Quality of Life in Screen-detected Celiac Disease Patients in the United States

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Background and Aims: Celiac disease (CD) is increasingly diagnosed through screening of at-risk groups (relatives of individuals and associated autoimmune disorders). The impact of diagnosis and treatment on screen-detected CD patients is poorly studied, particularly in the United States. We therefore compared the quality of life (QOL) between screen-detected and symptom-detected CD patients.

Methods: Patients with a known diagnosis of CD were invited to complete 3 validated survey instruments: the CD Quality of Life (CDQOL), the CD Adherence Test for dietary adherence and the general Psychological General Well-Being index. In addition, demographic details, mode of presentation, and compliance with gluten-free diet (GFD) were assessed.

Results: The overall response rate was high at 69%. Of 226 responses received, 211 were eligible for inclusion; the median age was 47, and the median duration of GFD was 4 years. One third of the sample (71, 34%) was screen detected. Of these, 57 (80%) had a relative diagnosed with CD, whereas 14 (20%) had an associated condition. Despite being screen detected, 49 (69%) reported symptoms before diagnosis. GFD adherence was excellent and did not differ between groups. Overall, there were no significant differences between screen-detected and symptom-detected patients with regard to CDQOL, CD Adherence Test, and Psychological General Well-Being scores.

Conclusions: Screen-detected and symptom-detected CD patients do not differ with regard to QOL or disease adherence as measured by validated disease-specific instruments. A high proportion of screen-detected patients reported symptoms before diagnosis, which often improve with GFD.

Key Words: celiac disease, small bowel, quality of life, screening

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Celiac disease (CD) is a common disorder that is widely underdiagnosed, in part due to its varied presentation.[1] Its pathophysiology involves an autoimmune response to ingestion of gluten, a protein component of cereals including wheat, barley, and rye. CD can affect many organ systems, but is classically described as an enteropathy, with gastrointestinal symptoms of diarrhea, bloating, and weight loss. The classic presentation, however, now comprises a minority of patients, and there is evidence of a trend toward atypical, extraintestinal, and silent presentations.[2,3]

Although the seroprevalence of CD approaches 1% in western populations, a majority of patients are not aware that they have the disease.[4] Underdiagnosis is particularly acute in the United States, where currently only 17% of those with the disease are diagnosed.[5] The perceived rarity of the disorder in North America has historically resulted in long delays in diagnosis and a poor awareness of the disease among clinicians.[6] Given that untreated CD has been associated with diminished quality of life (QOL) and increased mortality, there is growing interest in active identification of unrecognized patients through surveillance and screening.[7,8] The impact on patients of being diagnosed with CD through screening is unclear.

Although screening of high-risk groups (family members and autoimmune disorders) for CD is common and accounts for 10% to 25% of new diagnoses of adult and pediatric CDs, it is controversial.[9–11] Authorative recommendations concerning screening high-risk groups vary: the National Institute of Health consensus development conference and the American Gastroenterological Society do not recommend routine screening of high-risk groups, whereas the North American Society Pediatric Gastroenterology Hepatology And Nuntrition and United Kingdom guidelines do recommend screening.[12–15] There are also inconsistent guidelines and practices concerning the screening of type 1 diabetics who have a high prevalence of CD.[16]

Benefits stemming from early detection and treatment must be weighed against the potential consequences of labeling apparently asymptomatic individuals with a chronic disease.[17,18] A significant burden of the diagnosis of CD is the need to adhere to a gluten-free diet (GFD), which poses problems of cost, restrictions on where to eat, and suboptimal nutrition.[19–21] A GFD may be stigmatizing for some, and it is unclear if asymptomatic patients are equally adherent to the diet.[22–24] There is evidence, however, that screening frequently detects cases who are only symptomatic in retrospect, and even patients who report no or subtle symptoms before diagnosis show improvement with GFD.[25–27]

Arguments against screening high-risk groups include the lack of clear health benefits and the consideration that the diagnosis and treatment of CD may impair the QOL of these patients. We therefore aimed, in this study, to determine if differences exist between screen-detected and symptom-detected CD patients with regard to measures of QOL and dietary adherence. To our knowledge, this is the first study to investigate these groups in North America,

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The authors declare that they have nothing to disclose.

