

The Sting Challenge Test Shows High Negative Predictive Value in Patients Receiving Venom Immunotherapy

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■ Abstract

Background: The sting challenge test (SCT) is regarded as the most reliable method for assessing the effectiveness of venom immunotherapy (VIT). However, its predictive value in patients undergoing VIT is unclear.

Objective: This study aims to evaluate the predictive value of the SCT.

Methods: A multicenter retrospective observational study was conducted on patients receiving VIT who underwent SCT. The study gathered data on patient demographics, diagnosis, immunotherapy details, outcomes of the SCT, and subsequent field stings.

Results: A total of 261 patients were included, and 372 SCTs were recorded. Most patients (75.1%) were men. Mastocytosis was confirmed in 7.7%. The final diagnosis was allergy to *Apis mellifera* (48.7%), *Polistes dominula* (36.8%), *Vespula* species (2.7%), and *P. dominula* plus *Vespula* species (10.7%). SCTs were performed with *Apis* in 61.6% overall, *Polistes* in 34.1%, and *Vespula* in 4.3%. Most of the SCT results were negative (95.7%).

A total of 306 field stings were recorded for 146 patients (56.2%); of these, 95.1% were negative. Among these 146 affected patients, 137 had a negative SCT result, and 130 of these also had a subsequent negative field sting, resulting in a negative predictive value (NPV) for the SCT of 94.9%. Of the patients who experienced a field sting, 9 had a positive SCT, and only 3 had a positive field sting, resulting in a positive predictive value of 33.3%.

Conclusions: SCT is safe, and the high NPV emphasizes the usefulness of this test in assessing the effectiveness of VIT.

Key words: Hymenoptera venom allergy. Predictive value. Risk factors. Sting challenge test. Venom immunotherapy. Field sting.

■ Resumen

Antecedentes: La prueba de repicadura controlada hospitalaria (RCH) se considera el método más fiable para comprobar la eficacia de la inmunoterapia con veneno de himenópteros (ITV). Sin embargo, el valor predictivo de esta prueba en pacientes en tratamiento con ITV es desconocido.

Objetivo: El objetivo de nuestro estudio fue analizar el valor predictivo de la RCH.

Métodos: Se realizó un estudio multicéntrico, retrospectivo, observacional en pacientes tratados con ITV que se sometieron a RCH. Se recogieron datos demográficos, diagnóstico, tratamiento, resultado de las RCH y de picaduras espontáneas posteriores.

Resultados: Se incluyeron 261 pacientes en los que se realizaron 372 RCH. La mayor parte (75,1%) fueron varones. El 7,7% estaba diagnosticado de mastocitosis. Los diagnósticos fueron alergia a *Apis mellifera* (48,7%), *Polistes dominula* (36,8%), *Vespula* spp. (2,7%), y doble sensibilización *Polistes dominula* y *Vespula* spp. (10,7%). La RCH se realizó con *Apis* en el 61,6% de las pruebas, *Polistes* en 34,1% y *Vespula* en 4,3%. La mayoría de las RCH (95,7%) fueron negativas.

Respecto a las picaduras espontáneas, 146 pacientes (56,2%) sufrieron 306 picaduras, la mayoría (95,1%) negativas. De estos 146 pacientes, 137 habían tenido una RCH negativa y de éstos, 130 volvieron a tener una repicadura espontánea negativa, lo que resultó en un valor predictivo negativo (VPN) de 94,9%. De los pacientes que sufrieron picaduras espontáneas, 9 habían tenido una RCH positiva y de éstos sólo 3 tuvieron de nuevo una picadura espontánea positiva, lo que resultó en un valor predictivo positivo (VPP) de 33,3%.

Conclusiones: La RCH es una técnica segura y su alto VPN refuerza su valor en la monitorización de la eficacia de la ITV.

Palabras clave: Alergia a veneno de himenópteros. Valor predictivo. Factores de riesgo. Repicadura controlada hospitalaria. Inmunoterapia con veneno de himenópteros. Picadura espontánea.

