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The Vespid Allergy Quality of Life Questionnaire - cultural adaptation and translation to Portuguese

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KEY WORDS

Quality of Life; Hymenoptera allergy; Venom immunotherapy; Cross-cultural translation; Vespid allergy

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Summary

A cross-cultural translation of the Vespid Allergy Quality of Life Questionnaire (VQLQ) to the Portuguese population (VQLQ-P) was performed, assessing its applicability in wasp and in non-beekeeper bee venom allergic patients. Additionally, we evaluated a Visual Analogue Scale (VAS) to estimate hymenoptera allergy interference with daily life. **Methods.** Cross-cultural translation was performed according to recommendations. The final VQLQ-P version, the Expectation of Outcome questionnaire (EoQ), EQ-5D and VAS were applied to wasp ($n = 19$) and non-beekeeper bee venom allergic patients ($n = 30$). **Results.** VQLQ-P significantly correlated with EoQ, ($r = 0.76$, $p < 0.01$), EQ-5D (usual activities and anxiety / depression dimensions) and VAS, with a good internal consistency (Cronbach $\alpha = 0.88$) in wasp allergic individuals. VQLQ-P and EoQ correlation was also high ($r = 0.67$, $p < 0.01$) in bee allergy. **Conclusion.** The VQLQ-P is a valuable tool to evaluate quality of life impairment in Portuguese hymenoptera venom allergic individuals.

Background

Health-Related Quality of Life (HRQoL) and the psychological burden of allergic diseases has been increasingly studied (1). The use of patient-reported outcomes in the assessment of allergic diseases is currently recommended, both in clinical studies and in daily practice, as they provide a better understanding of the patient subjective assessment of his/her health condition and they estimate the effects of new interventions from the patient's perspective (1). Allergic diseases, such as asthma (2), rhinitis (3) and particularly food allergy (4), have a significant burden on quality of life and are associated with relevant direct, indirect, and also intangible costs (5). Hymenoptera venom allergy is a rare, but potentially life-threatening disease (6), and therefore,

the fear of a re-sting and new systemic reactions may have a profound impact on HRQoL.

The potential life threatening systemic reactions to insect stings are estimated to occur in only 0.3 to 0.4% of children and 3% of adults; so the true impact on health status and the negative effects on the emotional, social and sometimes professional functioning might be underestimated (6,7). Even those individuals that are on immunotherapy for venom allergy still present long-lasting debilitating beliefs and psychological impact of a threatening systemic reaction, independent of the years they were under immunotherapy (8). Studying HRQoL in these patients will allow a better understanding of the true burden of insect venom allergy according to the severity of the reaction,

social limitation, psychological well-being, fear, anxiety and uncertainty associated with this disease (8). The first published tool to measure HRQoL in adults with allergy to wasp venom was the Vespid Allergy Quality of Life Questionnaire (VQLQ) (7). This easy to use, validated instrument, showed an impairment of quality of life in yellow jacket allergic patients especially due to emotional distress (7). Furthermore, it showed a clinical important improvement in quality of life with venom immunotherapy (9). The main limitation of this instrument is that it may be inappropriate for beekeepers or their relatives (7) because of their frequent exposure and higher sting rate. Also, it is not validated in non-beekeeper patients with bee venom allergy and in patients with allergy to *Polistes* species. However, it is possible that this instrument is suitable for use in these populations. At the moment there is no questionnaire assessing quality of life in subjects with diagnosed or suspected hymenoptera allergy in the Portuguese population. Our primary aims were to perform a cross-cultural translation of the VQLQ to Portuguese and to assess its applicability in wasp venom and in non-beekeeper bee venom allergic patients. Our secondary aim was to assess the use of a Visual Analogue Scale to estimate hymenoptera allergy interference with daily life.

