

Letter to the Editor

Tolerated wasp sting challenge improves health-related quality of life in patients allergic to wasp venom*To the Editor:*

Health-related quality-of-life (HRQOL) questionnaires are increasingly used in both research and patient care. Recently, HRQOL research was implemented in the field of wasp venom allergies. The “Vespid Allergy Quality of Life Questionnaire” (VQLQ), developed by Oude Elberink et al,¹ has become a well-established diagnostic instrument. This questionnaire is based on the hypothesis that the experience of anaphylaxis, the diagnosis of wasp venom allergy, and the potential dangers associated with wasp stings reduce the HRQOL in patients allergic to wasp venom. To measure the HRQOL, we validated this instrument in German (VQLQ-d).² The VQLQ-d consists of 14 items, each scored on a scale from 1 to 7, which provides an overall 1 to 7 HRQOL score after division by 14. Scores of 5 or less, 5.1 to 6, and 6.1 or more represent the categories of “high impairment,” “moderate impairment,” and “no/low impairment,” respectively. In agreement with their hypothesis, Oude Elberink et al^{1,3} showed that carrying out venom immunotherapy in venom-allergic patients improved the HRQOL, leaving a persisting impairment of 4.35 in the mean VQLQ score. For wasp venom immunotherapy, a protection rate of 92% was reported.⁴ In Europe, guidelines (eg, according to the European Academy of Allergy and Clinical Immunology and the German Society of Allergy and Clinical Immunology) propose that sting challenge tests should be carried out to identify those patients in whom standard venom immunotherapy (100 µg) is not effective.⁴ Based on the assumption that wasp stings are able to also boost sensitization to the venom and counteract the beneficial effects of immunotherapy, sting challenge tests are recommended only during ongoing venom immunotherapy. We initiated our first study to investigate whether the experience of tolerated wasp sting challenges could further improve the HRQOL in patients allergic to wasp venom.

In this pilot study, we assessed the global quality of life by using the World Health Organization-quality-of-life questionnaire and the disease-specific HRQOL by using the VQLQ-d, 4 weeks before the sting challenge test and 4 weeks after the sting challenge test. All patients were enrolled during the season of 2009 at the Allergy Unit of the Department of Dermatology and after giving informed consent. The local ethics committee approved the study protocol. Inclusion criteria were age more than 18 years and German-speaking. The sting challenge tests were performed as inpatient treatment under the supervision of an emergency team. The primary outcome measure was change in the VQLQ-d score. SPSS version 19.0 for Windows (SPSS Inc, Chicago, Ill) was used to conduct statistical analysis. Statistical significance was set at an α level of .05.

From June to October 2009, sting challenge tests were performed in 107 patients allergic to wasp venom (101 > age 18 years; 6 < age 18 years). Five adults had a previous experience of failure of venom immunotherapy (anaphylaxis in 2 patients after inadvertent field sting and in 3 patients after previous sting challenge test). Patients with elevated tryptase levels or experience of failure of venom immunotherapy were treated with an increased

TABLE I. Patients' characteristics at baseline 4 weeks before the sting challenge test*

Patients included	n = 57
Sex ratio (M/F)	1.2:1 (31/26)
Age (y) (mean)	
Men	49.8 (range, 21-75)
Women	51.9 (range, 28-78)
No. of anaphylactic reactions in medical history (%)	
1 event	64.9
2 events	24.1
3 or more events	10.5
Severity of anaphylaxis (according to Mueller) (%)	
Grade I	17.5
Grade II	17.5
Grade III	14
Grade IV	51
Time between last anaphylaxis and consultation with an allergologist (median)	55 d (range, 0 d to 25 y)
Time between consultation and initiation of immunotherapy (median)	146 d (range, 12 d to 6.5 y)
Immunotherapy experience (y) (median)	3.0 (range, 2.4-12.1)
Inadvertent field sting	10.5% (n = 6)
Sex ratio (M/F)	5:1
Experience of failure of immunotherapy (%)	8.8 (n = 5)
Anaphylaxis after field sting	3.5 (n = 2)
Anaphylaxis after sting challenge test	5.3 (n = 3)
Atopic patients (%)	19.3
Elevated tryptase levels or mastocytosis (%)	14.0
Bee venom allergy (as a second allergy) (%)	5.3

F, Female; M, male.