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where potential disparities between screened and symptom-detected patients may be magnified by poorer clinician awareness, higher thresholds for testing, longer delays in diagnosis, greater cost, and more limited availability of GFD compared with Europe.[28]

METHODS

Patients and Study Design

We performed a cross-sectional survey of patients with known CD via online and paper questionnaires. The study was conducted at the Celiac Disease Center at Columbia University in New York. The investigational protocol was approved by the Institutional Review Board of Columbia University. Data collection occurred from September 2011 to September 2012. Adults (18 y and older) who were either symptomatic (classic, diarrhea predominant) at diagnosis or were diagnosed by screening of high-risk groups were recruited for the study in one of 3 ways: during visits with their physician at the Center, at CD support group conferences, or via mail/email invitations after having been identified from the Center's prospectively maintained database. Paper surveys were completed either at the physicians' office or at home, and returned by mail. Subjects were included if they reported a biopsy-confirmed diagnosis of CD. Patients were not included in the study if analysis of their responses revealed they had omitted the survey items on gender, age, or greater than half of the survey questions.

The demographic portion of the survey enquired about race, education level, and the method and timing of diagnosis. Patients were asked if their CD was diagnosed as part of screening, with one of 4 possible responses: (a) yes, I have a family member with celiac disease (specify family member); (b) yes, I have a disease associated with celiac disease (specify disease); (c) Yes, other reason (specify reason); or (d) no, I was diagnosed because I had symptoms (specify symptoms). The response to this question was used to determine if patients were screen detected or symptom detected. A separate question later on in the survey asked whether or not patients had symptoms before CD diagnosis.

QOL Assessment

The questionnaire incorporated 2 validated instruments to assess QOL, as well as several general questions regarding self-perceived health. The CD-specific quality of life (CDQOL) scale, consisting of 20 items across 4 clinically relevant subscales (CD-related limitations, dysphoria, health concerns, and inadequate treatment) was used to assess QOL issues specific to CD.[29] Items were scored on a 5-point Likert scale, and summed to give a score of 100, with higher scores suggestive of better QOL. For the purposes of dichotomization, patients in the lowest quartile of CDQOL were considered to have poor QOL.

The Psychological General Well-Being (PGWB) index was used to assess self-perceived health-related well-being. Although not a disease-specific instrument, the scale has been validated and used extensively in celiac research, including in screening studies.[23,30,31] The questionnaire contains 22 items over 6 domains: anxiety, depressed mood, positive well-being, self-control, general health, and vitality. Scores range from 22 to 132 with higher scores indicating better psychological well-being. As above, patients in the lowest quartile of PGWB scores were considered to have low psychological well-being for the purposes of dichotomization.

Patients were also asked questions regarding their perceived health, including whether they agreed with the statement "I am glad that I was diagnosed with celiac disease," and whether or not their symptoms improved after starting a GFD.

TABLE 1. Survey Responses, by Mode of Distribution

Item	Responses Received (n = 226)	Surveys Distributed	Response Rate
Support group meeting	105	132	0.79
Physician office	67	70	0.95
Mailed/emailed survey	54	126	0.42
Total	226	328	0.69

Dietary Adherence

Dietary adherence was assessed by use of the CD Adherence Test (CDAT). This validated 7-question survey instrument asks about persistent symptoms and attitudes to gluten exposure, and was validated for standardized evaluation of GFD adherence.[32] Scores range from 7 to 35, with higher scores implying worse adherence. For the purposes of dichotomization, a single cutoff of ≥ 13 (as we have used previously) was chosen to represent poor adherence.[33] Additional questions were included on dietitian use, and self-reported percent adherence to GFD.

Statistical Analysis

Scores were calculated for CDQOL, CDAT, and PGWB, and reported as mean values. The independent samples Mann-Whitney *U* test was used to compare values between the screen-detected and symptom-detected groups. Fisher exact test was used for cross tabulations where appropriate. Logistic regression was performed to determine if mode of detection was predictive of poor QOL (lowest quartile of CDQOL), poor psychological well-being (lowest quartile of PGWB), or poor adherence (CDAT ≥ 13). All testing was 2-sided, and P values < 0.05 were considered statistically significant. Statistical tests were performed using SAS version 9.2 (SAS institute, Cary, NC).

RESULTS

Sample Characteristics

Surveys were received from a total of 226 subjects (Table 1). The response rate overall was high at 69%. Of the 226 surveys received, 4 were incomplete, and a further 11 were excluded from the analysis because the respondent gave inconclusive information concerning the CD diagnosis, leaving 211 valid entries.

A majority of patients were female (78%), white (95%), and highly educated, with 93% holding a college or advanced degree (Table 2). Screen-detected patients comprised one third of the sample (71, 34%), and most reported a family history of CD as the prompt for their testing.

