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ORIGINAL ARTICLE

The diagnostic challenges presented by patients with medically unexplained symptoms in general practice

JOSÉ M. AIARZAGUENA¹, GONZALO GRANDES², AGUSTÍN SALAZAR¹,
IDOIA GAMINDE³ & ÁLVARO SÁNCHEZ²

¹San Inazio Health Care Centre, ²Primary Care Research Unit, Osakidetza/Basque Health Service, Bilbao, and ³Health Development, Research and Education Service, Department of Health, Government of Navarra, Pamplona, Spain

Abstract

Objective. To describe the complexity of somatizing patients' symptomatology and the difficulties involved in the diagnostic process. **Design.** Cross-sectional study of patients with medically unexplained symptoms. **Setting.** Basque Health Service primary care centres in Bizkaia, Spain. **Subjects.** The study comprised 156 patients selected at random from a list of 468 patients who had presented, over the course of their lives, six or more medically unexplained somatic symptoms for females and four or more for males, identified retrospectively by their practitioners. **Main outcome measures.** Physicians interviewed these patients using the somatoform symptoms section of the Composite International Diagnostic Interview (CIDI), and the Primary Care Evaluation of Mental Disorders (PRIME-MD). The Medical Outcomes Survey Short Form 36 (SF-36) was filled in at home. Organic diseases whose diagnosis was established during the previous year were included in the study by consulting patients' medical records. **Results.** Patients were found to have a median of three medically explained and 12 medically unexplained symptoms. Mental disorders were found in 83% of cases, associated with other morbidity categories in 78%. The predictive value of symptoms was lower than 26% for diagnosing broad disease categories. **Conclusions.** These results depict an extremely difficult scenario for dichotomous diagnostic strategies aimed at classifying patients' symptoms as either organic or functional. Rather than struggling to choose one of these hypotheses, it is suggested that both of them should always be addressed concurrently.

Key Words: *Family physician, family practice, general practitioner, health-related quality of life, predictive value, primary healthcare, somatization, somatizing patients*

Patients with medically unexplained symptoms (MUS) are high-rate users of healthcare and often receive expensive, unnecessary tests and treatments [1,2]. General practitioners in particular have been criticized for inadequate recognition and management of these problems [3]. There are two main factors that cause GPs to feel frustration with regard to this situation. On the one hand, they find it difficult not to be sceptical about the seriousness of these patients' conditions, something which they need to do in order to be able to make diagnostic and therapeutic decisions. On the other hand, they feel that their main responsibility with regard to these patients is to diagnose any serious diseases which may be present and not to allow them to go unrecognized [4,5].

A wide variety of reasons have been put forward to explain this complex clinical scenario: doctors with poor psychosocial attitudes [6]; differences between patient/doctor expectations regarding treatment [7]; a lack of competence in treating mental health problems [8]; patients' tendencies to make reference to psychosocial topics [9]; and the use of a biomedical model, which artificially separates the body from the mind, making it hard to understand the interaction of biological, psychological, interpersonal, and medical factors in the predisposition, precipitation, and perpetuation of functional somatic symptoms [10]. However, there are very few studies describing the clinical characteristics of these patients and the difficult diagnostic process that doctors have to face [11–13].

Correspondence: Dr Gonzalo Grandes, Unidad de Investigación de Atención Primaria-Osakidetza, Luis Power 18, 4^a, E-48014 Bilbao, Bizkaia, Spain. E-mail: Gonzalo.Grandes@osakidetza.net

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The diagnostic challenge represented by patients with medically unexplained symptoms causes GPs to feel frustration and also fear that a physical disease might go unnoticed.

- In patients who somatize, symptoms with a biomedical explanation coexist with others lacking any such explanation, in a ratio of 1 to 4, and it is extremely difficult to attribute individual symptoms to either purely physical or psychiatric terms.
- Their symptoms have an extremely low predictive value, lower than 26%, for diagnosing broad disease categories.
- Rather than struggling to choose an organic or functional explanation for somatising symptoms, we suggest that both hypotheses should always be addressed concurrently.

With the aim of helping to understand the complexity involved in diagnosing somatizing patients, we analysed the clinical characteristics of somatizing patients who had taken part in a clinical trial, in order to describe the symptoms most frequently encountered in these patients, the predictive value of their symptoms, their comorbidity, and their health-related quality of life.

