

Patient perspectives in sarcoidosis

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Purpose of review

The review presents an overview of the scientific publications about patient perspectives in sarcoidosis

Recent findings

The literature on patient perspectives in sarcoidosis is limited. Patient perspectives in sarcoidosis encompass a myriad of topics that have been addressed to some degree in the literature: patient needs and perceptions, patient-reported burden of sarcoidosis, and patient treatment priorities. Similar findings across studies were high levels of reported fatigue, a need to incorporate psychological support into the treatment plan and easy access to sarcoidosis expert centers. Furthermore, largely similar results were found across countries.

Summary

There is a growing tocus in patient perspectives in terms of sarcoidosis treatment. A multidisciplinary approach including psychological support and attention to fatigue, may better reflect the needs of sarcoidosis patients. Further research on sarcoidosis patient perspectives in sarcoidosis is needed to optimize care.

Keywords

patient perspectives, patient-reported outcomes, auality of life, sarcoidosis

INTRODUCTION

Sarcoidosis is a multisystemic, granulomatous disorder of unknown cause, which primarily affects the lungs but may involve any organ [1]. The clinical manifestations, natural history and prognosis are highly variable [2]. The clinical signs and symptoms are dependent on the organ/organs involved and may range from asymptomatic to life threatening, and the granulomatous inflammation may resolve spontaneously or with treatment [3]. In addition to organ-related symptoms, patients may suffer from a wide range of persistent nonspecific symptoms (sometimes referred to as 'parasarcoidosis') such as fatigue, small fiber neuropathy (SFN), fever, malaise, night sweats, weight loss, arthralgia, muscle pain, headache, general weakness, muscle weakness, reduced exercise capacity, cognitive impairment, and poor subjective sleep quality [1,4–11]. Nonspecific symptoms often do not correspond with objective physical evidence of disease and therefore are challenging to diagnose and to treat [6,12].

Both organ-related and nonspecific symptoms of sarcoidosis may be disabling and associated with psychological distress, anxiety, as well as depressive symptoms that may adversely affect a patient's quality of life (QoL) [5,6,13]. Consequently, the clinician's understanding of sarcoidosis patient's perspectives

will be important in tailoring an appropriate therapeutic regimen. Over the years, many tools for patient-reported outcomes (PROs) have been developed and validated to measure QoL, health status, fatigue, depression, anxiety, and stress in sarcoidosis [14]. However, most PRO measures (PROMs), while useful in clinical trials, are not generally considered to be reliable in individual patients [5]. The difficulties in applying traditional PROMs to individual sarcoidosis patients are two folds. First, there are inherent inadequacies of traditional PROMs instruments themselves. These PROMs are reliable to measure mean changes over time or between cohorts. However, the degree of intrapersonal variability makes it problematic to reliably follow QoL over time in individual

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Research from the patients' perspective in sarcoidosis is scarce. Receiving adequate information about the disease and easy access to an expert center for sarcoidosis are amongst main needs mentioned by patients. Data also suggest that clinicians should adopt a more holistic approach including pain management and psychological support. More research on patient perspectives in sarcoidosis should be prioritized by grant providers.

patients. Second, the phenotypic variability of sarcoidosis creates difficulties in developing PROMs that encompass the major QoL issues that affect the full range of sarcoidosis patients. It may be that accurate assessment of QoL in sarcoidosis requires the construction of PROMs based on 'personalized medicine,' where several of these instruments are developed so that they can be adapted and applied to individual sarcoidosis patients on the basis of their particular health and social situations. Therefore, despite the availability of multiple assessment tools, clinicians still have inadequate instruments to reliably determine what is most important to sarcoidosis patients.

Zanini et al. [15] reviewed several studies in various settings and defined the patient perspective as 'the self-perceived impact of the health condition on their life, their expectations of the consultation or the doctor, and their priorities regarding the outcomes of the treatment'. Despite knowledge of the burden of sarcoidosis, which may be associated with psychological, social, and physical limitations, very few studies have evaluated sarcoidosis patient perspectives. The aim of this review is to explore recently published literature concerning the sarcoidosis patient perspective and thereby to identify those topics most important to patients. Notably, the article was also literally written from a patient perspective, as the two first authors are both medical professionals (medical psychologist and physician) as well as sarcoidosis patients.