Differences Between Screen-detected and Symptom-detected Patients

Screen-detected and symptom-detected patients did not differ with regard to age, gender, race, or education (Table 3). A majority of both screen-detected (49, 69%) and symptom-detected patients (125, 89%) reported having

TABLE 2. Participant Characteristics

Item	Patients (n = 211)
Age [median (range)] (y)	
Current	47 (18-95)
At diagnosis	39 (0-75)
Gluten-free diet	4 (0-36)
Female [n (%)]	164 (78)
Race [n (%)]	
White	200 (95)
Hispanic	6 (3)
Asian	2 (1)
African American	1 (1)
Education [n (%)]	
High school	14 (7)
College	116 (55)
Graduate school	81 (38)
Diagnosis [n (%)]	
Symptom detected	140 (66)
Screened due to celiac family history	57 (27)
Screened due to personal history	
Type 1 diabetes mellitus	6 (3)
Autoimmune thyroid disease	4 (2)
Other associated condition	4 (2)

symptoms before diagnosis, although screen-detected patients were less likely to report improvement in their symptoms with GFD (54% vs. 71%, $P = 0.016$).

Self-perceived QOL—measured by the proportion of subjects who reported their QOL as very good or excellent on a 5-point Likert scale—did not differ between screen-detected and symptom-detected patients. Those who were screen detected were less likely to agree with the statement "I am glad that I was diagnosed with CD" (42% vs. 64%, $P = 0.005$).

There were no significant differences in QOL as measured by the CDQOL and PGWB scores between symptom-detected and screen-detected patients. Dietary adherence as measured by CDAT was also comparable, and similar numbers reported strict adherence to GFD, and having seen a dietitian. The 22 screen-detected patients who reported no symptoms before diagnosis were analyzed separately: when compared with symptom-detected patients, this subset demonstrated a trend toward higher CDQOL (81.8 vs. 73.5, $P = 0.057$) and PGWB (83.6 vs. 74.3, $P = 0.074$), without meeting significance. There was no difference in CDAT (12.5 vs. 12.0, $P = 0.59$).

On multivariate analysis, (Table 4) after adjusting for age, gender, education, dietitian use, self-reported dietary adherence, time since diagnosis, and survey location, there was no association between mode of detection and low CDQOL (suggestive of poor QOL), low PGWB (suggestive of poor psychological well-being), and high CDAT (suggestive of poor dietary adherence). Screen detection was, however, found to predict a lower tendency to agree with the statement "I was glad I was diagnosed with CD" (odds ratio = 0.34; 95% confidence interval, 0.15-0.77).

TABLE 3. Comparison of Screen-detected and Symptom-detected Participants

Item	Screen-detected Celiac Disease (n = 71)	Symptom-detected Celiac Disease (n = 140)	*P*
Age (mean) (y)	45	47	0.35
Female [n (%)]	52 (73)	112 (80)	0.25
Seen a dietitian [n (%)]	38 (55)	85 (63)	0.25
Always follow gluten-free diet [n (%)]	65 (93)	129 (95)	0.56
Symptoms before diagnosis [n (%)]	49 (69)	125 (89)	0.0005
Symptoms improved with gluten-free diet [n (%)]	37 (54)	98 (71)	0.016
Self-rate quality of life as very good or excellent [n (%)]	42 (64)	77 (60)	0.59
Glad they were diagnosed with celiac disease [n (%)]	28 (42)	82 (64)	0.005
CDQOL score (mean)	77.3	73.5	0.19
PGWB score (mean)	79.3	74.3	0.13
CDAT score (mean)	12.2	11.9	0.42

CDAT indicates Celiac Disease Adherence Test; CDQOL, celiac disease-specific quality of life; PGWB, Psychological General Well-Being.

DISCUSSION

The most important result of our study was that individuals diagnosed through screening of high-risk groups for CD had a similar QOL to those diagnosed because of the presence of symptoms. In addition, both groups had similar adherence to the GFD, as measured by a validated survey instrument. Other notable findings include a surprisingly high rate of symptoms before diagnosis even in screen-detected patients, and a lower frequency of improvement of symptoms with GFD.

The impact of being diagnosed with CD through screening has been the subject of a number of prior studies, with varied conclusions. Some of these studies, in keeping with our results, demonstrated no differences between screen-detected and symptom-detected patients with regard to QOL. One Finnish study of adults and children used the PGWB and Short Form health survey (SF-36) questionnaires to evaluate 53 screen-detected and 44 symptom-detected CD patients, and found no significant QOL differences between these groups, or between CD patients and healthy controls.[23] Kinos et al[34] surveyed 43 screen-detected and 83 symptom-detected children at the time of diagnosis and 1 year later: no differences were found between the 2 groups in parents' estimation of their child's overall health, although no validated QOL instrument was used. Screen-detected CD adolescents were compared with nonceliac controls in another Swedish study carried out by Nordyke et al,[35] with no impairment found in health-related QOL as measured by the EQ-5D instrument.

