Original article

Impact of stable angina on health status and quality of life perception of currently treated patients. The BRIDGE 2 survey

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ABSTRACT

Objective: to explore 1) the perception of stable angina (SA) - impact on quality of life (QoL) and current condition related to SA; 2) SA burden - symptoms and frequency of anginal episodes; 3) impairment attributable to SA - limitations in daily activities and impact on work; 4) characteristics that might affect the patients’ perception.

Method: a proprietary questionnaire was administered on-line to SA patients selected using a purpose-built screening program from general population panels collaborating with IQVIA in Italy, Germany, Spain, and the UK. Exploratory analyses were performed: descriptive statistics on the total sample and different stratifications (gender, age class, time since diagnosis) were provided; we used Chi-square tests to compare subgroups.

Results: of more than 25,000 subjects who accessed the survey, 268 were eligible and completed the questionnaire: mean age was 61 years and women accounted for 30%. Despite being treated, about 40% of patients reported that SA impacted “completely” or “very much” their QoL, 10% rated their condition as “not good”, and 45.1% stated that they felt “Fair”. The majority of patients were still symptomatic and many of them perceived that SA had a major impact on their working life. Women, younger patients and those with a more recent diagnosis reported a worse self-assessment of their condition, QoL and symptom burden.

Conclusions: the results of our survey provide new insights on how patients with SA perceived their own health status and suggest that any patient with SA deserves a more detailed and accurate evaluation by their physicians.

1. Introduction

Stable Angina (SA) is a common condition in patients with coronary heart disease, with a prevalence of around 2–4% of the general population in western European countries. In patients with cardiovascular disease, angina is a condition that substantially affects quality of life (QoL) [1,2], which is negatively related to the frequency of anginal episodes [3,4]. Despite a number of effective pharmacological treatments and the success of interventional cardiology, SA remains a cause of significant disability and impaired QoL for many patients [5]. Since angina is difficult to assess objectively, clinical decisions are based on physician evaluated symptom burden [6]: unfortunately, there is often discordance between physician evaluation of the burden of the disease with regard to its severity and/or its impact on the quality of life of the patients [3,5,7,8]. The CADENCE study showed that, in a relevant number of cases, general practitioners (GPs) consider angina well controlled even in patients with frequent attacks (≥ 1/week or daily) [3]. In a cross-sectional observational study, Quintar found that in
43.3% of patients, angina symptoms were underestimated. Physicians reported significantly less anginal episodes compared to that reported by the patients; this led to significantly less treatment escalation, diagnostic testing, hospitalizations and revascularization compared with more accurately assessed patients [8]. These data suggest a poor concordance between the physician and the patient with regard to the perception of the impact of the symptoms, both of which can affect adversely the clinical management and the QoL of the patient. There are several factors which may influence the impact of the disease on patients by physicians. Recently, the BRIDGE study, which was the first part of this project, explored physicians’ perception of SA patients’ needs, the impact of SA on QoL, and SA management. BRIDGE has involved 659 doctors (cardiologists and GPs) who entered data from 1965 SA eligible patients. The results demonstrated that physicians’ awareness of the limitations in daily activities was greater for recently diagnosed patients compared with patients with a longer diagnosis, irrespective of age and Canadian Cardiovascular Society (CCS) angina class [6]. Although women generally presented a more severe form of angina than men, physicians did not perceive differences between the condition of the two genders, with possible undertreatment of female patients, who less frequently underwent angiography, percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery [6].

We conducted a multinational survey, directly interviewing the patients, which is the BRIDGE 2: in line with the BRIDGE [6], and as completion of the previous study, we aimed to explore 1) the perception of SA (impact on QoL and current condition related to SA); 2) SA burden (symptoms and frequency of anginal episodes); 3) impairment attributable to SA (limitations in daily activities and impact on work). Also, we investigated whether the characteristics of the patients (age, gender, time since diagnosis, and previous treatment with PCI) may have an influence on all these aspects.

2. Methods

2.1. Study patients

The present study was an organized, prospective patient survey conducted in four European countries (Italy, Germany, Spain, United Kingdom [UK]), using computer-assisted web interviewing (CAWI), via a 30-min on-line quantitative proprietary questionnaire. The survey was conducted by IQVIA from March to May 2019. IQVIA is among the largest providers of solutions and information for the pharmaceutical and healthcare sector. IQVIA has a wide experience in reporting the pharmaceutical market phenomena with validated data comparable worldwide, and a long experience in real world data studies and in patient projects [9]. Respondents were part of global market research panels collaborating with IQVIA, and were invited by email to take part in the CAWI survey. Patients were eligible if they met inclusion criteria, investigated through a quantitative structured screening questionnaire designed to select patients with a diagnosis of angina currently under treatment. They had to be older than 18, and meet one of the following criteria to be enrolled in the core part of the study:

a) diagnosis and current treatment of SA
b) diagnosis of acute myocardial infarction (AMI) and/or diagnosis of coronary or heart disease/ischemia, with current or past SA symptoms and with current treatment for SA.