METHODS

Studies were identified using the electronic bibliographic database PubMed, using the Medical Subject Headings (MeSH) terms and keywords 'sarcoidosis' (and related terms), combined with MeSH terms and keywords as 'patients', 'surveys and questionnaires', or 'interview' (and related terms), and with keywords as 'needs', 'demands', 'perceptions', 'perspectives',

'experiences', 'priorities', 'burden', 'concerns', or 'expectations'. An additional search was done in the CINAHL (Cumulative Index to Nursing and Allied Health Literature) database. For the CINAHL search, the PubMed search was adapted: the supplementary concepts were removed and, when necessary, MeSH terms were replaced with comparable CINAHL subject headings. For example, the MeSH term 'surveys and questionnaires' was replaced with the CINAHL subject 'surveys'. Articles published in the last 18 months (between 1 September 2017 and 28 February 2019) were included, and articles in other languages than Dutch or English were excluded. References in retrieved articles were screened for additional relevant studies. Titles and abstracts of these articles were reviewed, articles were found to be eligible when they were original articles (no reviews) and assessed the patient perspective using questionnaires or interviews. Questionnaires must be broader than standardized and validated measures which measure a specific construct (e.g., fatigue or QoL). Patient perspectives included such topics as self-perceived impact of health condition (including self-reported symptoms), expectations of the consultation or the doctor, and priorities regarding treatment outcomes.

RESULTS

The PubMed search resulted in 29 articles, of which three articles met the inclusion criteria after screening the titles and abstracts for relevance [16^{••},17[•],18^{••}]. All selected studies were published recently: between August 2018 and February 2019. The CINAHL search resulted in one additional article, which did not met the inclusion criteria after screening the title and abstract for relevance. Checking the reference list of the retrieved articles yielded no additional original studies. An overview of the sarcoidosis cohorts and the results of the literature review can be found in Table 1.

Patient perspectives in sarcoidosis

Moor *et al.* [16**] evaluated the needs and perceptions of patients with sarcoidosis and their partners, using a live interactive voting system during two information meetings with sarcoidosis patients, in 2015 and 2017. Multiple questions were asked to both patients and partners on various topics. Forty percentage of sarcoidosis patients identified fatigue as their most disabling symptom, followed by painful joint/muscles (20%) and breathlessness (15%). Cough and ocular symptoms were the most disabling symptoms in less than 10% of the cohort and, and skin manifestations and depressive

Table 1. Overview and comparison of the literature review on patient perspectives

Study populations			
Source of patients	Two sarcoidosis patient information meetings for sarcoidosis patients from Erasmus University Medical Center in Rotterdam in 201 <i>5</i> and 201 <i>7</i>	A cross-sectional web-based anonymous survey among members of the Dutch Sarcoidosis Society, the Deutsche Sarkoidose Vereinigung, and a sarcoidosis clinic in Denmark	A web-based survey among members of patient organizations, patients were recruited through the PAG of the ELF
Sample size (n)	210	1072	1842
Sex, male (%)	Unknown	38.8°	Unknown
Age in years, mean (range) Study results sorted by t	Unknown	51.8 (12–80)	Unknown
Reported symptoms	Symptoms that affect patients most (n = 199) 40% Fatigue 20% Painful joints/muscles 15% Breathlessness 5–10% Cough, ocular, and other symptoms <5% Skin manifestations and depressive symptoms 50% Of patients and 40% of partners reported high levels of anxiety (elevated GAD-SI scores)	Sarcoidosis-associated symptoms (n = 1072) 90% Fatigue 86% SFN-related symptoms 72% Pulmonary 70% Musculoskeletal involvement 81% Reduced energy levels 54% Reduced concentration 51% Reduced memory 51% Sleeping problems	n/a
Reported needs (for treatment)	72% More attention and support for psychological problems 41% Receiving adequate information 36% Easy access to expert centers Contact with peers Practical and emotional support are important	n/a	More attention for quality of life and functionality Working in a multidisciplinary manner Treat patients as a whole, including pain management and psychological support Sarcoidosis specialists and expert centers are needed in every country

ELF, European Lung Foundation; GAD-SI, Generalized Anxiety Disorder-Single Item measure; PAG, Sarcoidosis Patient Advisory Group; SFN, small fiber neuropathy.

^aMean of the (significantly different) percentages: 31.9% male participants from Denmark, 38.0% male participants from Germany, and 46.6% male participants from the Netherlands.

symptoms in less than 5%. Almost three-quarters of both patients (n = 187) and partners (n = 121) reported sarcoidosis to have (very) much influence on their daily life (answering the questions 'What is the influence of sarcoidosis on your life at this moment?' or 'What is the influence of having a partner with sarcoidosis on your life at this moment?'). Levels of anxiety were elevated in the majority of patients and partners. The Generalized Anxiety Disorder Single Item questionnaire

identified approximately 50% of patients and 40% of partners who had experienced 'trouble relaxing' 'almost every day' or 'more than half the days' in the preceding 2 weeks. Almost three-quarters of patients would like more attention and support for their psychological problems and approximately 55% of patients and 65% of partners say they feel misunderstood because of the general unawareness of sarcoidosis. Patients reported receiving adequate information about the disease (41%) and easy access

to an expert center for sarcoidosis (36%) as main needs in care of patients with sarcoidosis. Moreover, contact with peers and the importance of emotional and practical support were mentioned. Concerning eHealth, the majority of participants desired to keep track of their data and symptoms on the internet and almost all patients were willing to measure lung function at home to optimize treatment. Given the interactive nature of the voting system, specific patient characteristics (including age, sex, and disease duration) could not be assessed, which complicates comparison with other research [16**].