Methods

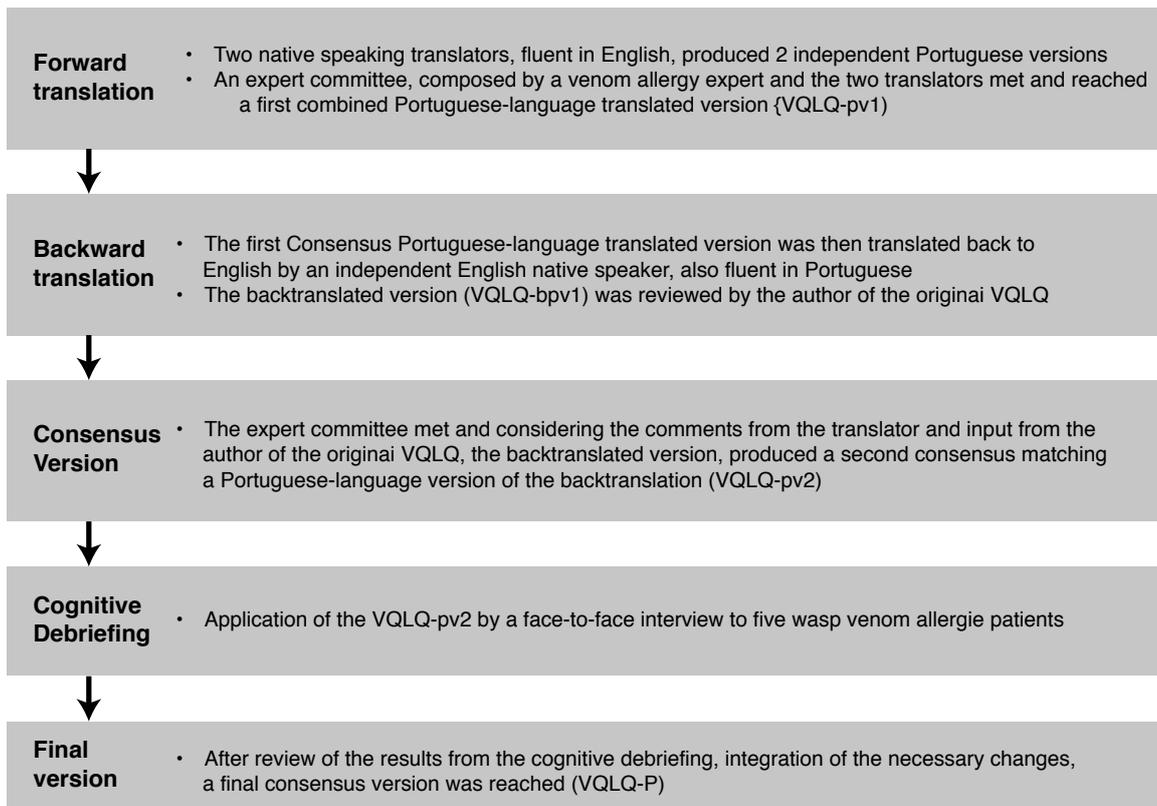
Cross-cultural translation

The cross-cultural translation of the VQLQ to Portuguese was performed, after author's permission, by forward and backward translation of the original English questionnaire and patient testing, according to published recommendations (1). The procedures are described in **figure 1**. During cognitive debriefing, the participants were informed that they should report the acceptability, understandability and clarity of the questionnaire and all comments were recorded by the investigators. After review of the results of the cognitive debriefing and integration of the necessary changes, the expert committee reached a final version, VQLQ-P.

Participants and study design

Participants were selected from two sources: 1) patients that were followed in the Allergy and Clinical Immunology Department of the São João Hospital in Porto due to hymenoptera venom allergy suspicion until December 2013; 2) individuals

Figure 1 - Cross cultural translation procedure.



with hymenoptera sting history who had specific IgE measurements to wasp or bee in the records of the Immunology Lab of the same hospital, from 2008 to 2011. All individuals with ≥ 18 years that had confirmed hymenoptera venom allergy to wasp or bee (history of hymenoptera sting systemic reaction and positive IgE or skin testing to the suspected hymenoptera) were included.

