. Although the author could not account for other direct medical costs, such as medication and physician visit expenses, and indirect costs due to changes in employment, it is reasonable to assume that vasculitis-related expenditures are substantial and negatively impact patients and their families (Herlyn et al., 2010). Five studies provide greater detail about the financial impact of vasculitis; they are summarized below.

Four studies have documented employment issues for Granulomatosis with polyangiitis (GPA) patients. In the first study, Hoffman and colleagues (1998) found that most patients (80%) were employed at the time of their vasculitis diagnosis; however, total household income was reduced by approximately 25%. Income reductions may have been due to patients' having to take at least 6 consecutive weeks of sick leave, receiving temporary disability status, or modifying their jobs. Similarly, Boomsma and associates (2002) found that GPA patients frequently missed work due to their disease, changed work duties, reduced work hours, and in rare cases (5%), had to resign from their jobs. Given these job-related changes, it is not surprising that 23% of patients reported a disease-related income reduction. A third study also found that patient financial quality of life was disrupted by vasculitis (Abdou et al., 2002). Specifically, 54% of patients reported losing 25% to 75% of their income, with almost half spending between $10,000 and $100,000 on their therapy and diagnosis. Additionally, 14% of patients reported having to retire due to their illness. In

addition, a study conducted by Reinhold-Keller and colleagues (2002), found that 27% of GPA patients were permanently unemployed as a result of their vasculitis and that women had a three-fold greater risk than men of losing their jobs. Patients who were employed reported missing a median of 14 days of work during the past year due to their vasculitis.
The fifth financial quality of life study involved Takayasu's arteritis (TA) patients (Abularrage et al., 2008). Almost half of those patients changed their work duties due to their TA. Additionally, approximately half of patients reported changing work hours and missing more than six consecutive weeks of work, while almost a third reported taking 6 consecutive months of sick leave from work. Moreover, TA caused almost a quarter of patients to resign from work and 15% to retire.

3. Impact on patients' relationships with social network members

Relatively little is known about the ways in which vasculitis impacts patients' relationships with spouses, family members, and friends. Many of the studies listed in Table 1 have measured social quality of life using the SF-36 (Ware & Kosinski, 2005), which includes two items about how the patient's physical health and emotional problems have interfered with his/her ability to engage in social activities. Overall, the results from these studies show that patient social functioning is compromised; however, the SF-36 social functioning items are so general that they offer limited utility in understanding *how* social relationships and activities have been affected. In this section, we will summarize existing research about the social impact of vasculitis as well as draw upon research from other disease populations to explain how a chronic, unpredictable illness like vasculitis can strain or enhance patients' relationships. We focus on the three studies that have documented social relationship issues in greater detail; Table 2 summarizes the results of these studies.

Relationship Effect	**Study**		
	Hoffman et al., 1998	Boomsma et al., 2002	Abularrage et al., 2008
Spouse/Partner			
No effect	25%	71%	44%
Improved relationship	56%	20%	36%
Worsened relationship	19%	9%	29%
Family			
No effect	40%	74%	35%
Improved relationship	47%	16%	41%
Worsened relationship	12%	10%	23%
Friends			
No effect	65%	70%	-
Improved relationship	14%	7%	-
Worsened relationship	21%	23%	-

Table 2. Percentage of patients reporting vasculitis-related effects on their relationship with their spouse/partner, family, and friends

3.1 Impact on spousal relationships

Chronic illness is a stressor that can affect the physical health and psychological well-being of patients as well as their spouses/partners (Baanders & Heijmans, 2007; Berg & Upchurch, 2007). Much of the stress that spouses experience may result from adapting to a new role as the patient's primary caregiver. For example, Marks and associates (2002) have shown that transitioning to a caregiving role increases depression in spouses of chronic disease patients. Vasculitis may be particularly mentally taxing for couples because spouses must be ready to act as a caregiver each time the patient experiences a relapse or disease flare-up. Because the severity of relapses varies considerably, the physical demands of caregiving for any particular relapse may range from minor to substantial, which requires additional adjustment on the part of the spouse. Moreover, patients often want to avoid being a burden on the caregiver, which can complicate interpersonal interactions as patients adapt to the sick role. These issues are discussed in greater detail by Koutantji and associates (2000).