Material and methods

Secondary cross-sectional analysis describing the baseline characteristics of 156 somatizing patients included in a randomized controlled clinical trial in November 2000 was undertaken [14]. A total of 39 family physicians from 28 general practices within the Basque Health Service (Osakidetza) took part in the trial. In the Basque health service, each general practitioner is allocated a specific number of patients for whom he or she cares throughout their lives. Each citizen has a single general practitioner who provides his/her primary care continuously over time and who acts as a gatekeeper to the rest of the healthcare system.

Family physicians were requested to select retrospectively at least 12 eligible patients. Eligibility characteristics were: patients aged between 18 and 65 years who had presented over the course of their lives six or more medically unexplained somatic symptoms for females and four or more for males, at least one of which had continued to be present during the preceding year [15]. Using this method, 478 eligible patients were identified. Four somatizing patients per GP were selected randomly. Exclusion criteria included dementia, psychotic disorders,

drug dependence, bipolar disorder, eating disorder, malingering patients, and patients engaged in psychotherapy. Eligible patients were asked to participate in the study by their family physician. If any patient refused, he or she was replaced by another randomly selected patient, in order to obtain a study sample of 156 patients (four per physician). The study protocol was approved by the reference hospital's Clinical Research Ethics Committee and patients gave written informed consent.

Each doctor interviewed those of his or her patients that were included in the study, to record their symptoms and active health problems. In order to identify the symptoms that had been active during the previous year and those present throughout the patient's life, physicians interviewed these patients using the somatoform symptoms section of the Composite International Diagnostic Interview (CIDI) [16]. Mental disorders were detected using the Primary Care Evaluation of Mental Disorders (PRIME-MD) [17]. Functional syndromes like irritable bowel syndrome, chronic fatigue syndrome, or fibromyalgia were not considered as diagnoses. Ongoing treatment and health-related problems diagnosed over the previous 12 months were recorded by the general practitioner after reviewing patients' electronic medical records. Diagnoses were sorted into the Adjusted Clinical Groups (ACGs) for classifying patients [18] under five broad categories of physical morbidity: acute minor (e.g. otitis media acute), acute severe disease (e.g. accident), recurrent disease (e.g. allergy), chronic stable disease (e.g. diabetes mellitus), and chronic unstable disease (e.g. asthma). Comorbidity was calculated by adding up the number of previous collapsed diagnoses and mental disorder diagnoses present in each patient. Patients were interviewed at home in order to collect sociodemographic data (educational level and socioeconomic class) and to assess health-related quality of life using the Medical Outcomes Survey Short Form 36 (SF-36) [19]. Quality of life scores were compared with the scores of a population-based sample from the Basque Country, and with scores of diabetic patients and patients with chronic obstructive pulmonary disease (COPD) [20,21]. The predictive value of the following somatoform symptoms active during the previous year was evaluated: gastric pain, excess gases, chest pain, dyspnoea, palpitations, urinary frequency, and dysuria. First, patients reporting any of the selected symptoms were identified. Subsequently, two investigators reviewed the active medical diagnoses recorded by physicians for each of the patients with the selected symptoms. In order to link a symptom or group of symptoms to the diseases with which they might be related, the primary care diagnostic assistance guide of the

Spanish Family Medicine Society was used [22] and only those symptoms that were directly related to organs or systems were selected. The group of medical diagnoses related to the organ or system indicated by each symptom was used as the gold standard. Thus, investigators linked gastric pain and vomiting to all pathologies of the digestive system; dysuria and urinary frequency with urinary tract infections; precordial pain, dyspnoea and palpitations with either some kind of cardiopulmonary disease, musculoskeletal pain, or gastro-oesophageal disease. The positive predictive value was estimated by calculating the conditioned probability of being diagnosed with a specific group of related diseases, given the presence of the symptom. In order to provide information on the accuracy of these estimators, 95% confidence intervals were built into the

data description for the means and percentages, taking into account the clustered structure of the sample in the standard error calculations.

Results

Of the 156 somatizing patients selected for the study, 81% were women. This group was found to have a median of 15 active, somatic symptoms for the previous year; for 12 of these, a satisfactory medical explanation had not been found, with only three symptoms being medically explained and considered by the doctor to be the consequence of an organic process. The most common medically unexplained symptoms are presented in Table I. Patients attributed their symptoms entirely to organic disorders in one-third of cases, to psychological problems in

Table I. Characteristics of 156 somatizing patients in primary care.