A structured survey was sent by mail to the homes of all eligible individuals; it included: demographic clinical data, type of reaction and symptoms, types of treatments and their related costs, as well as the VQLQ-P, EQ-5D, the Expectations of Outcome questionnaire (EoQ), and a Visual Analogue Scale (VAS) rating the interference of hymenoptera allergy in daily life. The survey was then returned by letter or in the next follow-up visit. In addition to the information obtained in the survey, all clinical records were reviewed to evaluate if the participants had diagnostic criteria of hymenoptera allergy, to assess hymenoptera sting reaction characteristics and reported beekeeper's activity. After analysis, the patients that met the inclusion criteria were selected. Despite being previously validated only in wasp venom allergic patients, the questionnaire was also sent to honey bee venom allergic patients, since it could be possibly used in non-beekeepers allergic to bee venom (7). Patients who were beekeepers, had beekeepers in their families or did not return the questionnaires were excluded from the analysis.

The participant selection flow chart is described in **figure 2**. The survey was returned by 80 patients (answer rate of 58%). A total of 49 individuals (19 with wasp venom and 30 with bee venom allergy) were included in the analysis. The characteristics of the included participants are described in **table 1**. There were no sig-

Figure 2 - Flowchart of the study participants. (VAS-visual analogue scale; EoQ-expectation of outcome questionnaire).

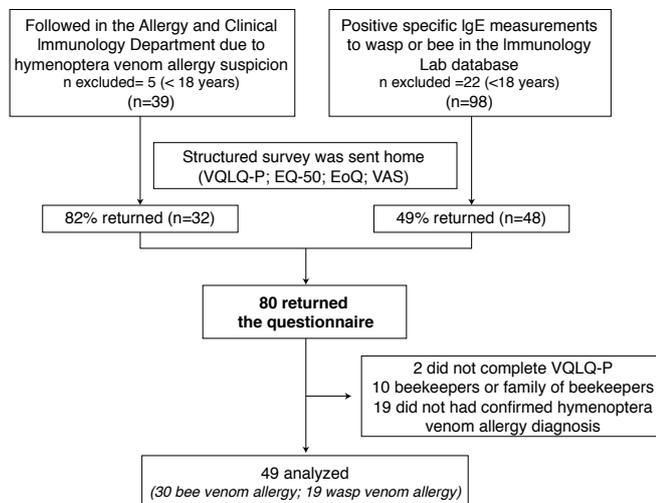


Table 1 - Demographic and clinical characteristics of the studied population.

	Participants (n = 49)
Age, years, median [IQR]	47 [38;56]
Gender, female	21 (43)
School education	
≤ 4 years	12 (25)
≥ 5 to 9 years	14 (29)
> 9 to ≤ 12 years	16 (33)
> 12 years	7 (14)
Confirmed hymenoptera allergy	
Bee	30 (61)
Wasp	19 (39)
Total IgE, UI/L, median [IQR]	90.0 [39.3; 148.3]
Wasp sIgE, kU/L, median [IQR]	0.9 [0.4;6.6]
Bee sIgE, kU/L, median [IQR]	2.1 [0.4;10.4]
Atopy	9 (18)
Asthma	6 (12)
Rhinitis	12 (25)
Cardiac disease	2 (4)
Severity of the systemic reaction (Müller)	
Grade I	7 (14)
Grade II	8 (16)
Grade III	18 (37)
Grade IV	16 (33)
Under venom Immunotherapy	32 (65)
Bee	20 (62)
Wasp	12 (38)

Results expressed as n (%), except if otherwise specified. IQR: interquartile range; sIgE: specific IgE

nificant differences between individuals that answered and those not returning the survey (**Online supplementary table 1**).

Instruments

The translated version of VQLQ-P (**Online supplementary file 1**) was used to measure HRQoL in wasp and non-beekeeper bee venom allergic individuals. The VQLQ-P has 14 questions. Each question is rated from 1 to 7 (1 the lowest and 7 the highest quality of life score). The scores are added and divided by the

number of items, excluding five questions (10 to 14) that have the option “does not apply” and are not counted.