(see Appendix A of Supplementary Materials for the patient screener with a detailed description of inclusion criteria). If the patients reported having been diagnosed with either of the above conditions, they were asked to specify which definition best described their situation, according to the CCS. The CCS scoring system, based on the degree of limitation that angina symptoms bring to daily activities, includes four classes, from 1 (less severe) to 4 (most severe) [10]. Fifteen patients who reported to be in line with the definition corresponding to the CCS class 4 were not included in the final analyses as we did within the BRIDGE study [6].

2.2. Questionnaire

Patients fulfilling inclusion criteria were enrolled in the survey and requested to complete the specific questionnaire. This was sub-divided into different sections. The first included collection of demographic data, SA therapy, working status, previous treatment with PCI, and questions about the main activities that the patient was able to do (by him/herself, with someone’s help or with complete assistance), or activities he/she did not do, or avoided. The second section focused on the patient experience with the condition, in particular: their perception about their condition (“Not good”, “Fair”, “Good”, “Very good”), how much the SA impacted on QoL (5 = “completely”, 4 = very much, 3 = somewhat, 2 = only a little, 1 = not at all, with a half-point scoring system implemented to capture all possible answers) and on the working activities, the limitations of daily activities induced by the symptoms. The third section explored the symptoms and the frequency of the attacks. Finally, the last part of the questionnaire was dedicated to the relationship of the patient with the physician (see Appendix B of Supplementary Materials for the full questionnaire).

According to the Code of Conduct of the European Pharmaceutical Market Research Association (EphMRA), the survey did not require Clinical Research Ethics Committee or Independent Review Board approval [11].

2.3. Statistical analysis

The survey collected anonymized data, analyzed in an aggregated form through descriptive statistics. Data are presented descriptively as mean and standard deviation (SD) for quantitative variables, or frequencies and percentages for qualitative variables. All patient data were analyzed for the overall study population, at European Level, and for different groups, stratified by age (<65 years, ≥65 years), gender, duration of diagnosis (≤2 years, >2 years) and previous PCI (yes, no), to explore possible differences in disease perception and experience. Because the presence of depression could have an impact on QoL and health perception, it was decided to perform a sensitivity analysis by excluding patients who reported having been diagnosed with depression (Supplementary Materials, Appendix E). To compare subgroups, Chi-square tests were used, and p-values <0.05 were considered statistically significant. Analyses were performed using SAS software, Version 9.4.

3. Results

In contrast to clinical studies, the number of invitations for web-based market research is much larger than the required sample size, because of the low response rate [6]. In our case 25,890 individuals were interviewed through the screening questionnaire; 322 (1.2%) refused to participate in the survey and did not send the disclaimer agreement; one responder was less than 18 years old; 24,026 (92.8%) did not report a diagnosis of stable angina, AMI, coronary or heart disease/ischaemia; 527 (2.0%) had been diagnosed with AMI or coronary or heart disease/ischaemia but had no symptoms of angina; 731 patients (2.8%) had received a diagnosis of angina but were not on treatment or did not remember. Fifteen patients (0.1%), who classified themselves according to the definition corresponding to the CCS class 4, completed the questionnaire but they were not included in the analysis. Data from 268 subjects were included in the final analysis (47 in Germany, 70 in Spain, 56 in Italy and 95 in UK) (Fig. 1).
3.1. Patients’ characteristics and differences among groups

Seventy per cent of the participants were men, with a mean age of 60.8 years and with a slight predominance of patients younger than 65 years (57.5%). 106 patients classified themselves as CCS class 1 (39.6%), 108 as CCS class 2 (40.3%), and 54 (20.1%) as CCS class 3; about 30% of patients had a recent diagnosis (<2 years before the survey) (Table 1). The severity of SA was greater in women compared to men. Although younger than men, women declared a higher CCS score; the patients with a less recent diagnosis (≥2 years) were older, more frequently men, and had a less severe symptom status in terms of CCS class (see Appendix C of Supplementary Materials). There were 144 patients who previously underwent PCI representing 53.8% of the participants (Table 1). Within the final Cohort, the most common diagnosis was angina alone (43.7%), but more than 14% of the patients reported having been diagnosed for as having all three conditions as per the inclusion criteria (angina, AMI, and coronary heart disease/ischaemia) (data not shown). A majority of the patients (67.5%) were treated for SA with monotherapy, 23.9% with two drugs, and only 8.6% with more than two therapies. The most frequently reported comorbidities were hypertension (54.9%), dyslipidemia (39.2%), and diabetes (28.4%). Although most patients were not smokers or had quit smoking, 17.9% of them reported that they were still smokers at the time of the survey. The majority of patients were overweight or obese (BMI ≥ 25 kg/m²), with this trend being slightly more pronounced among men (Table 1).

