Validation in Spain of the Quality of Life questionnaire PROSQOLI in patients with advanced prostate cancer

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Abstract
Objectives: Validation of the PROSQOLI questionnaire adapted to Spanish, pursing an instrument to evaluate, in the common clinical practice, the quality of life in patients with locally advanced or disseminated prostate cancer in our country.

Material and Methods: A cross-sectional prospective study was designed in 750 patients (150 centers) with disseminated or locally advanced prostate cancer (TNM criterion) who came to the scheduled check-up. Socio-demographic and clinical data of the participants were collected. The subjects filled out the PROSQOLI and EQ-5D questionnaires. The analysis included 561 cases that met the selection criteria. The psychometric characteristics (feasibility, validity and reliability) of the adapted PROSQOLI questionnaire were studied.

Results: Mean age was 73.63 (7.59) years. A total of 72.01\% of the participants had locally advanced disease. In 28.16\%, the primary treatment was radiotherapy, in 12.30\% it was prostatectomy. A total of 83.48\% received hormone treatment. The mean for each scale of the PROSQOLI questionnaire varied from 68.86 to 74.51. The percentage of no response was less than 3\% for each scale. The percentage of subjects with minimum score in any scale was negligible, and the maximum score did not surpass 5\%. Mean time to fill out the questionnaire was 109.42 (101.00) seconds. Cronbach’s $\alpha$ coefficient was 0.937 and the total item correlation was superior to 0.7 for all the items. Correlations with the EQ-5D questionnaire were moderate. Scores on the questionnaire were associated to all the parameters studied related to the disease.

Conclusions: The adapted questionnaire has adequate psychometric properties for its use in research and in the clinical practice.

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PALABRAS CLAVE
Cuestionario; Calidad de vida; Cáncer prostático

Validación en España del cuestionario de calidad de vida PROSQOLI en pacientes con cáncer de próstata avanzado

Resumen
Objetivos: Validación del cuestionario PROSQOLI adaptado al castellano, persiguiendo la obtención de un instrumento para evaluar, en la práctica clínica habitual, la calidad de vida en pacientes con cáncer de próstata localmente avanzado o disemorado en nuestro país.

Material y Métodos: Se diseñó un estudio transversal prospectivo en 750 pacientes (150 centros) con cáncer de próstata diseminado o localmente avanzado (criterio TNM) que acudían a revisión programada. Se recogieron datos socio-demográficos y clínicos de los participantes. Éstos cumplimentaron los cuestionarios PROSQOLI y EQ-5D. El análisis incluyó 561 casos que cumplieron criterios de selección. Se estudiaron las características psicométricas (factibilidad, validez y fiabilidad) del cuestionario PROSQOLI adaptado.

Resultados: La edad media fue de 73,63 (7,59) años. El 72,01% de los participantes sufría enfermedad localmente avanzada; en el 28,16% el tratamiento primario fue radioterapia y en el 12,30% prostatectomía. El 83,48% recibía tratamiento hormonal. La media para cada escala del cuestionario PROSQOLI varió entre 68,86 y 74,51. El porcentaje de no respuesta fue inferior al 3% para cada escala. El porcentaje de sujetos con puntuación mínima en alguna escala fue despreciable, y el de puntuación máxima no sobrepasó el 5%. El tiempo medio de cumplimentación fue 109,42 (101,00) segundos. El coeficiente α-Cronbach fue 0,937 y la correlación item-total superior a 0,7 para todos los ítems. Las correlaciones con el cuestionario EQ-5D fueron moderadas. Las puntuaciones en el cuestionario se asociaron con todos los parámetros estudiados relacionados con la enfermedad.

Conclusiones: el cuestionario adaptado presentó adecuadas propiedades psicométricas para su uso tanto en investigación como en la práctica clínica.