	Total (n = 156)	Mental disorder	
		Yes (n = 129)	No (n = 27)
Age, years (SD)	46.9 (11.1)	46.4 (11.0)	49.4 (11.8)
Women, %	81.4 (74.3–88.5)	83.7 (76.75–90.69)	70.4 (49.5–91.3)
Patients who attribute symptoms entirely to physical causes, %	30.8 (23.4–38.2)	31.8 (23.58–39.98)	25.9 (6.55–45.31)
Average number of active symptoms in the last year			
Medically unexplained	11.8 (10.6–12.9)	12.1 (10.8–13.4)	10.2 (8.0–12.4)
Medically explained	2.8 (2.2–3.3)	2.8 (2.2–3.4)	2.6 (1.5–3.7)
The 10 most frequent medically unexplained symptoms, %			
Headache	64.1 (56.2–72.0)	60.5 (50.8–70.1)	59.3 (35.29–83.2)
Excess gases	61.5 (51.8–71.3)	65.1 (56.4–73.8)	59.3 (38.7–79.8)
Gastric pain	60.3 (52.1–68.0)	61.2 (50.3–72.2)	63.0 (45.4–80.5)
Back pain	55.8 (46.7–64.8)	54.3 (45.2–63.3)	63.9 (39.2–86.7)
Dyspnoea	53.2 (43.9–62.5)	55.8 (46.19–65.44)	40.7 (18.41–63.07)
Palpitations	52.6 (42.8–62.3)	54.3 (43.9–64.6)	44.4 (20.0–68.9)
Articular pain	50.6 (40.8–60.4)	50.39 (39.7–61.1)	51.8 (27.6–76.1)
Pain in the lower limbs	50.6 (40.8–60.4)	51.9 (40.8–63.1)	44.4 (18.9–70.0)
Paraesthesia/numbness	48.7 (41.1–56.3)	50.4 (42.4–58.4)	40.7 (14.2–67.2)
Chest pain	46.1 (38.1–54.2)	48.8 (40.2–57.4)	33.3 (10.7–55.9)
Physical morbidity categories, %			
Acute minor	43.6 (34.0–53.2)	43.4 (32.9–53.9)	44.4 (23.5–65.4)
Severe acute	36.5 (29.0–44.6)	35.7 (28.3–43.0)	40.7 (18.9–62.5)
Recurrent	45.5 (35.5–55.5)	45.7 (35.0–56.4)	44.4 (20.9–68.0)
Chronic stable	37.2 (27.5–46.8)	38.8 (28.8–48.7)	29.6 (10.0–49.2)
Chronic unstable	11.5 (5.7–17.4)	11.6 (5.4–17.8)	11.1 (0.0–24.2)
Mental disorders, %			
Depression	33.3 (24.9–41.8)	40.3 (30.5–50.1)	–
Anxiety	5.8 (1.84–9.7)	7.0 (2.24–11.71)	–
Anxiety and depression	42.9 (33.2–52.7)	51.9 (41.3–62.6)	–
Comorbidity ¹ , %			
One or more categories	97.4 (93.4–100)	100	85.2 (63.0–100)
Two or more categories	78.2 (69.8–86.6)	82.2 (74.7–89.6)	59.2 (34.3–84.2)
Three or more categories	53.2 (43.5–62.9)	58.9 (49.1–68.7)	25.9 (6.5–45.3)
Four or more categories	22.4 (15.1–29.8)	27.1 (18.2–36.1)	–
Five or more categories	5.8 (1.8–9.9)	7.0 (2.2–11.7)	–

Notes: Unless otherwise indicated, values are the mean (95% CI). ¹Calculated by adding up physical morbidity and mental health diagnoses.

Table II. Predictive positive value of some symptoms analysed individually and as clusters.

Symptoms	n (%; CI 95%)	Positive predictive value (PPV)	IC 95% PPV
Digestive system pathology			
Gastric pain	119 (76.3; 67.6–85.0)	18/119 (15.2%)	8.3%–22.0%
Vomiting	114 (73.1; 65.7–80.5)	2/12 (16.7%)	0%–41.4%
Gastric pain or vomiting	123 (78.8; 70.8–86.8)	18/123 (14.6%)	8.1%–21.2%
Cardiopulmonary disease, musculoskeletal pain or gastro-oesophageal disease			
Chest pain	80 (51.3; 43.8–58.7)	21/80 (26.2%)	16.4%–36.1%
Dyspnoea	94 (60.3; 51.8–68.7)	17/94 (18.1%)	10.2%–26.0%
Palpitations	92 (59.0; 49.3–68.6)	18/92 (19.6%)	11.3%–27.8%
Chest pain or Dyspnoea or Palpitations	125 (80.1; 73.4–86.9)	26/125 (20.8%)	13.6%–28.0%
Urinary tract infection			
Urinary frequency	48 (30.8; 22.9–38.7)	8/48 (16.7%)	5.7%–27.6%
Dysuria	31 (19.9; 13.3–26.5)	6/31 (19.3%)	4.6%–34.1%
Dysuria or urinary frequency	65 (41.7; 32.7–50.7)	11/65 (16.9%)	7.6%–26.3%