Expectation of Outcome questionnaire (EoQ) (**Online supplementary file 2**) was used for comparison and validation purposes (7). This tool was previously used in the development of VQLQ as, in a patient who had sting anaphylaxis, the expected outcome of future stings interferes with quality of life and might be an important target for intervention. This questionnaire includes 2 questions with a 7-point scale in which patients are asked to indicate their expectation regarding the outcome of a future sting. A visual analogue scale was added to score the level of hymenoptera allergy interference in daily life, questioning “Do you think your insect allergy interferes with your daily life?” with a score ranging from 0 (no interference) to 10 (maximal interference). The EQ-5D, validated for the Portuguese population (10-12), is a health-related quality of life questionnaire. It comprises five dimensions (mobility, self-care, usual activities, pain / discomfort, anxiety / depression) with three levels each. It is able to define 243 different health states. It also includes a VAS reporting health-related quality of life, from zero (the worst health condition) to 100 (the best health condition). The index was calculated using the Portuguese population-based predicted preference weights for the 243 EQ-5D health states (11).

Statistical analysis

All data analyses were performed using SPSS® version 20.0 for Windows (IBM SPSS, Chicago, IL, USA). Categorical variables were described using absolute frequencies and proportions and compared using Chi-square or Fisher’s exact tests. Continuous variables were described using medians with interquartile range (IQR) and compared using the Mann-Whitney test (non-normal distribution of the included variables). To assess the internal consistency, the reliability coefficient Cronbach’s alpha was used. To test construct validity, bivariate Spearman correlations between VQLQ-P individual items and the mean of all items was determined using EoQ (individual as well as mean) and EQ-5D (individual dimensions, index and general health state VAS) as comparators. To evaluate the potential applicability of the VAS use to estimate hymenoptera allergy interference in daily life, spearman correlations were performed with VQLQ-P individual and total items, EoQ and EQ-5D parameters. To evaluate differences between the correlation coefficients of wasp and bee venom allergic individuals Fisher’ Z transformation test was applied. A p-value of < 0.05 was considered statistically significant.

Results

Cross-cultural translation of VQLQ-P

During the translation and back-translation procedure, doubts and corrections were raised due to slight differences in wording

and different meaning of the statements. The following items were questioned: “I am moderately frightened or scared”; “check certain places for stinging insects”; “Do you feel limited in your activities...”; “How often do you become frightened, because of your allergy, when you are stung by an insect”, different interpretations and the consensus version are specified in **Online supplementary table 2**. At all times, if comprehensibility was not affected, the approximation with the original version was preferred. During the phase of acquisition of author’s approval no questions or corrections were raised.

After reaching the consensus version, 5 participants were interviewed for cognitive debriefing. They had a mean age of 38 years, 3 were males, and all had wasp venom allergy. The following question presented some difficulties in interpretation by two participants: “How often do you, because of your allergy, check certain places for stinging insects (yellow jackets, hornets, and wasps)?”. Participants enquired if the question reported all stinging insects or specific species of wasps. As they avoided all stinging insects, it was suggested to simplify the statement. Therefore, in the final reconciliation phase, the expert committee agreed to simplify the examples to wasp and introduce the term bee, as participants could not distinguish a bee from a wasp at first sight. No more issues were reported or changes suggested by the participants of the cognitive debriefing. The final version of VQLQ-P is presented in **Online supplementary file 1**.

Internal consistency of the VQLQ-P

The Cronbach α of the 14 items was 0.85 for those with confirmed hymenoptera allergy, and higher for those with wasp venom allergy (0.88) than for bee venom allergic patients (0.83).

External consistency of the VQLQ-P

The Spearman correlations between VQLQ-P items and the expectation of outcomes are shown in **table 2**. The correlation coefficient (r) between the total score of the VQLQ-P and the mean of the 2 questions from the EoQ was 0.71, $p < 0.01$. The correlation remained significant when analyzing the individuals that were on venom immunotherapy (0.74, $p = 0.01$). In patients with a wasp venom allergy the correlation was higher (0.76, $p < 0.01$) compared to the bee venom allergic patients (0.67, $p < 0.01$). However, there was no significant difference between these correlations ($z = 0.58$, $p = 0.56$).