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Introduction
Prostate cancer (PC) is one of the most important medical problems affecting the male population. It is a disease that affects mostly older men, and it is thus a major threat in developed countries, where it accounts for 15% of cancers in men.¹ In the European Union, it is the most common cancer in men and it kills 0.03% men per year.² In Spain, in the last two decades, there has been a marked increase in the incidence of PC, especially in subjects under 65 years, due to improvement of screening of the disease, accompanied by a decrease in mortality.³

The treatments applied in this type of cancer and the symptoms of the disease have a significant impact on the quality of life of the patient for years.⁴-⁷ The treatment for PC can cause sexual dysfunction, infertility, and incontinence. The fact that the disease is detected in younger subjects and in many cases in the asymptomatic disease state makes the quality of life an important factor in assessing the most effective way to deal with the management of the disease. Moreover, in advanced patients, the treatment has a palliative purpose aimed at improving the duration and/or the quality of survival, the improvement in quality of life being the most realistic target. Thus, the assessment of health-related quality of life (HRQoL) of patients with locally advanced or disseminated PC is particularly relevant as a patient-based measure of the impact of the disease and the treatments.

Hormone treatment is that recommended as therapy in metastatic disease, although it is also used as adjuvant therapy in locally advanced disease.⁸

For correct analysis of the impact of the disease, the extent of HRQoL in men with PC requires the study of specific domains, not included in assessment tools of overall quality of life.⁸ There are different questionnaires to assess HRQoL in patients with PC.⁹-¹⁴ Of the instruments developed or validated in our country, the EPIC and EORTC QLQ-PR25 questionnaires include items to assess the impact of hormone treatment.¹⁵,¹⁶ These instruments, with 50 and 46 items, respectively, may be too long for use in clinical practice. Alternatively, shorter instruments aimed at specific groups of patients within the disease have been developed beyond our borders. The Prostate Cancer Specific Quality of Life Instrument (PROSQOLI), developed and validated for the assessment of HRQoL in patients with hormone-resistant and symptomatic disseminated PC,¹²,¹⁷,¹⁸ consists of 10 questions that assess the physical limitations in the perceived health status of the patient (pain, physical activity, fatigue, appetite, urinary problems, and constipation), their emotional state, their ability to enjoy social relations and overall health. It is structured in 9 linear analog self-assessment scales (LASA) to quantify symptoms, function, and general health status, and a 6-point adjectival ordinal scale that assesses the current intensity of pain taken from the McGill Pain Questionnaire.¹⁹ With respect to other questionnaires evaluated, the adjectival scale of intensity of pain highlighted the survival time based on the patient’s¹²,¹⁷,¹⁸ as univariate predictor. The reliable measure of the variable pain is particularly important in patients with disseminated or advanced disease, as it is a determining factor in their HRQoL, which can mask the effect of other disorders associated with the treatment. The psychometric
PROSQOLI

Please, place in each of the following lines a vertical mark (I) in the place that best describes your status in the last 24 hours. For example, you could describe how you feel about the weather putting a vertical mark on the line below:

BAD WEATHER
I hate it
I love it

1. PAIN
Extremely strong
No pain at all

2. PHYSICAL ACTIVITY
Completely unable to move
I can move my body normally

3. TIREDNESS
Extremely tired
Not tired at all

4. APPETITE
No appetite at all
Normal appetite

5. CONSTIPATION
I have no bowel movements
I have normal bowel movements

6. URINARY PROBLEMS
The worst imaginable
No problem at all

7. ENJOYMENT OF TIME WITH FRIENDS AND FAMILY
Severely limited by disease or treatment
Not limited at all by disease or treatment

8. MOOD
Very depressed
Not depressed at all

9. OVERALL STATUS
(How do you feel?)
Extremely ill
I feel good

10. Intensity of current pain (ICP)
Please, circle the number that best represents how much pain you felt, in general, in the last 24 hours.

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td>Mild pain</td>
<td>Annoying pain</td>
<td>Overwhelming pain</td>
<td>Horrible pain</td>
<td>Excruciating pain</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1 PROSQOLI questionnaire adapted to Spanish.

properties of this questionnaire and the brevity thereof have enabled their use as an outcome measure in both comparative studies of the effectiveness of treatments and in pharmacoeconomic evaluation studies thereof.