*Patients with elevated tryptase levels or experience of failure of venom immunotherapy were treated with increased dose of wasp venom (150 µg per injection) at least 1 year before the sting challenge test.

dose of wasp venom (150 µg per injection). This year no anaphylactic reactions occurred following sting challenge tests, and patients continued venom immunotherapy for at least another year. Eighty-four adults were included in this study, and 57 patients (26 women, 31 men) completed it by returning the questionnaire after the challenge test. There were no significant differences in the VQLQ score at baseline between completers and challenged patients who did not return the questionnaire after the challenge test. The characteristics of the sample are listed in Table I.

We found no impairment in the general quality of life, as measured by the World Health Organization-quality-of-life questionnaire, before (mean, 76.5 ± 13.4) or after sting challenge tests (mean, 75.8 ± 15.3), compared with normative German populations.⁵

In contrast, disease-specific HRQOL was impaired before the sting challenge test (mean, 5.57 ± 1.26). Consistent with the literature,³ the women in our study (mean, 5.08 ± 1.46) showed lower VQLQ-d scores during ongoing venom immunotherapy than did the men (mean, 5.99 ± 0.88) (Fig 1). More women than men reported “high impairment” of HRQOL (ratio M/F 1:2). In contrast, men were predominantly represented in the category “no/low impairment” (ratio M/F 2.3:1). In the category “moderate impairment,” the ratio of men to women was balanced (ratio M/F 1.1:1).

The HRQOL improved significantly after the sting challenge test. Mean VQLQ-d scores increased to 5.88 ± 1.06 (Wilcoxon $P = .001$). In our sample, 15 out of 57 patients (26.3%) reported “high impairment” of HRQOL (10 women, 5 men) before the

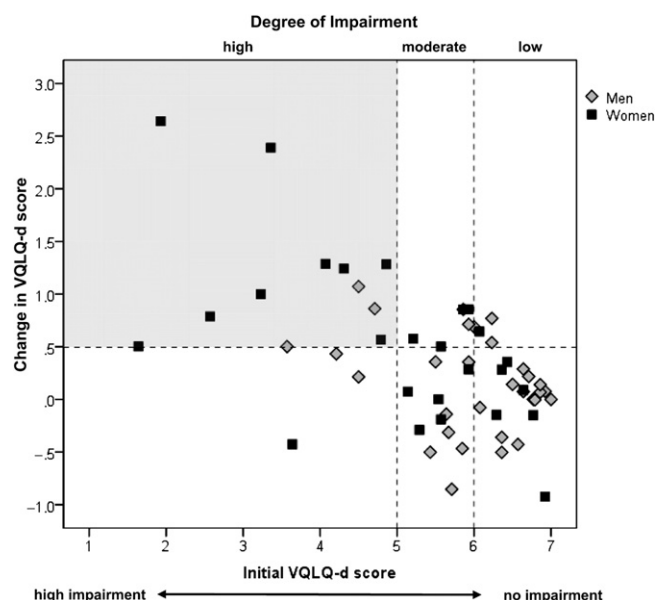


FIG 1. Changes in the VQLQ-d score after the sting challenge test, according to the VQLQ-d score before the sting challenge test. Scores of 5 or less, 5.1 to 6, and 6.1 or more represent the categories of "high impairment," "moderate impairment," and "no/low impairment," respectively. A clinically relevant change of .5 or more in the VQLQ-d score is defined, according to Juniper et al,⁶ as a minimally important difference.

sting challenge test. Defining a change of .5 or more in the VQLQ score as the minimal clinically important difference⁶ after the sting challenge test, 80% of these patients reported a clinically significant improvement in the HRQOL. Twenty percent reported no changes at all. None of these patients reported additional impairment due to sting challenge tests (Fig 1).