Of the three studies that investigated the effect of vasculitis on spouse/partner relationships, two were conducted with Granulomatosis with polyangiitis (GPA) patients (Hoffman et al., 1998; Boomsma et al., 2002) and another was conducted with Takayasu's arteritis (TA) patients (Abularrage et al., 2008). The results from these studies reveal substantial variation in the extent to which vasculitis affects spousal relationships (Table 2). For example, in the two studies of GPA patients, the percentages of patients who reported that vasculitis did not affect their relationship with their spouse were 25% and 71%. The percentage of TA patients reporting no effect was in the middle (44%) of the previous two estimates. In all three studies, patients were more likely to report that vasculitis had improved, rather than worsened, their relationship with their partner. Unfortunately, greater detail about how relationships improved has not yet been reported. Based on some Qualitative data patients and their partners have shared with us, positive effects may include: 1) feeling closer to one another, 2) more equal distribution of household labor, and 3) making one's relationship a priority after experiencing a severe relapse (Carpenter et al., under review).

There is also little insight into how relationships with partners have worsened; however, both GPA studies found that about 70% of spouses were concerned about the long-term effects of vasculitis and its treatment and approximately one-third were concerned about how vasculitis will affect their financial security. Additionally, Hoffman noted that spouses sometimes had to alter their employment situation in order to care for the patient. Thus, it seems that emotional strain (e.g. worry and concern) as well as financial strain may take a toll on marriages. While these additional strains did not lead divorced GPA patients to believe vasculitis was the cause of their divorce (Hoffman et al.; 1998), 37% of TA patients believed their vasculitis was largely responsible for the termination of their relationship (Abullarage et al.; 2008). Although this has not been reported in the literature, qualitative data from our Accessing Social Support in Symptom Treatment (ASSIST) Study reveals that patients' sex lives are often negatively impacted. Moreover, patients often report partners' becoming frustrated with mood swings that are a side effect of certain vasculitis medications.

The negative impact of vasculitis on marriages may be markedly reduced if couples learn how to effectively manage and cope with vasculitis dyadically, as discussed by Lewis and colleagues (2006). Specifically, patients and their partners may minimize the negative effect of vasculitis on HRQOL through communal coping, developing a high level of dyadic

efficacy, and effective communication (see Lewis et al. for a more thorough discussion of these topics). Effective dyadic coping may explain why spouses of vasculitis patients did not report a lower HRQOL when compared with the general U.S. population, even though the HRQOL of patients and spouses was moderately correlated, meaning that spouses were more likely to report reduced HRQOL if the patient did (Carpenter et al., 2009).

3.2 Impact on family relationships

As shown in Table 2, it was uncommon for patients to think that vasculitis negatively impacted relationships with family members. Although 74% of participants in the Boomsma et al. study believed that relationships with family were unaffected, between 40% and 50% of patients from the other two studies felt that their family relationships had improved. Again, details about how relationships had improved were not provided. It is likely that a serious life-threatening illness like vasculitis can cause patients to feel closer to their family, especially if they are emotionally and instrumentally supportive when the patient is experiencing a relapse. Indeed, qualitative data from the ASSIST Study supports this statement, with many patients reporting that they feel closer to family members, either through family members' increasing the frequency with which they interact with patients or telling the patient how concerned they are for the patient's well-being.

In all three studies, fewer than 25% of patients reported negative changes to family relationships. Between 5 and 10% of non-spousal family members of GPA patients changed their employment status in order to care for the patient, whereas 18% of family members of TA patients altered their work situation. Relationships are probably most at risk when a family member, like a child or parent, takes on a caregiving role, as those family members are under additional physical, mental, and financial strain.