In this study, the validation of the PROSQOLI questionnaire adapted to Spanish (see section 'Material and methods') is presented in order to obtain a specific instrument for the assessment of the HRQoL in patients with locally advanced or disseminated symptomatic PC, suitable for use in daily clinical practice in our country.

Material and methods

We designed a cross-sectional study in a sample of 750 patients with disseminated symptomatic or locally advanced PC of 150 research centers.

The eligible patients had to be adults, have a diagnosis of disseminated or locally advanced PC (TNM classification), attend a scheduled follow-up, be trained to understand the study and voluntarily give informed consent.

In a data collection logbook, the basic clinical information that made it possible to know the pre-treatment and current health status of the patients was obtained. They completed the adapted version of the PROSQOLI questionnaire, presented in Fig. 1, along with the EQ-5D Health Questionnaire.

The version of the PROSQOLI questionnaire submitted to validation comes from a cultural adaptation to Spanish previously performed by means of translation into Spanish of the original questionnaire, back translation (approved by the author), evaluation of the translated version by a panel of 6 experts and one of 30 patients, analysis of the results of the panels and resulting change in the
questionnaire approved by the panel of experts. Like the original questionnaire, the adapted questionnaire consists of nine linear analog self-assessment scales. The score of these scales ranges from 0 (worse state) to 100 (best state). The last item is a 6-point adjectival ordinal scale, taken from the McGill Pain Questionnaire,\(^{19}\) which assesses the current intensity of pain from lower to higher. The score of this item has been adapted to the rest of the questionnaire, scoring from 0 to 100 from better condition to worse. The questionnaire also includes a table for the assessment of daily intake of analgesics, which enables the calculation of an index of analgesia, 1 being given to the standard dose of non-narcotic analgesics and 2 to the standard dose of narcotic analgesics.

**Statistical analysis**

The analysis database consisted of data of 561 participants of the 737 received, after limiting the analysis to those participants who, according to the registered TNM classification, had disseminated (M1) or locally advanced (T3–T4) PC.

In all the exploratory and analytical statistical tests, a 0.05 significance level (\(\alpha\)) was used. The analyses were performed for the number of cases that responded to each particular item.

We performed a description of the sample with respect to socio-demographic and clinical variables. We studied the psychometric characteristics of the PROSQOLI questionnaire adapted to Spanish:

1. **Feasibility.** We evaluated the percentage of non-response for each item, the percentage of patients who did not respond to any item, time of completion, effect ceiling/floor for each item and for the overall questionnaire.

2. **Validity.** Validity of content was assessed by means of item-total correlation analysis; the convergent validity by means of an analysis of the correlation between the questionnaire under exam and the EQ-5D questionnaire; the discriminant validity from the analysis of the...
association of PROSQOLI questionnaire scores with clinical variables relating to the patient’s health status (type of cancer, PSA values before primary treatment, hormone treatment, and primary treatment).

3. **Reliability**. Internal consistency was assessed using Cronbach’s $\alpha$ coefficient.

The analyses were conducted using the statistical package Stata 10.

## Results

The analyzed sample consisted of 561 participants who had locally advanced or disseminated PC. The mean age was 73.63 (7.59) years, with a minimum age of 44 and maximum of 93.

Table 1 shows the description of the sample in clinical parameters. The predominant type of cancer was the locally advanced one, and most of the sample had not received prostatectomy or radiotherapy as primary treatment. 83.48% of the participants received hormone treatment (39.13% of the patients in the prostatectomy group, 73.42% in the radiotherapy group, and 97.58% of the group that had received no treatment).

Table 2 presents the descriptions for the scores in each item of the PROSQOLI questionnaire and for the summary scores of the EQ-5D questionnaire. 55% of the participants had an analgesic-score zero, i.e., they did not report analgesic consumption in the last 24h.

