Relationship Between Symptoms and Health-Related Quality of Life in Patients Treated for Hypertension

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Study Objective. To determine the relationship between symptoms and health-related quality of life (HRQOL) in patients receiving drug therapy for hypertension.

Design. Cross-sectional survey.

Setting. Outpatient general medicine and university-based hypertension clinics.

Patients. All patients prescribed one or more antihypertensive drugs seen during a 6-month period in the clinics.

Intervention. Data were obtained from a mailed questionnaire and medical records.

Measurements and Main Results. Symptoms were measured by a symptom count and total symptom distress. Two scores derived from the Short Form-36 (SF-36)—the Physical Component Summary (PCS) and the Mental Component Summary (MCS)—were used to assess HRQOL. Responses were received from 125 of 220 patients (56.8%). Mean ± SD values were 8.8 ± 7.8 for symptom count, 31.6 ± 46.2 for total symptom distress, 48.7 ± 9.3 for PCS, and 51.6 ± 10.1 for MCS. Higher symptom counts and symptom distress scores were strongly associated with lower HRQOL scores in multivariate models, with standardized coefficients from -0.62 to -0.41. These were greater in magnitude than any other predictor, including demographic information (age, sex, race, education level, income), disease variables (blood pressure, years of hypertension), and drug treatment (number of antihypertensive drugs and duration of regimen). Model-adjusted R^2 values were 0.22–0.41.

Conclusion. Symptoms have a greater impact on HRQOL than patient characteristics, blood pressure, or drug-related factors. Among patients receiving drug therapy for hypertension, detailed review of symptoms may yield important information for assessing and improving HRQOL.

Key Words: quality of life, hypertension, symptoms.

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Patients with hypertension frequently report symptoms that are similar to those reported by patients without the diagnosis.[1] Although hypertension is often thought to be asymptomatic, cognitive changes, mood alterations, and general symptoms, such as dizziness and headache attributable to hypertension, have been described.[2–7] Drugs used for the treatment of hypertension also may cause symptoms, some of which are specific to a particular drug, whereas others are similar to symptoms described or attributed to the disease of hypertension.[8]

Health-related quality of life (HRQOL) may be influenced by symptoms, whether these are derived from disease or treatment. The term HRQOL refers to the physical, emotional, and social impact of disease and treatments[9, 10] and is distinct from physiologic measures of disease.[9–12] The HRQOL of patients with hypertension may be influenced by blood pressure, adverse effects

of drugs used to treat hypertension, or other factors, such as the labeling effect, or beliefs and attitudes about illness and treatment. At issue is the determination of which variable or set of variables has the greatest influence on HRQOL.

The relationships between patient, disease, treatment variables, symptoms, and HRQOL were described by a model published in 1995.[13] This model proposes that physiologic changes due to illness or treatment lead to symptoms, which in turn influences functional status or HRQOL. These relationships are influenced by patient and environmental variables that may affect patient perception of symptoms and changes in HRQOL. This general model can be applied to data from clinical studies to ascertain the strength of relationships between HRQOL and patient, disease, and treatment variables.

We sought to determine the relationship between symptoms and HRQOL in patients receiving drug therapy for hypertension. Our population-based study used the published model[13] as a framework to identify and rank the relationships between patient, disease, and treatment variables and HRQOL. We hypothesized that those patients who report the most symptoms or the most distress associated with symptoms would have lowest HRQOL scores, independent of blood pressure and other variables related to patient or disease characteristics.

Methods

Study Setting and Patient Population

This study was a cross-sectional survey of patients who attended either an outpatient general medicine clinic or a university-based hypertension clinic. All patients had a documented diagnosis of hypertension and were prescribed one or more antihypertensive drugs. Patients were identified by a search of the billing database for the internal medicine and hypertension clinics for encounters with the *International Classification of Diseases, Ninth Revision*, diagnosis code for essential hypertension. The database was searched for all patients who had appointments at the clinics from July–December 1996. The medical records of the identified patients were reviewed to identify those meeting the study criteria.