3.3 Impact on friendships

Of the three relationships discussed in this chapter, friendships are the most likely to be negatively impacted by vasculitis. Although two studies in Table 2 document that approximately 20% of patients reported that vasculitis had worsened their friendships, a recent qualitative study has found that more than half of vasculitis patients experienced degradation in the quantity and quality of their friendships (Carpenter et al., under review). To be specific, 1 in 5 patients reported losing a friend as a result of their vasculitis diagnosis. Moreover, quality of friendships was compromised due to reduced social participation, with 25% of patients engaging in fewer social activities after their diagnosis. Reduced social participation was often attributed to friends' lack of understanding about vasculitis, vasculitis-related fatigue, lifestyle changes related to medication contraindications and infection precautions, as well as patient withdrawal.

Although previous research has found that between 7% and 14% of patients report that vasculitis led to improved friendships, more than 45% of patients reported positive friendship changes in the study by Carpenter and colleagues. Positive changes included becoming closer with friends and receiving social support. Supportive friends were described as those who showed some interest in vasculitis and its effects, understood and accepted that patients would not be able to engage in social activities at the same level as previous to illness onset, and were emotionally and instrumentally supportive. Many times, patients developed new friendships with other chronic disease patients. These relationships helped patients realize they were not alone and often became an avenue for sharing

personal accounts of the disease as well as helpful disease-specific information that patients were unable to get elsewhere.

4. Limitations of existing research

Table 1 highlights several methodological limitations in the HRQOL literature that are worthy of greater discussion. First, all but one of the HRQOL studies was cross-sectional in nature. Without longitudinal data, we cannot determine how HRQOL changes over time, which may be particularly important for a relapsing, remitting disease like vasculitis. Furthermore, cross-sectional studies limit our ability to identify moderators or mediators of the effect of vasculitis on HRQOL. Disease status, or whether a patient is in relapse or remission, is likely one such moderator. Preliminary evidence demonstrates that: 1) remission status was the only significant predictor of better mental quality of life for Takayasu's arteritis patients (Abularrage et al., 2008) and, 2) relapsing patients reported lower quality of life for 7 of 8 SF-36 subscales when compared with patients in remission (Carpenter et al., 2011). Other potential moderators include number of comorbidities (Ertam et al., 2009), whether the patient is taking immunosuppressive medications (Faurschou et al., 2010), vasculitis type (Koutantji et al., 2003), and patient age (Faurschou et al., 2010). Additionally, patient coping (Koutantji et al., 2000) and social support (Carpenter et al., 2011) may mediate the relationship between vasculitis and HRQOL.

A second limitation concerns the measurement of health-related quality of life. For example, the majority (79%) of studies used generic measures of HRQOL, including the Short Form 36 (SF-36; Ware & Kosinski,), the World Health Organization's WHOQOL-100 (WHO, 1997), and the EQ-5D (EuroQol group, 1990). Only a few studies (26%) used disease-specific measures, such as the quality of life questionnaire developed specifically for vasculitis patients by Hoffman and colleagues (Hoffman et al., 1998). The rationale for these choices is not always clear. Measurement is the link between the concepts and variables researchers want to examine and the numbers they collect and analyze. Unless the correspondence between the measures and the concepts is high, the numbers may be subject to misinterpretation. Under some circumstances, for example, illness-specific concepts and variables may be of interest. For example, the uncertainty patients with relapsing/remitting illnesses face may expose them to forms of stress that may not be a part of other chronic illnesses with a less variable trajectory. When that is the case, using a less specific assessment tool may not fully capture the concept of interest to the researcher. On the other hand, when investigators wish to examine the same variables across different conditions, using illness-specific measures may impede their ability to do so. Another important measurement distinction that is often overlooked differentiates measures comprising indicators sharing a common cause from those sharing a common effect. As an example, most depression scales fit a common-cause model, with the response to each item being determined by the same subjective state experienced by the respondent. In contrast, comorbidity checklists typically aggregate variables that have a common effect (i.e., each contributes a quantum of poor health to a total) but that do not necessarily share a common cause (i.e., the various comorbid conditions may not share a common etiology). Certain measurement procedures are more readily applicable to the common-cause than to the common-effect situation and some psychometric procedures, such as the computation of internal-consistency reliability, are inappropriate for measures based on common effects (e.g., DeVellis, 2012). More generally, it is essential that sufficient attention is paid to

measurement issues to ensure that the information gathered accurately reflects the precise nature of the variables the investigators intend to quantify.