Voortman et al. [17"] evaluated and compared the self-reported burden of sarcoidosis patients in Denmark, Germany, and the Netherlands, especially regarding the prevalence of fatigue and SFNrelated symptoms, using a cross-sectional web-based anonymous survey. Among 1072 patients completing the survey, almost all patients (95%) reported having sarcoidosis-associated symptoms (both organ-related and nonspecific, nonorgan-related symptoms). Fatigue was reported by 90% of the respondents (as measured with the Fatigue Assessment Scale), followed by SFN-related symptoms by 86% (as measured with the Small Fiber Neuropathy Screening List), pulmonary symptoms (72%), and musculoskeletal involvement (70%). In addition, reduced energy levels (81%), concentration (54%), memory (51%), and sleeping (51%) problems were reported [17^{*}].

Baughman et al. [18**] published an article concerning treatment priorities in Europe. In 2016, a European Respiratory Society task force was established to provide evidence-based guidelines on the treatment of sarcoidosis. Given that outcomes are generally based on objective laboratory data, imaging studies or pulmonary function tests (PFTs), a survey was developed to assess which treatment outcomes mattered most to patients. Through the Sarcoidosis Patient Advisory Group of the European Lung Foundation patients were asked to rate 7 outcomes including QoL, functionality, PFTs, blood tests, imaging, adverse events, and survival, using an online anonymous survey with a five-point Likert scale. Patients from six countries participated and 1842 surveys were completed (692 Dutch, 528 German, 338 English, 148 Italian, 107 Spanish, 29 French). Quantitative results from this study showed that QoL and functionality were rated as the most important outcomes for sarcoidosis patients, followed by survival, imaging, and adverse events, while blood tests and PFTs were rated as least important. Furthermore, based on both quantitative and qualitative results, the authors stated that QoL and functionality should be included in treatment outcomes. These authors suggest that their results show that clinicians should work in a multidisciplinary manner and focus on patient needs rather than the results of objective testing, and such an approach would include attention to pain management and psychological support when required. Moreover, the authors concluded that sarcoidosis specialists in specialist centers are needed in every country [18**].

DISCUSSION

The literature on patient perspectives in sarcoidosis is scarce. Although the number of studies included in the literature review may be too limited to draw firm conclusions, these results provide an overview of topics that are important to sarcoidosis patients. This literature review illustrates that patient perspectives in sarcoidosis span a vast range of concerns. Similarities across the studies include that fatigue was a major impactful symptom of sarcoidosis [16",17"], psychological support should be a major concern of clinicians, and easy access to sarcoidosis expert centers is important to sarcoidosis patients [16",18"]. We noted that the reported needs of patients with sarcoidosis concerning support or treatment are often about learning to live with their disease: the results suggest that clinicians should adopt a more holistic approach including pain management, psychological and practical support; more attention for QoL and functionality, and contact with peers [16**,18**]. These aspects may not be incorporated in standard care by most sarcoidosis caregivers. Therefore, a multidisciplinary approach focusing on somatic as well as psychosocial aspects is recommended for this wide-ranging disorder. The two European studies found largely similar results across countries, which suggest that these findings are relevant to people with sarcoidosis in different countries and health systems [17,18].

In the few published studies on patient perspectives in sarcoidosis, we noticed that patients are mostly recruited via patient societies [16**,17*,18**]. The downside of this recruitment method may be that it introduces a potential selection bias as patients who join these societies may be more likely to be symptomatic and, as a result, more likely to complete the surveys. To date, data on symptom burden in an unselected nationwide sarcoidosis patient population are scarce. In the study by Voortman et al. [17"], the Danish cohort were patients from a sarcoidosis clinic, whereby the German and Dutch cohorts were gathered through patient associations. The German and Dutch cohorts had similar patient-reported severity as the Danish cohort, that had detailed objective severity data. This finding provides some reassurance regarding the self-reported patient association data in this study $[17^{\bullet}]$.

The literature shows that almost three-quarter of patients reported a need for more attention and support for their psychological problems, which underlines the importance of including psychological support in standard care for sarcoidosis [16**]. Psychological symptoms in sarcoidosis are common and may include depressive symptoms, anxiety, and stress, cognitive impairment, memory loss, and fatigue [6]. Fatigue, depressive symptoms and anxiety are most probably interrelated; however, understanding the nature of the relationships remains problematic [6]. Sarcoidosis patients may benefit from various psychological interventions such as stress reduction, cognitive-behavioral therapy, and mindfulness-based cognitive therapy. Hence, not only fatigue but also anxiety and depressive symptoms should be an integral part of the multidisciplinary management of sarcoidosis patients [6].