Age above 30 years was a criterion for inclusion. Patients were excluded if they had other symptomatic chronic disease states, such as pulmonary disease (asthma or chronic obstructive pulmonary diseases), inflammatory rheumatic diseases, chronic heart failure (documented New York Heart Association functional classes III or IV), chronic pain syndromes, neurologic disorders or deficits, ischemic heart disease, or diabetes mellitus. Patients also were excluded if their medical record revealed conditions that would interfere with their ability to participate in the study, such as terminal illness, dementia, and severe functional impairment. Finally, patients were excluded if evidence of hypertension-related target organ damage was present (documentation of retinopathy, renal changes such as serum creatinine level > 2.0 mg/dl or albuminuria, chronic heart failure, stroke, peripheral arterial disease, and ischemic heart disease with a history of myocardial infarction, percutaneous coronary revascularization procedure, or coronary artery bypass graft surgery). Documentation of left ventricular hypertrophy in the medical record was an exclusion criteria. However, left ventricular hypertrophy was not universally assessed and could not be ruled out for all patients in the study. The study was reviewed and approved by the institutional review board of the university, and written informed consent was obtained from all patients.

Data Collection and Measures

Data were collected by self-administered questionnaires mailed to patients' homes. A follow-up reminder postcard was sent to nonrespondents 2 weeks after the initial survey packet was sent; those who still did not respond received a second survey packet 1 month after the mailing of the first survey. Telephone follow-up was attempted for nonrespondents, but few patients were accessible during normal business hours.

Symptoms were identified using a modification of the Symptom Distress Checklist (SDC), a

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questionnaire developed for use in clinical trials to identify the existence of symptoms related to hypertension and antihypertensive drug adverse effects and the impact they have on patients.[14–16] The SDC used for this study consisted of a list of 51 symptoms. We added an item related to sexual dysfunction. The questionnaire asks whether the patient experienced the symptom during the past 4 weeks (yes or no), the frequency of the problem in the past 4 weeks, and the extent to which it caused distress. For each symptom the patient documents as being present, the patient completes two additional questions to characterize the symptom. First, the patient indicates how frequently the symptom occurs by choosing one of four response options ranging from "once or twice" over the 4 weeks (assigned a value of 1) to "daily or more often" (assigned a value of 4). Next, the patient indicates the amount of distress the symptom caused during the past 4 weeks. There are five response options to quantify the distress caused by each symptom. If the patient indicates that a symptom caused minimal or no distress, the symptom is assigned a value of zero. The other end of the distress scale—extreme distress—has a value of 4. A symptom distress level then can be calculated for each documented symptom by multiplying the value assigned to the response for frequency of occurrence times the value assigned to the distress it causes. For example, if the symptom occurred twice/week (assigned a value of 2) and caused a moderate amount of distress (assigned a value of 3), the symptom distress level for that symptom is 6.

Two summary measures were calculated from the SDC symptoms. The first was the number of symptoms reported/patient (SDC count, range 0–51). The second was the overall distress level of reported symptoms (overall symptom distress [OSD]). The OSD equals the sum of individually reported symptom distress levels. For example, a patient who experienced three symptoms with distress levels of 6, 12, and 16 would have an OSD of 34. The range for the OSD score is 0–816.

The Short Form-36 (SF-36) Health Survey, version 1.0 (The Health Institute, New England Medical Center, Boston, MA)[17] was used to assess HRQOL. The SF-36 is a validated 36-item questionnaire that measures the health concepts of physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social function, role limitations due to emotional problems, and mental health. It also contains a single item that examines change in health over time. Summary measures of physical health (Physical Component Summary [PCS]) and mental health (Mental Component Summary [MCS]) are derived from the completed questionnaire. The PCS and MCS were used for this analysis. Item scores are coded, summed, and transformed to a scale ranging from 0 (worst health status) to 100 (best health status), then adjusted to norm-based scaling for final scores for PCS and MCS. The questionnaire uses a 4-week recall period. A scantron version of the SF-36 was used (Response Healthcare Information Management, Inc., East Greenwich, RI).