The global mean score of VQLQ-P was significantly correlated with EQ-5D index ($r = -0.34$, $p < 0.05$) and with the usual activities ($r = 0.48$, $p < 0.01$) and the anxiety / depression ($r = 0.49$, $p < 0.01$) dimensions of the same questionnaire. No significant correlations were found with EQ-5D mobility ($r = 0.11$), self-care ($r = 0.22$) or pain / discomfort ($r = 0.21$) dimensions. When considering only those with wasp venom al-

lergy the results were similar, however stronger correlations were found (**table 3**). No significant correlation was seen between the VAS reporting health-related state included in the EQ-5D and the VQLQ-P mean score ($r = -0.20$, $p = 0.29$).

Regarding the VAS assessing interference of hymenoptera allergy in patient's daily life it showed a significant correlation with the VQLQ-P mean score ($r = 0.68$, $p < 0.01$), as demonstrated in **figure 3** and with specific questions of the questionnaire (**ta-**

Table 2 - External Validity of VQLQ-P questionnaire in patients with confirmed hymenoptera venom allergy diagnosis ($n = 49$) and correlation with VAS assessing interference of hymenoptera allergy in patient's daily life. Spearman correlation coefficients between individual items. and the mean score (1-14) of VQLQ-P and the Expectation of Outcome (questions 1,2 and mean score) and VAS are presented.

VQLQ-P item	Expectation of Outcome Questionnaire item			VAS
	1	2	Mean score of 1 and 2	
1	0.664 ¹	0.392 ¹	0.514 ¹	0.642 ¹
2	0.571 ¹	0.397 ²	0.474 ¹	0.615 ¹
3	0.360 ²	0.388 ²	0.417 ²	0.300
4	0.692 ¹	0.497 ²	0.608 ¹	0.480 ²
5	0.502 ¹	0.456 ¹	0.485 ¹	0.466 ¹
6	0.452 ¹	0.279	0.384 ¹	0.314
7	0.665 ¹	0.565 ¹	0.640 ¹	0.713 ¹
8	0.679 ¹	0.512 ¹	0.613 ¹	0.588 ¹
9	0.705 ¹	0.530 ¹	0.638 ¹	0.599 ¹
10	0.260	0.102	0.150	0.156
11	0.049	0.057	0.053	0.117
12	0.489 ¹	0.294	0.419 ²	0.534 ¹
13	0.500 ¹	0.431 ¹	0.525 ¹	0.407 ²
14	0.410 ²	0.289	0.348	0.437 ²
Mean (1-14)	0.661 ¹	0.645 ¹	0.708 ¹	0.620 ¹
Wasp venom allergic participants ($n = 19$)	Mean (1-14)	0.638 ¹	0.712 ¹	0.758 ¹
Bee venom allergic participants ($n = 30$)	Mean (1-14)	0.667 ¹	0.603 ¹	0.669 ¹

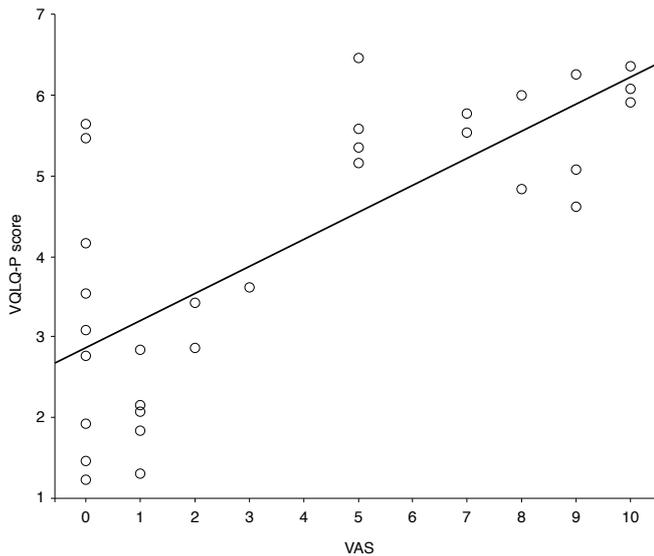
¹ $p < 0.01$; ² $p < 0.05$

Table 3 - External Validity of VQLQ-P questionnaire: Spearman correlation coefficients between the mean VQLQ-P score and EQ-5D dimensions and Index.