Summary box

- **What do we know about this topic?**

The negative predictive value (NPV) of the sting challenge test (SCT) has been analyzed in patients not receiving venom immunotherapy (VIT), with values of 85.4% for bees and 89.9% for vespids.

- **How does this study impact our current understanding and/or clinical management of this topic?**

This is the first report on the predictive value of SCT in patients undergoing VIT. The NPV was found to be 94.9%, indicating that negative results are highly reliable in the event of new field stings.

Introduction

The occurrence of stings by Hymenoptera is influenced by geographical, environmental, and ecological factors, all of which can change rapidly [1,2]. More than half of adults worldwide (56%-94%) have been stung by a Hymenoptera insect in their lifetime. Systemic reactions (SRs) to these stings affect between 0.3% and 8.9% of the population, with lower rates in children and higher rates among individuals with frequent exposure, such as beekeepers [3]. These reactions range from mild symptoms, such as urticaria, to severe and potentially life-threatening anaphylaxis or anaphylactic shock, which require immediate medical intervention [4].

Venom immunotherapy (VIT) for allergic reactions to Hymenoptera stings has proven to be highly effective in protecting allergic individuals in 77%-85% of cases of bee venom allergy and in 91%-96% of cases of vespid venom allergy [5-7], reducing the occurrence of SRs in allergic individuals. VIT induces long-term tolerance and provides sustained protection. Studies show that VIT becomes effective immediately after the first maintenance dose is reached [8,9]. However, individual responses to VIT can vary, underlining the importance of reliable methods for monitoring efficacy. The main risk factors for failure of immunotherapy are immunotherapy with bee venom, high tryptase levels, mastocytosis, SRs associated with immunotherapy, and severe initial reactions [10].

It is essential to identify patients who are not protected by VIT. However, there are no biomarkers that enable us to determine the degree of protection reached by an individual patient. Determination of specific IgE (sIgE) and IgG4 and skin test results have not been found to be useful as biomarkers [11-14]. The basophil activation test has shown a correlation with protection in some studies, although it is not standardized and is not available as

a routine diagnostic tool [15,16]. The most reliable method for monitoring immunotherapy is the sting challenge test (SCT) [6].

The SCT should be performed as early as possible after the maintenance dose of 100 µg is reached to identify patients who may not be fully protected [6]. When SCTs are not feasible, reports of field stings can provide useful insights, although this approach is limited by factors such as insect misidentification and nonstandardized sting conditions [17].

Beyond assessing the clinical effectiveness of VIT, SCTs also play a key role in improving health-related quality of life, especially for patients experiencing high levels of anxiety about future stings [18-20]. Quality-of-life questionnaires, such as HiCaVi, the Spanish version of the Health-Related Quality of Life Questionnaire for Hymenoptera Venom Allergy (HRQLHA) [19,21,22], are valuable tools for monitoring patient well-being and success of treatment in daily clinical practice.

Despite its advantages, the SCT is limited by the fact that its predictive value in patients undergoing VIT is unknown [17], and it has been questioned whether the results of the SCT under controlled conditions are the same as with field stings. Therefore, the objectives of this study were to analyze the predictive value of the SCT in patients treated with VIT and to compare the results of this test with field stings subsequently experienced by patients.

Material and Methods

We conducted a multicenter, retrospective, observational study of patients treated with VIT who underwent an SCT between the years 2017 and 2023. The participating centers were all in Spain (Reina Sofía University Hospital, Córdoba;

Guadalajara University Hospital, Guadalajara; Arnau de Vilanova University Hospital, Lleida; and University Hospital Foundation Alcorcón, Alcorcón). VIT was conducted using aqueous extracts from various companies in line with the clinical practices of each center.

