

Health-Related Quality of Life (HRQoL)

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HRQoL is a multi-dimensional concept that reflects the degree to which a health condition interferes with participation in and fulfillment of important life areas. HRQoL is intended to capture the composite degree of physical, physiologic, psychological, and social impairment resulting from symptom burden, patient-perceived disease severity, and treatment side effects.

Keywords: sarcoidosis ; quality of life ; symptom burden ; symptom distress ; shared decision making ; patient-centeredness ; patient centered care ; mindfulness ; exercise ; physical activity

1. Introduction

Sarcoidosis is a phenotypically heterogeneous, systemic disease of unknown etiology characterized pathologically by the presence of non-caseating granulomas in one or multiple organs. Though sarcoidosis potentially resides in any organ and most commonly recognized with pulmonary, cutaneous, ophthalmologic involvement; neurologic, cardiac, gastrointestinal, hepatic, and renal involvement are likely under-recognized. The presence of granulomas may be silent or cause severe or life-threatening organ dysfunction resulting in multiple and diverse symptoms that impair physical function and psychosocial realms of function due to direct effects of disease or treatment effects. Sarcoidosis-related impairments can impede routine activities of daily living (ADLs) and disrupt critical life areas: work, family, and social/leisure; and also impact psychological well-being.

When relying predominantly on positive biomarkers, radiologic, and physiologic testing to guide treatment, a patient's physical, psychological, and cognitive impairment in sarcoidosis can often be overlooked by clinicians ^{[1][2]}. Clinician-recognition that "absence of evidence does not mean evidence of absence", especially when PET/CT is not available, is crucial in considering patient history. It should be acknowledged that sarcoidosis patients prioritize quality of life issues over most objective clinical tests to assess their disease ^{[1][2]}.

Health-related quality of life (HRQoL), though rarely a primary endpoint in clinical trials, may be the single outcome most reflective of patient priorities when living with a health condition ^[3]. HRQoL is a multi-dimensional concept that reflects the degree to which one's health condition impairs the ease with which one is able to interface with crucial areas of life activity: making a living, engaging with loved ones, and pursuing life's interests ^[4]. Health status, or physical function, is only one component of HRQoL, and therefore measures that are specific to health status/physical function do not measure the extent of HRQoL ^[5]. HRQoL reflects how important life areas are enhanced or diminished by the health condition, treatment, and environmental influences.

2. Medication-Related and Complication-Related HRQoL

Management of medication side effects, offers further opportunity to improve HRQoL. Clinician acknowledgement that, although anti-sarcoidosis medication may effectively treat sarcoidosis and thereby improve HRQoL, the side effects of medication may paradoxically worsen HRQoL. Again, if the clinician focuses solely on objective measures of physiologic improvement and lessening of granulomatous inflammation, medication side effects that impair HRQoL may go undetected.

The impact of glucocorticoids on HRQoL and adverse outcomes cannot be overstressed. While in some cases life-saving, glucocorticoids predictably create short-term intolerability and pose long-term risk of lasting detrimental harm to multiple organ systems. Long-term use of glucocorticoids has resulted in reports of multiple and diverse adverse events in sarcoidosis patients on prednisone and similar glucocorticoids ^{[6][7][8][9][10]}, including severe infection, psychosis, insomnia, cataracts, glaucoma, gastrointestinal bleeding, myopathy, hormonal dysfunction, and skin and mucosal fragility ^[11].

One study demonstrated a significantly worse HRQoL for patients receiving even mild doses of prednisone [6]. Across >900 sarcoidosis patients from the UK, U.S., and the Netherlands, the strongest association between a reported side effect and drug use was that of weight gain associated with increased appetite among prednisone use [7]. Avascular necrosis, a source of severe pain, disability, and cause for surgery, and low bone density with a fracture, commonly complicate long-term use of glucocorticoids [12][13][14]. Discussions in the expert community favor elevated BMI, the presence of cardiovascular disease, diabetes, low bone mineral density, prior avascular necrosis, prior gastrointestinal bleeding or ulceration, and psychiatric history as relative contraindications to glucocorticoid use.

Other anti-sarcoidosis medications, if implemented and monitored appropriately, have good safety profiles. The authors employ prednisone judiciously, as dictated by disease severity, and only as a bridge to on-boarding steroid-sparing anti-sarcoidosis treatment, such as methotrexate. This is followed by vigilant proactive tapering of prednisone as the steroid-sparing treatment gains efficacy 4outline common adverse events, contraindications, and protective measures with glucocorticoid use.