It should be noted that most issues discussed in the literature about patient perspectives, such as fatigue, psychological symptoms, and a need for a more holistic treatment approach, are not specific for sarcoidosis. These issues are likely to be prevalent in other chronic diseases such as neurological disorders, autoimmune diseases, cancer, diabetes, pulmonary disease, heart disease, and arthritis [19–22]. Most of these chronic diseases are more common than sarcoidosis, and the consequences and potential treatment strategies in these diseases are likely to have been more thoroughly investigated. Therefore, it may be useful to extrapolate knowledge of patient perspectives of those suffering from other chronic disease to sarcoidosis in an attempt to uncover beneficial patient interventions.

Based on these data, we suspect that a paradigm shift towards more patient centered care, with more attention to fatigue, psychological symptoms and QoL will be required to optimize care for sarcoidosis patients. For this to occur, more attention needs to be paid to patient QoL issues, that will mandate that sarcoidosis patients are more actively engaged in their medical care. In addition, clinicians need to reprioritize their priorities giving more credence to patient concerns while downgrading the importance of objective laboratory data, which often relates poorly to patient concerns [5].

Traditionally, clinicians and basic scientists have formulated research protocols aimed at improving the understanding and treatment of disease. However, these data suggest that consideration should be given to incorporating issues that are important to patients into research trials.

Improving the currently limited understanding of sarcoidosis patient perspectives may facilitate the construction of such sarcoidosis research protocols that include significant relevant patient input. Therefore, it is very important to incorporate the patients themselves in developing new research questions and performing research. Qualitative research may be a good way for investigating patient perspectives. Furthermore, given the potential selection bias in studies initiated by sarcoidosis societies, research on the symptom burden in unselected patient populations would be interesting and useful. Performing randomized control trials in sarcoidosis cohorts may not be feasible in most general hospitals, due to the rarity of this disease. Patient samples are mostly small, especially when looking at each manifestation or phenotype separately. Therefore, larger studies should be carried out in sarcoidosis expert centers. Currently, interesting new qualitative research is being conducted about the experience of living with sarcoidosis, in which patients and family members are interviewed about their experience of living with (a family member that has) sarcoidosis. Results are expected summer 2019 (personal communication with Kerri Hall from Northcentral University on 4 February 2019).

Moreover, more research is needed on PROMs to evaluate QoL, health status, fatigue, and psychological symptoms in sarcoidosis patients over time. As mentioned above, most PROMs are useful in clinical trials, but they are not generally considered to be reliable in an individual patient [5]. Therefore, it is important to develop and validate PROMs, or to validate more general PROMs in sarcoidosis patients, that are applicable in an individual clinical setting over time. Item response theory (IRT) is a measurement approach that is often precise enough to provide reliable PRO assessments in individuals [5,23]. With IRT, each item response is individually 'scaled' to assess the state of the trait, the individual's responses to the items of the PROM are not summed but analyzed to see where the individual's responses lie on the continuum of the trait [5,23]. IRT allows the use of computer adaptive testing whereby the traits are selected in an iterative fashion based on the patient's previous responses so that an accurate location on the continuum of a particular trait (i.e., mild, moderate, and severe) and is able to compute a minimally important difference or clinically important difference [23,24]. Therefore, we currently have the technology available to assess patient concerns accurately and quickly in real time not only at the time of their visit but regularly between visits. However, we suspect that such technology has not been implemented even at sarcoidosis centers of excellence. Moreover, it would be of interest to investigate how sarcoidosis centers of excellence currently use assessment tools to evaluate QoL, health status, fatigue, and psychological symptoms in their evaluation of patients. Points of interest may be whether or not sarcoidosis centers of excellence use assessment tools and why; which tools do they use; how do they use them clinically; do they have the capacity to follow their patients over time both in and outside the center? In addition, it would be interesting to investigate what therapeutic approaches are used by experts as a follow-up to the PRO assessments.

CONCLUSION

Although the literature on patient perspectives in sarcoidosis is scarce, the few recently published studies show that there is a growing interest in this perspective. Patient perspectives encompass a variety of topics. The available literature shows that psychological symptoms and fatigue may need more attention in standard care for sarcoidosis, for example by adopting a more holistic treatment approach. Largely similar results across (European) countries suggest that findings may be relevant to people with sarcoidosis in different countries and health systems. More research on patient perspectives in sarcoidosis is needed.

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Conflicts of interest

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