Mean VQLQ-P (1-14)	EQ-5D dimensions					EQ-5D Index
	mobility	self-care	usual activities	pain / discomfort	anxiety / depression	
Total ($n = 49$)	0.117	0.228	0.482 ¹	0.210	0.494 ¹	- 0.335 ²
Wasp venom allergy ($n = 19$)	0.237	0.344	0.553 ¹	0.445	0.561 ¹	- 0.512 ²
Bee venom allergy ($n = 30$)	0.000	0.000	0.415 ²	0.034	0.412 ²	- 0.198

¹ $p < 0.05$; ² $p < 0.01$

Figure 3 - Correlation between the Visual Analogue Scale assessing hymenoptera allergy interference with daily life and VQLQ-P mean score ($r = 0.68$, $p < 0.01$).



ble 2). The results from the VAS also correlated with each of the EoQ specific questions ($r = 0.64$ and $r = 0.56$ for questions 1 and 2, respectively; $p < 0.01$) and the mean EoQ score ($r = 0.62$, $p < 0.01$). No significant correlation was found between this VAS and the one assessing global health-related state from EQ-5D ($r = -0.12$, $p = 0.610$), but a mild correlation was noticed with the activity and anxiety dimensions ($r = 0.42$, $r = 0.41$, $p = 0.05$; respectively).

When evaluating the mean VQLQ-P there were no differences between the grades of reaction to the hymenoptera sting, genders or being on venom-specific immunotherapy.

Discussion

The translated and culturally adapted Portuguese version of the Vespid Allergy Quality of Life Questionnaire showed a good cross-sectional correlation with the Expectation of Outcome questionnaire as well as EQ-5D, a health-related quality of life measure instrument. In the non-beekeeper bee venom-allergic patients a good correlation was also seen. The applied VAS presented a good correlation with the VQLQ-P and EoQ. This translated version of the Vespid Allergy Quality of Life Questionnaire and the VAS evaluating the hymenoptera allergy interference with daily life appear to be two easy tools to evaluate quality of life impairment in Portuguese hymenoptera venom allergic individuals. However, a longitudinal evaluation of their applicability is needed in non-beekeeper allergic patients.

This is the first tool translated into Portuguese to evaluate quality of life in wasp venom allergic individuals. The procedure of translation and cultural adaptation followed the recommendations of the GA2LEN guidelines (1). Another strength of our study is that the translated questionnaire was compared with other quality of life measurements, namely with the widely used health-related quality of life measurement, the EQ-5D, the Expectation of Outcome questionnaire, previously used in the development and validation of the original VQLQ, and also with VAS. In line with previous studies that suggested the VQLQ could be suitable for bee venom allergic individuals (7), we also evaluated allergic individuals that were not beekeepers and did not have relatives with beekeeping activities. Although the questionnaire was not validated to this specific group, it also showed good correlation with other quality of life outcome measurements.

Our study has some limitations, namely a small sample size. Due to its wide recruitment strategy, including all individuals followed in our Hymenoptera Allergy Unit and also those who had a past positive IgE to wasp or bee venom, we had a low response rate (58%). Furthermore, as only those with a confirmed diagnosis were included, the number of selected participants was even smaller. However, a strong and significant correlation was still found. A visual analogue scale was also used to evaluate the interference of hymenoptera allergy in daily life and, despite not being previously validated, it showed a good correlation with the VQLQ-P and EoQ. The cross-sectional design of this study did not allow to establish if this tool can measure a change in quality of life with an intervention, namely venom immunotherapy (VIT). Nonetheless, the original questionnaire had previously measured a clinically important improvement in health-related quality of life with VIT (9). Therefore, it is likely that VQLQ-P may also be used to measure VIT outcomes in Portuguese patients. When evaluating the correlation between each of the questions and the EoQ, there were some items that presented non-significant or significant mild correlations, namely those related to vigilance in places where individuals might be in contact with wasps or bees. This could be due to the small sample size which lacked the power to adequately evaluate these correlations. Another possible explanation, previously reported in the literature (7), is that the level of vigilance might not be so significant in individuals living in urban environments, leading to weaker correlations in these items, when comparing with those that live in rural places. However, in our study no data is available on the area of residence and we could not test this hypothesis. Furthermore, individuals with hymenoptera venom allergy might intentionally avoid places where the probability of contact with wasps or bees is higher, therefore choosing vacations, hobbies and places where they feel they do not need to be so alert. The environment interaction with stress and anxiety is particularly