Third, although there are over 15 types of vasculitis, quality of life has been reported for only six different vasculitis types: ANCA-associated (Granulomatosis with polyangiitis, Churg-Strauss Syndrome, Microscopic polyangiitis), Takayasu's arteritis, giant cell arteritis, and Bechet's disease. GPA and Behçet's disease have received the most attention in the literature thus far. Because recruiting patients with a rare illness is often costly and logistically difficult, researchers' ability to describe HRQOL is limited, especially with rarer forms of vasculitis. Difficulties with recruitment are why many studies included fewer than 100 patients. Vasculitis researchers must strike a balance recruiting larger convenience samples versus using smaller randomly-selected samples.

Last, most research to date has focused on physical, functional, and psychological quality of life, with fewer studies investigating financial and social domains. To garner an understanding of how vasculitis affects patients' total well-being requires more data about non-physical consequences of the disease. Simply documenting the percentage of patients experiencing positive, negative, or no changes in these life domains is not enough to make concrete recommendations for how to enhance patient care. For example, more information about *how* social relationships have changed is needed to identify how family members can help patients manage the physical and emotional burden of vasculitis.

5. Future research directions

In attempting to summarize the vasculitis quality of life literature, we have identified several areas for future research. First, as noted in the previous section, we believe longitudinal studies are needed to help identify important moderators and mediators of the effect of vasculitis on patient quality of life. Longitudinal studies could be conducted in a cost-effective manner using web-based surveys. Carpenter and colleagues (2011) had a 98% retention rate for a 3-month, web-based longitudinal study of vasculitis patients. Although Internet-based studies are subject to selection bias, as the number of patients using the Internet continues to increase, selection bias will become less of an issue.

We also endorse mixed methods studies that qualitatively and quantitatively ascertain patients' quality of life. Qualitative studies would help illuminate how patients are positively affected by vasculitis and reveal quality of life domains that are untapped by existing measures. For example, even though we know that vasculitis and its treatment can affect patients' sex drive and fertility (Seo, 2007), no studies have documented how these issues are related to patients' psychological and social health. Telephone interviews may be the most feasible method for collecting in-depth qualitative data on these topics, though focus groups conducted at patient support groups or conferences may yield qualitative data on less sensitive topics, like positive effects of the disease.

Finally, greater attention to measurement issues would be beneficial. As mentioned earlier, measurement is a vital link between what investigators intend to learn and the actual data their studies produce. It is incumbent on investigators to explain why their measures have been chosen. Unfortunately, the only justification offered in some studies is that the instrument used was a "validated scale." In fact, neither reliability nor validity are properties of a scale per se, but of how a scale is used. Thus, a demonstration of a scale's validity in one instance does not guarantee it in a separate instance, especially if the two differ in important ways.

6. Conclusion

Although we have discussed several domains of HRQOL individually, they are inter-related. Physical health influences mental health, which is also affected by social functioning and the patients' financial situation. Together, these components make up the multidimensional construct of HRQOL. Between the years of 2000 and 2010, we have seen a marked increase in the number of studies that document quality of life issues for vasculitis patients. These studies show that vasculitis impairs patient quality of life in every domain but offer little insight into the mechanisms through which the disease affects patients psychologically and socially. The challenge for researchers is to build upon this base of studies and draw theoretical insights from research with other chronic diseases to identify areas where the negative impact of the disease can be reduced. During the coming years, we are confident that additional quality of life studies will better describe how vasculitis positively and negatively influences the quality of life of patients and their social network members. Additionally, we foresee that the field will shift from a focus on describing quality of life to developing non-medical interventions to improve quality of life.

7. References

Abdou, N.I.; Kullman, G.J.; Hoffman, G.S.; Sharp, G.C.; Specks, U.; McDonald, T.; Garrity, J.; Goeken, J.A.; Allen, N.B. (2002). Wegener's granulomatosis: survey of 701 patients in North America. Changes in outcome in the 1990s. *The Journal of Rheumatology*, Vol.29, No.2, pp. 309-316.