This pilot study is the first to assess the HRQOL before and after sting challenge tests and extends existing knowledge about the HRQOL in patients allergic to wasp venom. Previous studies have shown that HRQOL impairment improves after 1 year of venom immunotherapy.^{1,7} These studies on venom immunotherapy also demonstrated that the degree of HRQOL improvement due to venom immunotherapy depended on the magnitude of the HRQOL impairment before this therapy began.^{3,7} Compared with the general population,⁵ patients allergic to wasp venom displayed no relevant differences in their general quality of life. Of note, the data assessed with the VQLQ-d as a disease-specific instrument demonstrate the significant burdens borne by patients with wasp venom allergies. These data also clearly show that the experience of tolerated sting challenge tests improves the HRQOL, especially in patients reporting high impairment in HRQOL before the sting challenge test.

Our findings encourage the implementation of sting challenge tests not only for the purpose of evaluating the efficiency of venom immunotherapy but also for the purpose of fostering individual belief in disease-specific safety. This might help overcome worries on wasp venom allergy and improve self-efficacy, resulting in improvements in the HRQOL.

We thank Mrs Oude Elberink for allowing the original Dutch Version of the VQLQ to be used in the development of the German Version, VQLQ-d, and Mrs Aline Neumann of Eberhard Karls University, Faculty of Medicine, Department of Medical Biometry, for her advice on statistical analysis.

Jörg Fischer, MD^{a,*}

Martin Teufel, MD^{b,*}

Alexandra Feidt, MD^{a,b}

Katrin Elisabeth Giel, PhD^b

Stephan Zipfel, MD^b

Tilo Biedermann, MD^d

From ^athe Faculty of Medicine, Department of Dermatology, Allergy Unit, and ^bthe Faculty of Medicine, Department of Internal Medicine, Psychosomatic Medicine and Psychotherapy Unit, Eberhard Karls University, Tübingen, Germany. E-mail: tilo.biedermann@med.uni-tuebingen.de.

*These authors contributed equally to this work.

Disclosure of potential conflict of interest: M. Teufel, K.E. Giel, and S. Zipfel have received research support from the German Federal Ministry of Education and Research and the Center for Nutritional Medicine, Tübingen & Hohenheim, Germany. T. Biedermann has received research support from the Deutsche Forschungsgemeinschaft (SPP 1394). The rest of the authors declare that they have no relevant conflicts of interest.

REFERENCES

- Oude Elberink JN, De Monchy JG, Van Der Heide S, Guyatt GH, Dubois AE. Venom immunotherapy improves health-related quality of life in patients allergic to yellow jacket venom. *J Allergy Clin Immunol* 2002;110:174-82.
- Fischer J, Feidt A, Giel KE, Martens U, Zipfel S, Biedermann T, et al. Quality-of-life in wasp venom allergy – validation of the German version of the "Vespid Allergy Quality of Life Questionnaire" (VQLQ-d). *J Dtsch Dermatol Ges* 2011; 9:379-85.
- Oude Elberink JN, Dubois AE. Quality of life in insect venom allergic patients. *Curr Opin Allergy Clin Immunol* 2003;3:287-93.
- Rüeff F, Wenderoth A, Przybilla B. Patients still reacting to a sting challenge while receiving conventional Hymenoptera venom immunotherapy are protected by increased venom doses. *J Allergy Clin Immunol* 2001;108:1027-32.
- Angermeyer MC, Kilian R, Matschinger H. WHOQOL-100 und WHOQOL-BREF. Handbuch für die deutsche Version der WHO Instrumente zur Erfassung von Lebensqualität. Göttingen: Hogrefe; 2000.
- Juniper EF, Guyatt GH, Willan A, Griffith LE. Determining a minimal important change in a disease-specific quality of life questionnaire. *J Clin Epidemiol* 1994; 47:81-7.
- Oude Elberink JN, van der Heide S, Guyatt GH, Dubois AE. Immunotherapy improves health-related quality of life of adult patients with dermal reactions following yellow jacket stings. *Clin Exp Allergy* 2009;39:883-9.

<http://dx.doi.org/10.1016/j.jaci.2013.03.010>