In order to assess the feasibility of the questionnaire, an analysis of the percentage of non-response in each item was carried out, as well as the percentage of participants who did not respond to some items and the floor and ceiling effects. As it can be seen in Table 2, 1.60% of the participants did not respond to any item in the questionnaire, including those in the 10.52% of the participants who left some of them blank. The percentage of subjects with minimum score is negligible, while the percentage of subjects with maximum score ranges between 3 and 5% for LASA scales and reached 33.40% in the IDA.

The mean time of filling in was 109.42 (101.00) s. 50% of the participants completed the questionnaire in less than 80 seconds and only 25% of the patients needed more than two minutes.

We analyzed the construct validity using the item-total correlation. As shown in Table 3, this correlation is greater than 0.7 for each item of the questionnaire.

For the analysis of convergent validity, the correlation between the scores in the PROSQOLI questionnaire and the scores in the EQ-5D generic questionnaire was studied. Table 4 shows that the correlation of all the items of the PROSQOLI with the summary scores of the EQ-5D questionnaire is moderate or moderate-high. It also shows the correlation between each item of both questionnaires, the correlations between related items appearing in bold.

In order to analyze the discriminant validity, the mean difference in each score of the questionnaire was studied for groups defined according to relevant clinical variables such as type of cancer, primary treatment, current hormone therapy, and analgesia (analgesic intake in the last 24h or not). We also studied the correlation with the PSA parameter before the treatment. Table 5 shows that the association between all the scales of the questionnaire and the variables considered is significant.

As for reliability, the Cronbach’s $\alpha$ coefficient of the questionnaire as a whole is 0.937 (mean inter-item covariance: 267.69).

## Discussion

This paper presents the results of the study to validate the PROSQOLI questionnaire adapted to Spanish in a sample of patients with locally advanced or disseminated PC.

According to the trend noted in other studies,1,7 in the sample, the existence of a large group of subjects who had not received prostatectomy or radiotherapy as primary treatment is reflected, of whom almost all were being treated with hormone treatment.

The mean score in the scales of the questionnaire is higher than in the original validation, except for the scales ‘urinary problems’, ‘use of time in the company of family and friends’ and ‘mood’, being lower for the first two and almost equal for the last one. The best score in most scales can be explained by the characteristics inherent to the samples, the original validation of the sample being

<table>
<thead>
<tr>
<th>No.</th>
<th>Item-total</th>
<th>Mean inter-item covariance</th>
<th>$\alpha$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item1 - pain</td>
<td>549</td>
<td>0.799</td>
<td>262.50</td>
</tr>
<tr>
<td>Item2 - physical activity</td>
<td>549</td>
<td>0.838</td>
<td>261.14</td>
</tr>
<tr>
<td>Item3 - tiredness</td>
<td>551</td>
<td>0.858</td>
<td>257.05</td>
</tr>
<tr>
<td>Item4 - apetite</td>
<td>552</td>
<td>0.820</td>
<td>264.24</td>
</tr>
<tr>
<td>Item5 - constipation</td>
<td>547</td>
<td>0.749</td>
<td>266.80</td>
</tr>
<tr>
<td>Item6 - urinary problems</td>
<td>547</td>
<td>0.787</td>
<td>266.47</td>
</tr>
<tr>
<td>Item7 - use of time with family and friends</td>
<td>551</td>
<td>0.899</td>
<td>256.88</td>
</tr>
<tr>
<td>Item8 - mood</td>
<td>549</td>
<td>0.852</td>
<td>257.29</td>
</tr>
<tr>
<td>Item9 - general state of health</td>
<td>547</td>
<td>0.893</td>
<td>255.21</td>
</tr>
<tr>
<td>IDA</td>
<td>524</td>
<td>0.704</td>
<td>328.63</td>
</tr>
</tbody>
</table>
Validation in Spain of the quality of life questionnaire PROSQOLI in advanced prostate cancer

Table 4 Correlation (Spearman) between the PROSQOLI questionnaire items and the EQ-5D questionnaire.