Abularrage, C.J.; Slidell, M.B.; Sidawy, A.N.; Kreishman, P.; Amdur, R.L.; Arora; S. (2008). Quality of life of patients with Takayasu's arteritis. *Journal of Vascular Surgery*, Vol.47, pp. 131-136.

Akar, S.; Can, G.; Binicier, O.; Aksu, K.; Akinci, B; Solmaz, D.; Birlik, M.; Keser, G.; Akkoc, N.; Onen, F. (2008). Quality of life in patients with Takayasu's arteritis is impaired and comparable with rheumatoid arthritis and ankylosing spondylitis patients. *Clinical Rheumatology*, Vol.27, pp. 859-865.

Baanders, A.N. & Heijmans, M. (2007). The impact of chronic diseases: the partner's perspective. *Family & Community Health*,Vol.30, pp. 305–417.

Basu, N.; Jones, G.; Fluck, N.; MacDonald, A.; Pang, D.; Dospinescu, P.; Reid, D.M.; Macfarlane, J.G. (2010). Fatigue: a principal contributor to impaired quality of life in ANCA-associated vasculitis. *Rheumatology*, Vol.49, pp. 1383-1390.

Berg, C.A. & Upchurch, R. (2007). A developmental-contextual model of couples coping with chronic illness across the adult lifespan. *Psychological Bulletin*, Vol.133, pp. 920–954.

Bernabé, E.; Marcenes, W.; Mather, J.; Phillips, C.; Fortune, F. (2010). Impact of Behçet's syndrome on health-related quality of life: influence of the type and number of symptoms. *Rheumatology*, Vol.49, No.11, pp. 2165-2171.

Boomsma, M.M.; Bijl, M.; Stegeman, C.A.; Kallenberg, C.G.; Hoffman, G.S.; Tervaert, J.W. (2002). Patients' perceptions of the effects of systemic lupus erythmatosus on health, function, income, and interpersonal relationships: a comparison with Wegener's granulomatosis. *Arthritis Care & Research*, Vol.47, No.2, pp. 196-201.

Buhaescu, I.; Covic, A.; Levy, J. (2005). Systemic vasculitis: Still a challenging disease. *American Journal of Kidney Diseases*, Vol.46, No.2, pp. 173-185.

Carpenter, D.M.; Thorpe, C.; Lewis, M.; DeVellis, R.; Hogan, S. (2009). Health-related quality of life for patients with vasculitis and their spouses. *Arthritis Care & Research*, Vol.61, No.2, pp. 259-265.

Carpenter, D.M.; Kadis, J.; DeVellis, R.; Hogan, S.; Jordan, J. (2011). The effect of medication-related support on the quality of life of patients with vasculitis in relapse and remission. *Journal of Rheumatology,* epub ahead of print; DOI: 10.3899 / jrheum. 100808.

Carpenter, D.M.; Meador, A.E.; Elstad, E.A., Hogan, S.L., DeVellis, R.F. (under review) The impact of vasculitis on patient social participation and friendships. Participation and friendships. Clinical and Experimental Rheumatology

Cella, D. (1994). Quality of life: Concepts and definitions. *Journal of Pain and Symptom Management*, Vol.9, No.3, pp. 186-192.

Cotch, M.F. (2000). The socioeconomic impact of vasculitis. *Current Opinion in Rheumatology*, Vol.12, pp. 20-23.

DeVellis, R. F. (2012). *Scale development: Theory and applications (Third Ed.)*. Thousand Oaks, CA: Sage Publications.

DiMatteo, M.R.; Lepper, H.S.; Croghan, T.W. (2000). Depression is a risk factor for noncompliance with medical treatment: a meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine*, Vol.160, pp. 2101–2107.

Ertam, I.; Kitapcioglu, G.; Aksu, K.; Keser, G.; Ozaksar, A.; Elbi, H.; Unal, I.; Alper, S. (2009). Quality of life and its relation with disease severity in Behçet's disease. *Clinical and Experimental Rheumatology*, Vol.27, pp. S18-S22.

Euro-Qol Group. (1990). EuroQol–a new facility for the measurement of health-related quality of life. The EuroQol Group. *Health Policy*,Vol.16, pp. 199-208.