Patient-related data obtained from the self-administered questionnaire included age, sex, race, income, education level, and self-reported length since diagnosis of hypertension. Information also was collected on prescribed drugs, including drug name, dose, and frequency, as well as length of current therapy. The medical record was used to confirm age, sex, and race. Disease characteristics such as blood pressures, other documented diseases, and prescribed antihypertensive drugs were obtained from the medical record. Self-reported treatment information matched that found in the medical record for all patients. All systolic and diastolic blood pressures documented in the medical record in the year preceding the study were recorded. The most recent blood pressure recorded in the medical record was used for analysis. Although a statistically significant difference ($p=0.01$) existed between mean 1-year systolic blood pressure (143.7 mm Hg) and most recent systolic blood pressure (104.3 mm Hg), we felt that the relative difference between the values was insignificant. Data obtained from the medical record were used in part for a nonresponse bias assessment.

Data Analysis

Descriptive data are presented as mean ± SD or frequency (%). Multivariable linear regression was used to determine the relationship of symptom data to PCS and MCS. Patient, disease, and treatment variables were added first to the model, followed by one of the SDC summary variables (SDC count or OSD). The final regression model was developed through stepwise elimination of variables that lacked statistical significance ($p>0.05$). Separate models were run for each SDC summary variable (SDC count and OSD) and each SF-36 variable (PCS and MCS).

Results

The inclusion criteria were met by 222 patients. Two questionnaire packets were undeliverable, leaving a sample of 220 patients. A total of 125 patients responded to the survey for a 56.8% response rate.

Nonresponse bias assessment showed no differences between respondents and nonrespondents based on blood pressure, sex, or number of prescribed antihypertensive entities. However, more patients over 65 years of age responded (58.9% respondents vs 55.5% nonrespondents, p=0.03) whereas fewer African-American patients responded (17.1% respondents vs 35.8% nonrespondents, p=0.005).

Patient characteristics are listed in Table 1. There was a fairly equal distribution with regard to sex and income. There were more Caucasian than minority patients. Patients tended to have had the disease for many years and had relatively stable drug regimens. The drug classes most commonly reported were diuretics (33.3%), followed by angiotensin-converting enzyme inhibitors (20.6%), β-blockers (18.4%), and calcium channel blockers (15.8%). Other drugs were peripheral α-blockers (terazosin and prazosin), centrally acting agents (clonidine and methyldopa), and direct-acting agents (minoxidil). Patients took an average of one to two antihypertensive drugs.

Nearly all respondents (122 of 125 [97.5%]) indicated that they experienced at least one symptom. The mean number of reported symptoms (SDC count) was 8.8 ± 7.8 (range 0–35). The mean OSD was 31.6 ± 46.2 (range 0–261). Symptoms reported by more than 30% of patients were lethargy, fatigue, tiredness, lightheadedness, nocturia, dryness of mouth, and heartburn. The mean PCS was 48.7 ± 9.3 (range 21.9–63.1). The mean MCS was 51.6 ± 10.1 (range 16.6–67.0).

The results of final regression models for the relationships between number of reported symptoms (SDC count); characteristics of the patient, disease, and treatment; and HRQOL (PCS and MCS) are presented in Table 2. Age, length of current drug therapy, and SDC count all had negative influences on the physical-related HRQOL score (PCS), with older age, longer therapy, and greater number of reported symptoms being associated with lower scores. The SDC count had the strongest relationship with the PCS score of all variables evaluated. For the MCS model, sex and SDC count were the only variables. Women reported more symptoms and had lower mental-related HRQOL (MCS) scores than men. The SDC count variable had an even stronger relationship with MCS score than did sex. The explained variance in the final SDC count models was 0.31 and 0.41 for the PCS and MCS models, respectively.