addressed in VQLQ, however, for precise characterization, comparative studies with different environmental settings and populations may be needed, as previously suggested (13).

The Vespid Allergy Quality of Life Questionnaire was originally developed in Dutch (7) and latter translated and validated in English (7), German (13), Polish (14) and Spanish (15). All the cross cultural translated versions showed a good internal consistency, as our Portuguese version. We did not find a significant correlation with age, grade of reaction or VIT. Conflicting results have been seen for gender, with some studies reporting a stronger impact in quality of life in women versus men (16) and others reporting otherwise (15). Another study found a stronger correlation with the severity of reaction, in which those with a severe anaphylaxis had greater impairment in quality of life (14). Our study showed a strong positive correlation (0.8) between the mean score of VQLQ-P and the mean EoQ, which was similar to the German and Dutch versions (0.7), but higher than the Spanish version (0.5). This may be explained by the inclusion of individuals with allergic reactions to *Apis*, *Vespula* and *Polistes* in the Spanish study (15). Nevertheless, we also found a good correlation between these tools in non-beekeeper bee venom allergic individuals. A good correlation was reported with other measures of QoL, namely with the WHOQOL-BREF, used for comparison in the German validation study, particularly with the “physical well-being” and “psychological well-being” dimensions, and with the SF-12, used in the Spanish study (15). This was reproduced in our study with a good correlation seen with the usual activities and anxiety / depression dimensions of the EQ-5D. The resemblance with a health-related quality of life measure might support the use of VQLQ-P to evaluate the cost-effectiveness of future intervention studies in hymenoptera venom allergic individuals.

Venom immunotherapy has been shown to improve health-related quality of life in wasp venom allergic patients (9). In another study, even in venom allergic patients on VIT, debilitating beliefs associated with the fear of a systemic reaction were seen (8). Two recent studies showed that quality of life (evaluated by VQLQ) improved significantly in hymenoptera venom allergy individuals currently on VIT (16,17). Therefore, the VQLQ may be particularly relevant when evaluating VIT's cost-effectiveness.

A study analyzing the economic burden linked to VIT, showed that it is associated with a cost of up to €23 million per year (18). This systematic review, focusing in the life saving aspect of VIT, was limited by the poor quality of the included studies and the lack of studies evaluating HRQoL. Therefore, as expected, it was associated with a very high cost per QALY gained (18). This strategy to evaluate cost-effectiveness, using only survival data, has been criticized as the specific effects on quality of life should also be taken into account (19). In this way, VQLQ-P can have a role in the patient-centered approach to decision-making

when initiating VIT. Recently, VIT is no longer covered by the health care system in Portugal and the cost of the treatment is totally supported by the patient. The evaluation of specific QoL in hymenoptera venom allergic patients could be useful to evaluate QALY in this population and thereafter the need for the health care system to support this treatment in venom allergic patients. For this questionnaire to be further used, a longitudinal validation is needed with a larger sample and using a multi-centered approach.

In conclusion, the Portuguese version of VQLQ and the hymenoptera allergy interference in daily life VAS can be used in future research and clinical contexts to evaluate quality of life in wasp venom allergic patients. Despite not being previously validated in non-beekeeper bee venom allergic patients, VQLQ-P and VAS also showed to have a good reliability in this setting. The application of VQLQ-P in the initial approach to a hymenoptera venom-allergic patient, may also guide the allergist to actively promote reassurance of the patient and provide support in the decision to start venom specific immunotherapy.

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