Exley, A.R.; Bacon, P.A. (1996). Clinical disease activity in systemic vasculitis. *Current Opinion in Rheumatology*, Vol.8, pp. 12-18.

Faurshcou, M.; Sigaard, L.; Bjorner, J.B.; Baslund, B. (2010). Impaired health-related quality of life in patients treated for Wegener's granulomatosis. *Journal of Rheumatology*, Vol.37, No.10, pp. 2081-2085.

Flossmann, O.; Bacon, P.; de Groot, K.; Jayne, D.; Rasmussen, N.; Seo, P.; Westman, K.; Luqmani, R. (2007). Development of comprehensive disease assessment in systemic vasculitis. *Annals of the Rheumatic Diseases*, Vol.66, pp. 283-292.

Hajj-Ali, R.A.; Wilke, W.S.; Calabrese, D.O.; Hoffman, G.S.; Liu, X.; Clark, T.; Langford, C.A. (2011). A pilot study to assess the frequency of fibromyalgia, depression and sleep disorders in patients with Wegener granulomatosis. *Arthritis Care & Research*, Vol. 63, No. 6, pp. 827-833.; DOI 10.1002/acr.20442.

Hays, R.D.; Anderson, R.; Revicki, D. (1993). Psychometric considerations in evaluating health-related quality of life measures. *Quality of Life Research*, Vol.2, No.6, pp. 441-449.

Hellmann, D.B.; Ehlfelder, M.L.; Stone, J.H.; Jenckes, M.W.; Cid, M.C.; Guillevin, L.; Moreland, L.; Dellaripa, P.F.; Hoffman, G.S.; Merkel, P.A.; Spiera, R.; Brown, L.; Hernández-Rodriquez, J.; Rubin, H.R. (2003). *Arthritis Care & Research*, Vol.49, No.6, pp. 819-825.

Herlyn, K.; Reinhold-Keller, E.; Zeidler, A.; Raspe, H.; Gutfleisch, J.; Peter, H.H.; Gross, W.L. (1998) Health-related quality of life in primary systemic vasculitides. *Arthritis & Rheumatism*, Vol.41,p. S538.

Herlyn, K.; Hellmich, B.; Seo, P.; Merkel, P.A. (2010). Patient-reported outcome assessment in vasculitis may provide important data and a unique perspective. *Arthritis Care & Research*, Vol.62, No.11, pp. 1639-1645.

Hoffman, G.S.; Drucker, Y.; Cotch, M.F.; Locker, G.A.; Easley, K.; Kwoh, K. (1998). Wegener's granulomatosis: Patient-reported effects of disease on health, function, and income. *Arthritis & Rheumatism*, Vol.41, No.12, pp. 2257-2262.

Koutantji, M.; Pearch, S.; Harrold, E. (2000). Psychological aspects of vasculitis. Rheumatology; Vol.39, pp. 1173-1179.

Koutantji, M.; Harrold, E.; Lane, S.E.; Pearce, S.; Watts, R.A.; Scott, D.G. (2003). Investigation of quality of life, mood, pain, disability, and disease status in primary systemic vasculitis. *Arthritis Care & Research*, Vol.49, No.6, pp. 826-837.

Langford, C. A. (2005). Update on Wegener Granulomatosis. *Cleveland Clinic Journal of Medicine,* Vol.72,No.8, pp. 689-697.

Lewis, M.A.; Kalinowski, C.T.; Sterba, K.R.; Barrett, T.M.; DeVellis, R.F. (2006). Interpersonal processes and vasculitis management. *Arthritis Care & Research*, Vol.55, pp.670-675.

Marks, N.F.; Lambert, J.D.; Choi, H. (2002). Transitions to caregiving, gender, and psychological well-being: a prospective US national study. *Journal of Marriage & Family*, Vol.64, pp. 657–667.

Moses Alder, N.; Fisher, M.; Yazici, Y. (2008). Behçet's syndrome patients have high levels of functional disability, fatigue and pain as measured by a Multi-dimensional Health Assessment Questionnaire (MDHAQ). *Clinical and Experimental Rheumatology*, Vol.26, (Suppl. 50), pp. S110-S113.