3.2. SA perception

3.2.1. QoL

Overall, about 40% of patients reported that SA impacted “completely” or “very much” their QoL (points 3.5–5). With regard to subgroups of interest, the proportion of patients who reported only a minor impact on their QoL was higher among older patients: 16.7% of them stated that angina had little or no impact (points 1–1.5), compared to 8.4% for the younger group. However, differences were not statistically significant. Focusing on results by gender, it should be noted that 15.4% of men declared that angina had “little” or “no impact” (points 1–1.5) on their QoL, which is significantly greater than the 3.8% observed among women. In addition, the proportion of patients who declared to be “not at all” or “only a little” impacted by the condition was significantly greater among patients with a longer history of the disease (14.5% vs. 5.3%). No differences in terms of impact on QoL emerged based on previous PCI presence or absence (Fig. 2). Similar trends were found in the sensitivity analysis (see Appendix E of Supplementary Materials, Fig. 2s).

3.2.2. Current SA related condition

10.1% of patients rated their condition as being “not good”, and 45.1% stated to feel “Fair” (Fig. 3). Looking at results from stratified analyses, older patients reported a more positive perception of the disease: more than 15% of them defined their condition as being “very good”, compared to the 6.5% observed among younger patients, these differences being statistically significant. The proportion of patients who defined their condition as “fair” or “not good” was 70% among women, and 50% among men, while less than 4% of women reported their condition as being “very good”, compared with the 13% observed among men; these differences being statistically significant. A longer history of angina seemed to induce a more positive perception of the condition, although results from this analysis were not statistically significant. Finally, no differences emerged with regard to disease perception between patients with or without previous PCI. Similar trends were found in the sensitivity analysis (see Appendix E of Supplementary Materials, Fig. 3s).
3.3. SA burden

3.3.1. SA symptoms

Overall, chest pain/tightness, fatigue, and shortness of breath were the most frequently reported effort-related-symptoms, with rates of 74.6%, 72%, and 67.5%, respectively. In the stratified analyses, it emerged that the proportion of patients who reported having atypical symptoms was significantly greater among women. In particular, we found a statistically significant greater prevalence of arm pain, fatigue, shortness of breath and headache than those observed among men (Fig. 4). Similar trends were found in the sensitivity analysis (see Appendix E of Supplementary Materials, Fig. 4s).

3.3.2. Number of angina attacks

Overall, 52.9% of the patients reported at least one angina attack per month. A statistically significant difference in the distribution of the number of attacks was observed depending on gender, while no differences were observed depending on age, history of disease and presence or absence of a previous PCI. In particular, the proportion of patients who reported at least one attack per month was 63.9% and 48.2% for women and men, respectively (Fig. 5). Similar trends were found in the sensitivity analysis (see Appendix E of Supplementary Materials, Fig. 5s).

3.4. Impairment attributable to SA

3.4.1. Limitations in daily activities

Overall, the daily activity for which patients perceived the highest level of limitation was playing sports, with almost 70% of them avoiding or not performing such activity at all. Stratified analyses revealed that the proportions of patients who declared avoiding or not playing sports at all were significantly greater among older patients and those with a longer history of the disease (data not shown). About half of the patients declared avoiding doing housework, or requiring help to perform this activity; the stratified analyses revealed a statistically significant difference between women and men: although a lower proportion of women declared avoiding or not doing housework at all, at the same time, a higher proportion of them needed some help or full assistance for this activity. Among all daily activities, climbing stairs was the one for which we observed a higher proportion of patients performing this activity unaided. No statistically significant differences emerged from the stratified analysis, except for the comparison between older and younger patients: interestingly among younger subjects we found a significantly lower proportion of patients who declared climbing stairs without assistance. 32.6% of females avoid or need assistance in climbing stairs compared to 22.3% of males but it was not statistically significant (Fig. 6). Similar trends were found in the sensitivity analysis (see Appendix E of Supplementary Materials, Fig. 6s).