<table>
<thead>
<tr>
<th>PROSQOLI 1</th>
<th>PROSQOLI 2</th>
<th>PROSQOLI 3</th>
<th>PROSQOLI 4</th>
<th>PROSQOLI 5</th>
<th>PROSQOLI 6</th>
<th>PROSQOLI 7</th>
<th>PROSQOLI 8</th>
<th>PROSQOLI 9</th>
<th>PROSQOLI 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D item 1</td>
<td>0.43</td>
<td>0.45</td>
<td>0.47</td>
<td>0.48</td>
<td>0.50</td>
<td>0.53</td>
<td>0.55</td>
<td>0.56</td>
<td>0.57</td>
</tr>
<tr>
<td>EQ-5D item 2</td>
<td>0.39</td>
<td>0.41</td>
<td>0.43</td>
<td>0.45</td>
<td>0.47</td>
<td>0.49</td>
<td>0.50</td>
<td>0.51</td>
<td>0.52</td>
</tr>
<tr>
<td>EQ-5D item 3</td>
<td>0.44</td>
<td>0.46</td>
<td>0.48</td>
<td>0.49</td>
<td>0.50</td>
<td>0.52</td>
<td>0.53</td>
<td>0.54</td>
<td>0.55</td>
</tr>
<tr>
<td>EQ-5D item 4</td>
<td>0.45</td>
<td>0.47</td>
<td>0.49</td>
<td>0.50</td>
<td>0.52</td>
<td>0.53</td>
<td>0.54</td>
<td>0.55</td>
<td>0.56</td>
</tr>
<tr>
<td>EQ-5D item 5</td>
<td>0.46</td>
<td>0.48</td>
<td>0.50</td>
<td>0.51</td>
<td>0.52</td>
<td>0.53</td>
<td>0.54</td>
<td>0.55</td>
<td>0.56</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>0.47</td>
<td>0.49</td>
<td>0.51</td>
<td>0.52</td>
<td>0.53</td>
<td>0.54</td>
<td>0.55</td>
<td>0.56</td>
<td>0.57</td>
</tr>
<tr>
<td>AVS</td>
<td>0.48</td>
<td>0.50</td>
<td>0.52</td>
<td>0.53</td>
<td>0.54</td>
<td>0.55</td>
<td>0.56</td>
<td>0.57</td>
<td>0.58</td>
</tr>
</tbody>
</table>

The associations between related items are marked in bold.

made of patients with metastatic disease and in our sample mostly by patients with localized disease. The results for the sub-sample with disseminated cancer are actually much closer to those described in the original validation. It should be noted that the scales 'urinary problems' and 'use of time in the company of family and friends' are not equivalent to those presented in the original validation (passing urine and family-marriage relations), as the Spanish adaptation has been made on a later version of the questionnaire provided by the author.

The questionnaire has adequate feasibility. The percentages of non-response were low, so no difficulties were identified in the compression or filling in of the questionnaire. The mean filling in time was low enough to allow for implementation in clinical practice. The floor and ceiling effects for all scales were equally low. The IDA item, with 5 response options, has 33% of the subjects with maximum score in the sense of minimal pain. This correlates with the high percentage of subjects, more than half of the participants, who reported not having required analgesia in the last 12 h.