Mumcu, G.; Inanc, N.; Ergun, T.; Ikiz, K.; Gunes, M.; Islek, U.; Yavuz, S.; Sur; H.; Atalay, T.; Direskeneli, H. (2006). Oral health related quality of life is affected by disease activity in Behçet's disease. *Oral Diseases*, Vol.12, pp. 145-151.

Newall, C.; Schinke, S.; Savage, C.O.; Hill, S.; Harper, L. (2005). Impairment of lung function, health status and functional capacity in patients with ANCA-associated vasculitis. *Rheumatology*, Vol.44, pp. 623-628.

Penninx, B.; Kriegsman, D.; van Eijk, J.; Boeke, A.; Deeg, D. (1996). Differential effect of social support on the course of chronic disease: a criteria-based literature study. *Families, Systems & Health*, Vol.14, pp. 223-244.

Reinhold-Keller, E.; Herlyn, K.; Wagner-Bastmeyer, R.; Gutfleisch, J.; Peter, H.H.; Gross, W.L. (2002). Effect of Wegener's Granulomatosis on work disability, need for medical care, and quality of life in patients younger than 40 years at diagnosis. *Arthritis Care & Research*, Vol.47, No.3, pp. 320-325.

Seo, P. (2007). Pregnancy and vasculitis. *Rheumatic Disease Clinics of North America*, Vol.33, pp. 299-317.

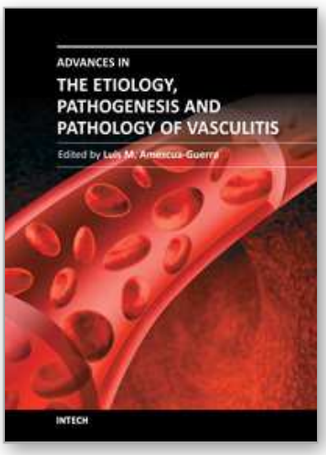
Seo, p.; Yuan-I, M.; Holbrook, J.T.; Hoffman, G.S.; Merkel, P.A.; Spiera, R.; Davis, J.C.; Ytterberg, S.R.; et al. (2005).Damage caused by Wegener's Granulomatosis and its treatment. *Arthritis & Rheumatism*, Vol.52, No.7, pp. 2168-2178.

Srouji, I.; Lund, V.; Andrews, P.; Edwards, C. (2008). Rhinologic symptoms and quality-of-life in patients with Churg-Strauss syndrome vasculitis. *American Journal of Rhinology*,Vol.22,No.4, pp.406-409.

Uguz, F.; Dursun, R.; Kaya, N.; Cilli, A. (2007). Quality of life in patients with Behçet's disease: the impact of major depression. *General Hospital Psychiatry*,Vol.29, pp.21-4.

Ware, J.E., Kosinski, M. (2005). *SF-36 physical & mental health summary scales: A manual for users of Version 1.* Lincoln, RI: QualityMetric Incorporated.

World Health Organization (1997). *WHOQOL: Measuring Quality of Life.* Available online at: http://www.who.int/mental_health/media/68.pdf.



Advances in the Etiology, Pathogenesis and Pathology of Vasculitis

Edited by Dr. Luis M Amezcua-Guerra

ISBN 978-953-307-651-5
Hard cover, 438 pages
Publisher InTech
Published online 17, October, 2011
Published in print edition October, 2011

This book represents the culmination of the efforts of a group of outstanding experts in vasculitis from all over the world, who have endeavored to devote their work to this book by keeping both the text and the accompanying figures and tables lucid and memorable. Here, you will find an amalgam between evidence-based medicine to one based on eminence, through an exciting combination of original contributions, structured reviews, overviews, state-of the-art articles, and even the proposal of novel pathogenetic models of disease. The book contains contributions on the etiology and pathology of vasculitis, the potential role of endothelial cells and cytokines in vascular damage and repair as well as summaries of the latest information on several primary and secondary vasculitis syndromes. It also covers selected topics such as organ-specific vasculitic involvement and quality of life issues in vasculitis. The editor and each of the authors invite you to share this journey through one of the most exciting fields of the medicine, the world of Vasculitis.

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
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中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
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