3.4.2. Impact on working activities

Table 2 reports the working status of the subjects. The majority of them were retired or unemployed at the time of the survey, while about 40% were currently working (part-time, full-time or self-employed) (Table 2).

Patients declared a very high limitation on work activities: only 25.1% of them reported that the disease had no impact on their work, while more than one third had to change job, reduce the amount of work time, or stop working completely (Fig. 7). In addition, among patients at work, about 65% declared the requirement to take sick leave because of the condition, with 24% of them reporting sick leave more than once a month (data not shown).

4. Discussion

To our knowledge, this is the first survey which extensively explores the patients' perception of their SA, its burden as reported by the patients, and patients' impairment attributable to SA. The study has also evaluated the factors that contribute to all these aspects, with particular attention given to the influence that age, gender, time since diagnosis and previous treatment with PCI may have. The results have shown that women, younger patients and patients with a shorter time from diagnosis reported a worse perception of SA, along with more frequent and severe symptoms. Also, a very high limitation on working activities has been reported by the patients overall. Patients included in our survey had a mean age of 61 years, which is lower compared with the mean age reported by previous studies [3,6–8,12]; this is probably because the selection of patients was made through web-based interviews. Our patients stated a slightly more severe condition in terms of CCS class compared with that observed in the BRIDGE study (20% CCS 3 vs 14%), and reported a longer time from diagnosis (time since diagnosis >10 years 29.9% and 4.3% respectively) [6]. The longer history of disease observed in the present study may be due to the fact that in surveys where the selection of patients...
was performed by doctors, they probably tend to report data from subjects with a more recent diagnosis.

The severity of SA was greater in women compared to men: although younger than men, women reported a greater CCS score, a greater frequency of symptoms, and had a greater number of attacks. Consistently, most did not have a positive perception of their condition, and the percentage of women reporting a significant impact on QoL was greater than among men. Our results are consistent with those found in other studies [3,13–15]. The CADENCE survey recorded a greater frequency of the angina attacks (≥ 1/week) in women, and a direct relationship between the number of attacks and QoL, assessed with a specific validated questionnaire [3,13]; also Dryer reported that women suffered significantly more angina attacks, with a poorer QoL as assessed by the Seattle Angina Questionnaire (SAQ) [14]; a higher impact of the disease on women is possibly caused by less aggressive pharmacological therapy and less revascularization observed in female patients [15,16]. In addition, women with coronary heart disease are less likely to achieve therapeutic targets in the management of risk factors such as dyslipidemia, diabetes and obesity, and tend to be less physically active [17–19].

![Fig. 2. Impact of “angina or chest pain” on patients’ quality of life, for overall population and subgroups by age, gender, time since diagnosis and previous treatment with PCI. *Statistically significant difference between the groups (p-value < 0.05).](image)

![Fig. 3. Definition of the current condition of angina or chest pain for the overall population and for subgroups stratified by age, gender, time since diagnosis and previous treatment with PCI. *Statistically significant difference between the groups (p-value < 0.05).](image)
The survey found a greater impact of SA in younger patients, who, when compared with older ones, reported more symptoms and anginal episodes, as well as a worse perception of their condition, with a higher impact of SA on QoL. The greater impairment of QoL perceived by younger patients may be partly due to more severe angina. Also, coping with limitations imposed by the condition may be more difficult for younger people, who generally have a more active life. It has been previously reported that the elderly may be better able to control their emotions by minimizing negative emotions and maximizing positive emotions more effectively than younger individuals [13]. These findings are similar to those recorded in other surveys [3,13,20]; in particular, in the CADENCE study, elderly and very old patients reported a better QoL and more frequently achieved treatment targets than younger patients, despite similar disease characteristics and greater physical limitations [13].

Patients with a more remote diagnosis were older, more frequently men, and had less severe symptoms with respect to their self-assessed CCS class than patients with a more recent diagnosis. Consistently, among patients with a more recent diagnosis higher proportions of symptoms were observed, almost half of them declared that the SA impacted “completely” or “very much” on their QoL and, only one-third of them defined their condition as “good” or “very good”. Also in this case, the greater severity of the SA could partially account for these results, but we can also speculate that patients with a longer history of illness become resigned to their SA and limit and/or avoid some of their daily activities because they tend to restrict their comfort zone.

Fig. 4. Symptoms occurring during activities such as climbing stairs, walking, dressing, showering or running in the overall population and stratified by gender. *Statistically significant differences between the groups (p-value < 0.05).