one-third, and to both types (organic and psychological) in the remaining third. We did not find any differences in morbidity or psychiatric diagnoses between these three categories.

All patients had been diagnosed by their physician with some biomedically explained active health problem during the previous year. These diseases were grouped into morbidity categories, listed below along with the percentage of patients who had displayed one or more diseases within each category: acute minor disease (44%), acute severe disease (36%), recurrent illness (45%), chronic stable disease (37%), and chronic unstable disease (11%). Mental disorder was present in 83% of patients, mainly anxiety and depression combined (see Table I). Regarding patients' comorbidity, at least two diagnostic categories were present in 78% of the 156 somatizing patients, at least three in 53%, at least four in 22%, and five categories were present in 6% of patients (see Table I).

Some of the most frequent somatic symptoms present during the previous year showed the following predictive values: 15% (18/123) of subjects with gastric pain or vomiting were diagnosed with some digestive system pathology; 17% (11/65) of subjects with dysuria and urinary frequency were diagnosed with urinary tract infection; and 21% (26/125) of patients with pain in the precordial region, dyspnoea, or palpitations were diagnosed with either some type of cardiopulmonary disease, musculoskeletal pain, or gastro-oesophageal disease (see Table II).

As shown in Figure 1, somatizing patients' quality of life scored two standard deviations below the population-based sample from our community, and was lower than diabetic patients and patients with chronic obstructive pulmonary disease.

Discussion

In somatizing patients, a limited number of symptoms with a biomedical explanation coexists with a large number of symptoms lacking any such explanation, in a ratio of 1 to 4. In 83% of cases, these are also accompanied by mental disorders, mainly anxiety and depression. These results are consistent with the literature [11–13].

The positive predictive values of these symptoms in the somatizing population are lower than the already low predictive values described for these symptoms in primary care. Klinkman et al. [23] found that 47% of patients who presented with chest pain in primary care were diagnosed with musculoskeletal pain, costochondritis and reflux oesophagitis and an additional 12% with coronary disease. However, in our study this symptom displayed a positive predictive value of 26% for all these diagnoses combined. In the case of dysuria, Medina-Bombardó et al. [24] found that 40% of women presenting urinary complaints had positive urinary culture. In our study, however, this symptom was associated with urinary infections in 20% of cases. For other symptoms, such as abdominal pain, our results were similar to the predictive values reported by Muris et al. [25], who found that 14.5% of patients with non-acute abdominal complaints were diagnosed as having organic disease. This low predictive value means that diagnostic hypotheses are rarely confirmed and, even given positive test results, a wide variety of further detection tests as well as diagnostic confirmation is required, which leads to the possibility of iatrogeny as well as increased cost. This has an impact on all of us and it is all too easy to collude with patients and their