As for the validity of the questionnaire, the degree of correlation with the EQ-5D questionnaire is moderate, indicating good convergent validity. The highest correlations are obtained for the general condition, as it is expected, the EQ-5D questionnaire being a generic quality of life questionnaire. Regarding discriminant validity, the scores show association with the clinical variables considered. As it was expected, the means in the score in all scales of the questionnaire are higher for lower-impact groups, according to the type of cancer and the consumption of analgesics. On the other hand, the correlation with pretreatment PSA is negative, indicating that for a worse initial state (higher PSA values), worse scores in the scales are obtained. In our sample, better scores for the patients who have undergone prostatectomy than for those who have not are also found. Therefore, a greater impact on urinary function for prostatectomy patients with respect to those treated with radiotherapy described in some studies is not observed. It should be borne in mind that in the radiotherapy group, 11% of the patients having received brachytherapy, treatment of which it has been described to have more impact on urinary function than prostatectomy, are included. On the other hand, the fact that the patients with prostatectomy have better HRQoL might be correlated with the presence of hormone treatment, since in the prostatectomy group, only a minority received this type of treatment, whereas in the radiotherapy group, they were the majority, and almost all in the 'none' group.

The questionnaire as a whole has a high α Cronbach coefficient value, as it is expected in a specific assessment questionnaire, in line and even higher than that recorded in the validations of those that assess HRQoL for pathology available in Spanish. Also, the item-total correlation ranged from 0.70 to 0.90 for each item in the questionnaire. All these are indicative of a high internal consistency and, hence, of a high reliability thereof.

As it has been shown, the instrument has good psychometric properties that, along with the characteristics of brevity and specificity inherent to the questionnaire itself, make it a useful tool for the assessment of HRQoL in
Table 5  Mean differences in the questionnaire score (*) or association (**) for the variables considered.

<table>
<thead>
<tr>
<th>Type of cancer*</th>
<th>PSA**</th>
<th>Primary treatment*</th>
<th>Hormone therapy*</th>
<th>Analgesia*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Rho p</td>
<td>Prostatectomy</td>
<td>Radiotherapy</td>
</tr>
<tr>
<td>Locally advanced</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disseminated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item1 - pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Locally advanced</td>
<td>77.98</td>
<td>65.78 &lt;0 0.0101</td>
<td>79.54 (24.05)</td>
<td>78.41 (21.87)</td>
</tr>
<tr>
<td>Disseminated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item2 - physical activity</td>
<td>76.89</td>
<td>67.48 &lt;0 0.0101</td>
<td>82.69 (19.17)</td>
<td>78.99 (20.17)</td>
</tr>
<tr>
<td>Item3 - tiredness</td>
<td>71.44</td>
<td>62.29 &lt;0 0.0101</td>
<td>77.94 (20.03)</td>
<td>71.94 (20.04)</td>
</tr>
<tr>
<td>Item4 - apetite</td>
<td>76.78</td>
<td>68.57 &lt;0 0.0101</td>
<td>82.37 (20.70)</td>
<td>76.30 (19.95)</td>
</tr>
<tr>
<td>Item5 - constipation</td>
<td>73.09</td>
<td>64.25 &lt;0 0.0101</td>
<td>77.55 (22.94)</td>
<td>70.66 (24.12)</td>
</tr>
<tr>
<td>Item6 - urinary problems</td>
<td>70.80</td>
<td>63.84 &lt;0 0.0101</td>
<td>77.62 (21.32)</td>
<td>71.10 (21.18)</td>
</tr>
<tr>
<td>Item7 - use of time with family and friends</td>
<td>76.48</td>
<td>65.48 &lt;0 0.0101</td>
<td>81.90 (18.82)</td>
<td>77.12 (19.32)</td>
</tr>
<tr>
<td>Item8 - mood</td>
<td>72.78</td>
<td>64.40 &lt;0 0.0101</td>
<td>78.45 (23.67)</td>
<td>73.10 (22.27)</td>
</tr>
<tr>
<td>Item9 - general state of health</td>
<td>72.93</td>
<td>64.75 &lt;0 0.0101</td>
<td>77.31 (22.52)</td>
<td>72.88 (21.95)</td>
</tr>
</tbody>
</table>

* Mann–Whitney.
** Spearman.
patients with advanced PC, both in research and in clinical practice.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgements

I appreciate the cooperation of all the urologists who participated in the PROSQOLI study, for providing the data necessary for its performance, and I thank the IPSEN PHARMA Inc. laboratories, whose collaboration has made this study possible.

References