Health-Related Quality of Life Instruments in Studies of Adult Men with Testosterone Deficiency Syndrome: A Critical Assessment

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ABSTRACT

Introduction. Health-related quality of life (HRQOL) is a multidimensional concept, which subjectively measures a patient's physical, social, and emotional well-being. This information is becoming increasingly important in policy and clinical decisions. With such a wide range of tools available, careful selection is required to ensure they adequately reflect patient's concerns.

Aim. To critically assess HRQOL instruments used in studies of testosterone deficiency syndrome (TDS) to see whether they accurately measure these concerns.

Methods. A systematic review identified published articles. Studies were included if the population was adult men with TDS, with or without comorbid disease; used one or more HRQOL tools; and described the impact of treatment, the impact of TDS on the patient or the development of a questionnaire. Measurement properties and their use in clinical studies were described. Each study was assessed against 10 clinical face validity criteria to evaluate whether the questionnaires reflected issues that were of concern to patients.

Main Outcome Measure. Review of published literature.

Results. The study identified 29 articles that included 14 HRQOL questionnaires selected for use in 20 intervention studies, seven studies of the impact of TDS on the patient, and two studies describing the development of a HRQOL tool. Questionnaires displayed variable measurement properties and only nine studies complied with more than 50% of the clinical face validity criteria. Disease-specific instruments achieved a higher rate of compliance and more often demonstrated a positive effect of treatment on HRQOL compared to generic instruments.

Conclusion. Instruments used to measure HRQOL display variable measurement properties and often lack adequate clinical face validity. There are well-validated disease-specific HRQOL measures for age-related TDS, but none for classical TDS patients. Clinical and political decision-makers require HRQOL information using a combination of well-validated generic questionnaires and patient-focused, disease specific instruments relevant to the target TDS population under study. **Langham S, Maggi M, Schulman C, Quinton R, and Uhl-Hochgraeber K. Health-related quality of life instruments in studies of adult men with testosterone deficiency syndrome: A critical assessment. J Sex Med 2008;5:2842–2852.**

Key Words. Testosterone Deficiency; Patient-Reported Outcomes; Health-related Quality of Life; Hypogonadism

Introduction

Testosterone deficiency syndrome (TDS) is characterized by abnormally low testosterone levels. This clinical syndrome complex can cause significant morbidity, which alongside other associated comorbidities such as metabolic syndrome [1,2], can potentially lead to substantial economic and quality of life implications [3]. Classical forms of TDS are categorized according to whether the underlying cause is testicular (primary hypogonadism) or pituitary–hypothalmic (secondary

hypogonadism). More recently, a third category has emerged resulting from impairment at both sites; age-related TDS.

The range of symptoms associated with TDS are extensive, and though men with age-related TDS exhibit symptoms similar to those with classical TDS, it is likely that they will be less well established [4]. According to recent clinical guidelines, the more specific symptoms include sexual dysfunction, gynaecomastia, small testes, reduced fertility, loss of body hair, low bone mineral density, loss of muscle mass, and hot flushes; combined with the less specific symptoms of decreased energy, low mood, cognitive impairment, sleep disturbance, anaemia, increased body fat, and reduced work performance [5]. Such symptoms can be difficult to recognize and overlap with those of aging and comorbid disease in all but the most severe cases. Consequently, a number of inventories have been developed to aid in the screening of TDS in clinical practice [6].

Treatment of TDS aims to alleviate symptoms, and from a clinical perspective, testosterone treatment has been shown to be effective at doing just that for most symptoms [7,8]. However, the impact of TDS on the patients themselves from their own perspective is less well defined. In order to fill this gap, a number of patient reported outcome (PRO) measures have thus been used with increasing regularity.

A PRO is a measurement of any aspect of a patient's health that comes directly from the patients themselves, with no interpretation of the patients' responses by a physician or anyone else. The most widely used PRO is health-related quality of life (HRQOL), a multidomain concept, which includes at a minimum physical, psychological, and social functioning [9]. The importance of the patients' perspective on the impact of a disease has been widely recognized and the information provided by HRQOL measures is becoming increasingly important for input into policy decisions and clinical decisions on patient management [10]. It is now an accepted measure of the effectiveness of a new intervention by organizations such as the European Medicines Agency (EMEA) and U.S. Food and Drug Administration (FDA) [11]. The FDA has recently issued guidance on the use of HRQOL measures [12] and suggest that often inadequate attention is given to patients' experiences [9]. Therefore studies using such tools may not necessarily be accurately measuring the primary concerns of patients with that particular condition [13] and therefore providing inadequate or inappropriate information on which to make clinical or policy decisions.

With this background, the aim of our study was to critically assess HRQOL instruments used in studies of TDS to see whether they accurately measure the concerns and experiences of adult men with testosterone deficiency syndrome.

Methods

A systematic literature review was conducted to identify published reports of studies using multidimensional HRQOL measures from 1966 to 2008 using the following databases: MEDLINE, EMBASE, PUBMED, Cochrane library, several health economic databases, and the use of one internet search engine. Search terms for TDS included hypogonadism, male menopause, testosterone deficiency, androgen deficiency, andropause, male climacteric, androgen deficiency in the aging male, late onset hypogonadism, and partial androgen decline in the aging male. These were combined with patient-based search terms including quality of life, health status, patient reported outcomes, questionnaires, and interviews. Abstracts from the initial search were reviewed to identify relevant articles. A full article review was then conducted on all those that met the general inclusion criteria. Reference lists of relevant studies were also hand searched to identify additional data.

Articles were included if they met the following inclusion criteria: (i) the population studied was adult men with TDS (classical or age-related), with or without comorbid disease; (ii) one or more patient-based outcome measure was selected measuring HRQOL and were either generic or TDS disease-specific; (iii) the aim of the study was to describe the impact of TDS on the patient and/or the effect of TDS treatment and/or the development of a TDS disease-specific questionnaire aimed at measuring HRQOL.

In this study, HRQOL is defined as a multidimensional construct measuring the physical, social and emotional aspects that are relevant and important to a patient's well-being. In this way it embraces the World Health Organisation's definition of health [14]. Furthermore, the evaluation of HRQOL is subjective in that the person being assessed rates his or her own health status. Assessment of HRQOL can either be in the form of multiple questions asking about the impact on a range of domains or a single global question measuring overall quality of life or well-being.