Fig. 5. Number of attacks per month reported by the overall population and by subgroups stratified by age, gender, time since diagnosis and previous treatment with PCI. *Statistically significant differences between the groups (p-value < 0.05).
In addition, it is worth remembering that within Maslow’s Hierarchy of Needs, for human beings the feelings of safety rank second, after physiological requirements (food, water, shelter) [21]. This powerful need is a strong reason for reducing or avoiding activities and situations which might lead to symptoms or SA attacks and a reduction of the comfort zone.

Our data confirm the high impact of SA on working life: many patients had to quit working or to reduce working time; in addition, among patients who were still working, the disease results in a significant amount of sick leave. This phenomenon, as reported by previous studies, can be caused by a variety of factors, such as patient characteristics, type of job, and the severity of the symptoms [22,23].

Overall health-related QoL is defined as a multidimensional model integrating biological and psychological aspects [24,25], and patient’s perception of their own condition is an important independent contributor to QoL in angina [26], and generally in chronic diseases [27]. These factors must be taken into consideration as they are not always concordant with the perception of the physicians, and therefore can impact on treatment and clinical outcomes. This is particularly true since angina cannot be objectively assessed, and appropriate clinical

<table>
<thead>
<tr>
<th>Working status</th>
<th>Total (N = 268)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-time employee</td>
<td>57 (21.27%)</td>
</tr>
<tr>
<td>Part-time employee</td>
<td>25 (9.33%)</td>
</tr>
<tr>
<td>Self-employed</td>
<td>19 (7.09%)</td>
</tr>
<tr>
<td>Retired</td>
<td>142 (52.99%)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>20 (7.46%)</td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>5 (1.87%)</td>
</tr>
</tbody>
</table>

Fig. 6. Limitations in main daily activities, overall population and groups stratified by age, gender, time since diagnosis and previous treatment with PCI. *Statistically significant differences between the groups (p-value < 0.05).

Table 2
SA patients working status.

![Image] Fig. 7. Impact of angina/chest pain on working activity.
decisions are largely guided by a physician’s recognition and judgment of
symptoms burden [6].

Another interesting finding of this survey is that, although all pa-
tients were on treatment for SA, many of them were still symptomatic, 40% declared to be impacted “completely” or “very much” by the
disease, and half of them judged their general condition as being “not
good”. This underlines the needs for better understanding and better
management of the patient, particularly in women and in younger and
more recently diagnosed patients.

Our study has some limitations. First, the selection of patients was
possibly influenced by the ability to access the web and the familiarity
with web navigation, which is observed more often in younger subjects
[20]. This factor could have led to an unusual SA population in terms of
age, working status and condition severity. Second, our direct recruit-
ment through panels, and not through a selection made by physicians,
did not allow specific and precise clinical details to be obtained.

Nevertheless, our survey was not made to characterize the condition
epidemiologically but to give an insight into patients’ perception of
their angina. In addition, the younger age of the population and the
slightly greater severity of the symptoms observed do not seem to have
influenced the results. In fact, the consistency of our data with similar
studies support our results as reliable and representative of the real-life
population over different European countries. Moreover, the direct re-
cruitment of SA patients through panels, can be considered as an ad-

cantage, in as much as the survey avoided some potential biases such as
physicians recruiting patients that they see more and patients they
believe to be more cooperative. Also, the adoption of an ad-hoc
 screener which implies rigorous inclusion criteria, allowed completely
objective patient selection. The method used permitted exploration of
issues such as workers vs non-workers and younger vs older patients,
which are not usually evaluated studies of SA.

5. Conclusions

This study, and the previously conducted BRIDGE study [6] have
been complementary projects related to angina management, which have
allowed the exploration of different perspectives from the physi-
cian and the patient.

The results of our survey provide new insights on how patients suffering from SA perceive their own health status, revealing that
women, younger patients and patients with a more recent diagnosis
report a worse self-assessment of their condition, their QoL and
symptom burdens. Thus, our survey supports the results of the BRIDGE
study [6], and extend its findings showing that SA patients develop a
form of tolerance to their condition over time, limiting their activities,
concealing the extent of their disability and therefore restricting their
comfort zone [21]. For the above reasons our data would suggest that
any patient with SA deserves a more detailed and accurate evaluation by
their physicians.

Declaration of Competing Interest

AJM, GA, AJC, PC, RD and JLS have acted as consultant to Menarini
Group, PC has disclosed that he received speaker fees from Menarini
Group, and VP has disclosed that she is an employee of IQVIA.

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Supplementary materials

Supplementary material associated with this article can be found in

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