More frequent visits, or checking in with patients during the initiation of medication, can intercept problems, early strategies, such as temporary dose reduction, drug holidays, dose timing, dose splitting, formulation changes, or concomitant PRN medications to improve tolerability. For example, most patients tolerate methotrexate very well; however, a few patients experience nausea or fatigue. Taking with food helps to reduce nausea symptoms, and if taken with evening meal; nausea/fatigue may not be noticeable during sleep. Splitting the methotrexate dose over two days, switching from oral to self-injection; PRN anti-emetics or modulating concomitant folic acid dosing all may help to mitigate symptoms.

Checklists, again, can help navigate patient experience and prevent complications; supplied below are preventive strategies. Regularly planned testing for medication toxicity monitoring to ensure avoidance of medication interruption and, at the same time, patient safety [15][16]. Prescribe sufficient medication, only up until the time for the next toxicity screening test to avoid prolonged use of medication without toxicity check. Counseling on medication-related red flags for complications and preventive measures for each medication. Counseling on sunscreen use and sun exposure with certain DMARDs and biologic use [16]. Supporting exercise as medicine and a stress reduction strategy are expanded upon below.

3. HRQoL Self-Management Strategies for Patients and Family Members

As discussed above, in regards to PEMS, patient education about the disease, medications that treat disease, and elements of the healthcare system are essential to motivating engagement, enhancing adherence, and increasing ability to detect and avert potential complications, and therefore protect HRQoL. Making connections with patient organizations, as described above, can provide sustenance to patients and family. Exposure to interventions that, if habituated to some degree into practice, enhance HRQoL through potential amelioration of disease activity, increased fitness, and physical function and enhancing psychological well-being.

Wellness interventions, such as mindfulness [17], yoga, tai chi, and physical activity can help fortify a patient's ability to cope more easefully with psychological, physical and with logistical healthcare burdens [18][19][20]. The myogenic influence, discussed below in Section 7.2., and other activities that reduce the stress response, induce diffuse physiologic activity, of which vagus nerve stimulation and conditioning is an important component that sets in motion multi-faceted mechanisms within cardiopulmonary, immune system, brain, and central nervous system, and cultivated gastrointestinal responses. As an example, with reduced stress response, the myocardium relaxes in response to parasympathetic drive, with heart rate slowing that, over time, leads to strengthening heart rate variability. While chronic stress shortens chromosomal telomeres associated malignancy, autoimmunity and fibrosis, integrative interventions halt and appear to increase telomere length [21][22].

Exercise cultivates a fitness that can offset cardiopulmonary deficiency, thus facilitating greater ease, capacity and reserve for patients to interface with life experience and activities. Thus, a critical component to HRQoL is the clinician supporting, or enlisting other care team members, in safe exercise as a central part of sarcoidosis care. The focus of counseling is promoting muscular and cardiopulmonary fitness, stimulating disease-modifying mechanisms of exercise, and increasing physical activity and physical capacity. Clinician-initiated discussions on obesity are unlikely to help the patient feel connected with the important message of fitness [23].

Aerobic and muscle-strengthening exercise is recognized across healthy populations and health conditions to significantly improve HRQoL as well as cardiovascular, endothelial, metabolic/glandular, muscle structure and function, lung mechanics, mobility and systemic inflammation, fatigue and depressive symptoms, with overall beneficial effect on a wide spectrum of physiological and psychological attributes. Pulmonary rehabilitation is a feasible, safe, and effective [24][25]

strategy for improving breathing, exercise tolerance, fatigue, and cough through education, regardless of underlying diagnosis (e.g., ILD, PH). Exercise safety and safety parameters in sarcoidosis-related cardiopulmonary involvement [25] [26] and programmatic considerations, and enhancements in this population [27].

Evidence for the role of physical training in sarcoidosis is limited, but promising, and includes improved exercise capacity [28][29][30], muscle strength [28], and HRQoL [30], and decreased fatigue after a 12-week outpatient physical training intervention. Enduring effects on exercise capacity (VO₂max and 6MWD) and HRQoL as measured by the St. George's Respiratory Questionnaire (SGRQ) were maintained at a 6-month follow-up [30].

Exercise being a practiced coordination of movement with breath, increases skilled capacity for complex, weighty, or effort intense activities. Diaphragmatic strengthening, a consequence of many forms of exercise, is another example of exercise's ability to fortify respiratory dynamics and to improve attributes that support respiratory capacity, e.g., balance, core strength and lower back health [31]. A large muscle, the diaphragm, potentially supports amplification of healthful myogenic pathways related to inflammation, fibrosis, mental health and cardiovascular health. Thus diaphragmatic multi-impact health strategies are increasingly being studied in inflammatory and cardiopulmonary conditions, such as singing for lung health [32][33][34], yogic breathing, tai chi [18][19][20][35], as well as some yoga and dance techniques [36].

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