The results of regression models demonstrating the relationship between OSD and HRQOL are shown in Table 3. The final PCS model retained the length of current therapy, systolic blood pressure, and OSD. Lower PCS scores were

Table 1. Characteristics of the 125 Respondents

Characteristic	Value
	Mean ± SD
Age (yrs)	59.0 ± 11.2
Most recent blood pressure (mm Hg)	
Systolic	139.6 ± 20.7
Diastolic	85.5 ± 11.8
Duration of hypertension diagnosis (yrs)	16.5 ± 12.2
Duration of current antihypertensive drug regimen (yrs)	3.8 ± 4.6
No. of hypertensive drugs	1.5 ± 0.7
	No. (%)
Sex	
Male	59 (47.2)
Female	66 (52.8)
Race[a]	
Caucasian	91 (75.2)
African-American	22 (18.2)
Other	8 (6.6)
Yearly household income ($)[b]	
< 20,000	12 (10.7)
20,000–39,999	17 (15.2)
40,000–59,999	32 (28.6)
60,000–79,999	20 (17.9)
≥ 80,000	31 (27.7)

[a]Only 121 responded.
[b]Only 112 responded.

Table 2. Standardized Regression Coefficients for Final Models Relating Symptom Count (SDC Count) to Health-Related Quality of Life

Variable	PCS	MCS
Adjusted R^2	0.31	0.41
Age	-0.28[a]	
Sex		-0.15[b]
Duration of current therapy	-0.21[c]	
No. of symptoms reported (SDC count)	-0.51[d]	-0.62[d]

PCS = SF-36 Physical Component Scale; MCS = SF-36 Mental Component Scale; SDC = Symptom Distress Checklist.
[a]p=0.001.
[b]p=0.03
[c]p=0.01.
[d]p<0.001.

associated with longer duration of current therapy, higher systolic pressure, and more symptom-related distress. The OSD variable had a stronger relationship to PCS than did the length of therapy or the systolic blood pressure variables. The final MCS model included a number of patient and disease variables, including age (older age, better MCS score), sex (women had lower MCS scores), systolic blood pressure (patients with higher systolic blood pressures had lower MCS scores), and OSD. Younger patients, women, patients with higher systolic blood pressures, and patients reporting greater total symptom distress had lower MCS scores than other categories of patients. The OSD variable demonstrated the greatest relationship to the MCS score. The explained variance in the final OSD models was 0.22 and 0.40 for the final PCS and the MCS models, respectively.

Table 3. Standardized Regression Coefficients for Final Models Relating Overall Symptom Distress (OSD) to Health-Related Quality of Life

Variable	PCS	MCS
Adjusted R^2	0.22	0.40
Age		0.18[a]
Sex		-0.22[b]
Systolic blood pressure	-0.22[c]	-0.21[d]
Duration of current therapy	-0.28[b]	
Overall symptom distress	-0.41[e]	-0.55[e]

PCS = SF-36 Physical Component Scale; MCS = SF-36 Mental Component Scale.
[a]p=0.04.
[b]p=0.01.
[c]p=0.03.
[d]p=0.02.
[e]p<0.001.

Discussion

The presence of symptoms, regardless of their source, may influence the HRQOL of patients receiving drug therapy for hypertension. A previously published model[13] provided a useful framework for demonstrating the relationship between symptoms and HRQOL. When we controlled for patient, disease, and treatment characteristics, the summary symptom measures emerged as the strongest predictors of both physical and mental HRQOL measures. The source of symptoms may derive from the illness (elevated blood pressure) or from adverse effects of treatment. Moreover, some symptoms may have no identifiable cause, such as somatoform symptoms common in the general population. Other studies have reached similar conclusions; that is, they have shown a strong association between symptoms and HRQOL in patients receiving treatment for hypertension.[18, 19] Our findings are consistent with and help justify the previously published causal model,[13] in which symptoms mediate effects between root causes, such as disease or drugs, and HRQOL.