A proportion of studies have, however, reported worse QOL in patients with symptom-detected CD compared with those detected by screening. A small study of 19 screen-detected and 21 symptom-detected patients found lower baseline PGWB scores in the symptom-detected cohort—a difference which persisted after 1 year on a GFD with similar rates of adherence.[30] Johnston et al[36] found that QOL in screen-detected CD patients mirrored healthy controls, but was significantly lower in symptom-detected CD patients across several SF-36 domains. Another study found screen-detected CD patients and nonceliac controls

TABLE 4. Multivariable Analysis; Screen-detected Status as a Covariate for Low CDQOL, Low PGWB, High CDAT, or Agreement With the Statement "I was Glad I was Diagnosed With CD"

	Low CDQOL (Lowest Quartile)		Low PGWB (Lowest Quartile)		High CDAT (CDAT $\geq$ 13)		"I was Glad I was Diagnosed With CD"	
Item	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Covariate								
Symptom detected	1		1		1		1	
Screen detected	1.15	0.36-3.72	0.91	0.30-2.70	1.20	0.52-2.70	0.34	0.15-0.77

CDAT indicates Celiac Disease Adherence Test; CDQOL, celiac disease-specific quality of life; CI, confidence interval; OR, odds ratio; PGWB, Psychological General Well-Being.

to be similar, in contrast to symptom-detected CD patients who scored lower on the SF-36 scale but were unchanged with regard to PGWB scores.[37]

The reason for these varied results regarding the relationship between screen detection and QOL are not entirely clear. Of note, there is significant heterogeneity among these studies with regard to the sample size, criteria for screening, and the timing of QOL assessment. Given that GFD is highly effective at improving the symptoms of CD, it is logical that differences between symptomatic CD and screen-detected CD patients may diminish with time from diagnosis if both groups are adherent to GFD. As such, prospective studies that assess QOL at the time of diagnosis or soon after might be more likely to detect a difference than cross-sectional study designs such as ours, where the duration on GFD ranged from 0 to 36 years and averaged 4 years. The general survey instruments used previously to quantify QOL may lack sensitivity in detecting differences that are relevant to patients with CD. With this in mind, we elected to use a CD-specific instrument, which to our knowledge has not been applied previously in this setting. This instrument is particularly applicable to this study as it was developed in the United States.

One argument against screening apparently asymptomatic patients for CD is that they may be less willing to adhere to a GFD, given that they may not be subject to the same consequences of dietary transgressions as symptomatic patients. The results of our work are consistent with multiple prior studies in refuting this hypothesis: patients who are diagnosed with CD through screening can be equally adherent to GFD as those who are symptom detected.[23,31,34,37,38] Although 2 prior studies found poorer adherence in screen-detected patients, both of these studies enrolled patients who were identified in mass population-based serologic screening programs rather than patients who were targeted for screening due to at-risk status.[24,39] This distinction is crucial, as at-risk patients frequently have family members already diagnosed with CD. These patients, as adults, voluntarily submit to testing, are aware of the consequences of diagnosis, have familiarity with GFD, and are more likely to adhere. Those diagnosed through population screening do not have this exposure.

A key finding of several prior studies, as well as ours, is that patients who are diagnosed with CD through screening are frequently symptomatic in retrospect, and find that their symptoms often improve with a GFD.[30,31,34] Although there may be a component of recall bias driving this finding, it also suggests that many undiagnosed CD patients are in fact chronically experiencing a subtle degree of health impairment that is subclinical and only recognized following initiation of GFD, which argues in favor of active efforts to diagnose more patients with CD. Indeed, screen-detected patients may in fact seek out screening because they are aware of symptoms, even though they identify themselves as screen detected.

Several limitations of the study are acknowledged. The surveyed sample may not reflect the overall celiac population. Those who attend support groups and respond to questionnaires may be more motivated to follow a GFD. Recruitment occurred at 1 tertiary-referral clinic, and patients were well educated and racially homogeneous, limiting generalizability. CD does, however, appear to be diagnosed more frequently in higher socioeconomic groups.[33,40,41] Screen-detected patients in this sample were mostly relatives of celiac patients, and may differ from patients diagnosed through population-wide screening measures. The female preponderence, although consistent with prior survey data in CD, limits generalization to men. Although all patients reported histologically confirmed CD, biopsy reports were not available for confirmation. The cross-sectional design only captures data at 1 time point, and may underestimate differences that occur closer to the time of diagnosis. Although our findings may not be widely applicable to other settings, they do represent an initial attempt to compare these groups in the United States, where limited data are available regarding screen-detected patients.

In conclusion, we found that screen-detected and symptom-detected CD patients do not differ with regard to QOL or disease adherence as measured by validated disease-specific instruments. A high proportion of both screen-detected and symptom-detected patients reported symptoms before diagnosis, which frequently improve with GFD. Adherence to GFD was excellent in both groups. The results of this study suggest that screening efforts do identify patients who are symptomatic in retrospect, and that diagnosis may therefore result in improved symptoms and QOL.

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