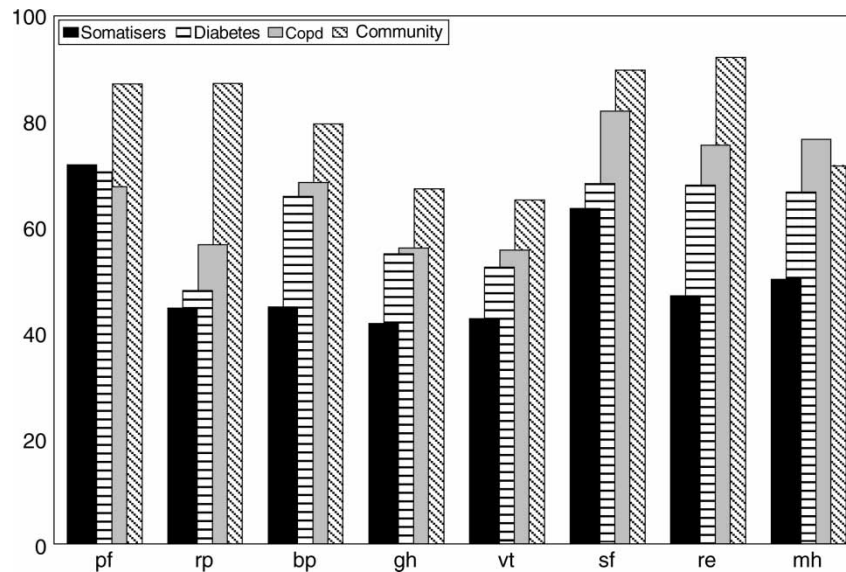


Figure 1. Health-related quality of life in somatizing patients compared with a population-based community sample, patients with diabetes mellitus, and patients with chronic obstructive pulmonary disease (COPD). Abbreviations: pf=physical functioning; rp=role-physical; bp=bodily pain; gh=general health; vt=vitality; sf=social functioning; re=role-emotional; and mh=mental health.

families in order to avoid leaving any 'organic' stone unturned [26].

GPs are used to considering clusters of symptoms and using contextual information to reach a diagnosis, usually classified in a dichotomous manner as serious versus non-serious, in an attempt to 'sort the wheat from the chaff' in a context where GPs have to decide whether a serious disease should be ruled out or not. [27] In MUS patients this strategy may not be useful for the following reasons: (i) ruling out a serious disease does not satisfy the patient, who wants to know what is wrong with him or her, not simply what is not wrong [28,29]; (ii) the 'chaff' is very important in MUS patients, as it reduces health-related quality of life two standard deviations below that of the reference population; and (iii) negative test results do not rule out the possibility that the physical disease in question may appear in the future; somatization is no protection against physical disease. We have to take into account the fact that somatization is a chronic condition, a way of life for certain patients, or a permanent characteristic of some individuals [30].

Somatizing patients therefore present a continuous flow of symptoms and, while they may herald a serious condition, the probability that this is the case (PPV) is very low. For this reason the current dichotomizing strategy in which GPs have been trained, which is a product of a biomedical model that focuses on the exclusion of physical disease, may lead to the perpetuation of the problem of diagnosing these patients. Kroenke et al. [31] reached a similar conclusion when studying common symptoms in ambulatory care; they found that 16% of

symptoms had an organic cause, 10% were considered psychological, whereas the aetiology of nearly three-quarters of the symptoms remained unknown, and they suggested that diagnostic strategies giving precedence to organic causes may be inadequate.

Given this situation, rather than struggling to choose either an organic or a functional explanation for somatizing symptoms we suggest a comprehensive diagnostic strategy to address both hypotheses concurrently. First, we explore the possibility of a hypothetical physical or psychiatric disease (a fear shared by both doctors and patients). Second, we assess the role of psychosocial factors in patients' complaints and explain in a physical, tangible way how psychosocial factors and the patients' way of dealing with life can generate homeostatic disorders, i.e. hormonal disturbances related to patients' symptoms. And finally, it is recognized that both previous hypotheses (physical or psychiatric disease vs. hormonal imbalance associated with psychosocial factors) interact in generating their symptoms, and therefore both have to be addressed concurrently. [14]

The validity of the results of this study is limited by the study design. These results are based on secondary analysis of the base-level data from a clinical trial, designed to evaluate the effectiveness of a new intervention, in which eligible patients were selected retrospectively. A prospective cohort study design would have been preferable. The present selection bias limits the generalizability of the results. The conclusions of the present study are particularly valid for the group of somatizing patients that create the most problems for doctors (i.e. those who readily

came to doctors' minds). However, the fact that a large number of somatizing patients were recruited, and these by 39 general practitioners from 28 Basque Health Service primary care centres, a service providing free healthcare to every citizen of the Basque Country, confers external validity to the study. Symptoms were identified by physicians interviewing patients with a validated instrument, the Composite International Diagnostic Interview (CIDI) [16], but physical diseases were identified retrospectively, which might reduce the value of the information with regard to the presence/absence of physical disease and its classification. While the large number of diagnostic tests carried out on these patients suggests that few diseases would have been overlooked, we do not have any data on the diagnostic process used by the doctors.

Conclusion

These results depict an extremely difficult scenario for dichotomous diagnostic strategies aimed at classifying patients' symptoms as either organic or functional. Rather than struggling to choose one of these hypotheses, we suggest that both of them should always be addressed concurrently.

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Ethical approval

Cruces Clinical Research Ethics Committee.

Conflicts of interest

None.

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