Symptoms in the patient receiving treatment for hypertension may have many causes. Although often regarded as an asymptomatic illness, hypertension has been associated with headache, blurred vision, nocturia, unsteadiness, dizziness, sexual problems, cognitive impairment, and tiredness.[20–26] Many symptoms reported by patients with hypertension are similar to nonspecific symptoms seen in the general clinic population.[27, 28] To compound the issue, most antihypertensive drug therapies are associated with adverse effects that are similar to commonly reported symptoms in primary care.[8, 29]

In a recent study, patients experiencing drug-related side effects in association with their treatment for hypertension reported the lowest assigned value for HRQOL, using utility analysis, of all patients in the study.[30] Other studies have documented that antihypertensive drugs do cause troublesome adverse effects that may affect HRQOL to various degrees, depending on the specific agent.[31–33] An interesting observation is that systolic blood pressure was related to both the PCS and MCS HRQOL scores in their respective models using OSD but not for the symptom frequency models. Other research also has demonstrated an influence of blood pressure on HRQOL.[1] However, the presence of an increasing number of symptoms as well as distress associated with the symptoms have an overall greater effect on HRQOL than blood pressure.

Previous research has demonstrated that patients with hypertension have lower HRQOL than the general population.[34] The Medical Outcomes Study found lower general health perception in patients with hypertension than in patients without chronic conditions.[19] The investigators postulated that most variance in functioning and well-being (HRQOL) was not explained by the presence of a chronic condition such as hypertension; rather, they suggested that other variables, such as severity and duration of the condition, type of treatment provided, style of medical care (reassurance or information), and other patient characteristics (exercise habits, weight, or will to function) influenced perceived

outcomes. Other research has suggested similar hypotheses.[34] Our study adds to this literature by suggesting that a significant proportion of HRQOL variance can be explained by patients' symptoms, regardless of root cause.

Patient drug-taking behavior may be influenced by both the presence of symptoms, particularly distressful symptoms, and changes in level of functioning. Patients may decide that a therapy is not indicated if they perceive it to be the cause of symptoms.[35] There is evidence that lack of motivation to take a treatment often arises from mistaken beliefs about the necessity of the treatment or from concerns about potential adverse effects.[36, 37] Often, these beliefs are influenced by perceived symptoms.[38] This is particularly an issue with hypertension, an illness that commonly is perceived by patients and health care providers as asymptomatic. Patient decisions often reflect perceptions that may be inappropriately linked to symptoms or changes in functioning.[39, 40]

Symptom monitoring and management are central to the improvement of patients' HRQOL. Our study provides evidence for a model that links patients' status with regard to biology, symptoms, and functionality (HRQOL) and may prove useful in guiding follow-up of patients who receive treatment for hypertension. The study also provides evidence that patients often have multiple symptoms that cause distress. By learning to identify symptoms and changes in functioning, clinicians can increase their effectiveness in helping patients maintain adherent behavior with drug and nondrug interventions in chronic diseases such as hypertension. Periodic administration of a symptom and/or functional status (HRQOL) questionnaire may be one method for identifying issues that are not discussed during a normal clinic visit. Limited time and resources can make it difficult to administer functional status questionnaires or interpret symptoms during office visits. However, advancing computer and personal device technologies soon may make these interventions feasible.

The cross-sectional design of our study enabled us to explore the relationship between symptoms and HRQOL, but it did not allow us to directly determine cause and effect. For this, a more sophisticated study design using longitudinal data collection and larger numbers of patients is necessary. Another limitation of our study is that study patients did not have other, more symptomatic illnesses that may impair HRQOL. Examples of highly symptomatic illnesses that are often comorbidities with hypertension are diabetes, ischemic heart disease, and other conditions associated with hypertension-related end-organ damage. However, our study does provide clinicians and researchers with evidence of an association between symptoms and HRQOL as measured by the SF-36.

Conclusion

Symptoms have a greater impact on SF-36 physical-related and mental-related scores than patient characteristics, blood pressure, or drug-related factors. Clinicians should be aware that detailed understanding of patients' symptoms, perhaps measured through available instruments, may provide important insights that can help assess and improve patients' HRQOL.

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