We collected demographic data, clinical data on the initial reaction, diagnosis (intradermal tests and sIgE), immunotherapy received, SCT results, and tolerance to field stings following the test. We used the World Allergy Organization classification of systemic reactions [23,24] (see Table in Supplementary material). Reactions of grades 1-2 were considered mild, grade 3 moderate, and grades 4-5 severe.

The SCT was performed following the protocol of the Hymenoptera Allergy Committee of the Spanish Society of Allergology and Clinical Immunology (SEAIC) [17]. The result of the challenge was considered negative when no systemic reaction occurred and positive when such a reaction was recorded.

Table 1. Demographic and Clinical Data.

		N=261 No. (%)
Sex	Male	196 (75.1%)
	Female	65 (24.9%)
Median (IQR) age, y		49.32 (38-59)
Occupation	Beekeepers	35 (14.6%)
	Nonprofessional beekeepers	13 (5.4%)
	Farmers	47 (19.6%)
	Maintenance workers	26 (10.8%)
	Construction workers	10 (4.2%)
	Retired	29 (12%)
	Students	15 (6.2%)
Grade of initial reaction ^a	1	41 (15.9%)
	2	45 (17.4%)
	3	86 (33.3%)
	4	36 (14%)
	5	50 (19.4%)
REMA score	≥2	51 (19.8%)
	<2	207 (80.2%)
Mastocytosis	Confirmed	20 (7.7%)
		N=372 No. (%)
Hymenoptera used	<i>Apis</i>	229 (61.6%)
	<i>Polistes</i>	127 (34.1%)
	<i>Vespula</i>	16 (4.3%)
Result of sting challenge test	Positive	16 (4.3%)
	Negative	356 (95.7%)

Abbreviation: REMA, Red Española de Mastocitosis (Spanish Mastocytosis Network).

^aWorld Allergy Organization classification.

The study was authorized by the clinical research ethics committees of the corresponding hospitals. All patients were informed and gave their consent to participate in the study.

The statistical analysis was performed using SPSS Version 17.0 (SPSS Inc.). Quantitative data are expressed as mean (SD) or median (IQR); qualitative data are expressed as absolute and relative frequencies. Differences in the demographic characteristics of the participants were analyzed according to the result of the SCT. Qualitative variables were analyzed using the χ^2 test; quantitative variables were analyzed using the Mann-Whitney test. The Wilcoxon signed-rank test was used to evaluate the change in quantitative markers. All tests were 2-tailed, and a *P* value of less than .05 was considered statistically significant.

Results

The study population comprised 261 patients enrolled from 4 hospitals in the south, center, and north of Spain (Córdoba, Guadalajara, Madrid, and Lleida). The median age was 49.32 years (38-59). Seventy five percent of patients were male. With regard to occupation, 60% of patients had professions with a high risk of exposure; of these, 21% were beekeepers and 39% worked in the open air (farmers, maintenance workers, and construction workers) (Table 1).

The initial reaction was severe in 33% of patients. The REMA score [25] was positive (≥2) in 20% of patients, and a diagnosis of mastocytosis was confirmed in 7.7% of patients (Table 1). The insect suspected of producing the reaction was identified by the patients as a bee in 47.9% of cases, a wasp (*Vespula* or *Polistes*) in 46.3%, and an unknown insect in 5.7% of cases.

Intradermal tests were performed, and sIgE was determined to whole venom of *Apis mellifera*, *Vespula* species, and *Polistes dominula* and to the main allergens of these venoms in order to establish a diagnosis. The intradermal skin tests were positive for *P dominula* in 55% of patients, for *A mellifera* in 46.9%, and for *Vespula* species in 28.9% (Table 2). The median sIgE values for whole venoms and their components are shown in Table 2. The final diagnosis was allergy to *A mellifera* in 48.7%, *P dominula* in 36.87%, double sensitization to *Polistes* and *Vespula* in 10.7%, and allergy to *Vespula* in 2.6%. Two patients were diagnosed as being allergic to *Apis* and *Polistes*, and 1 patient to *Apis* and *Vespula*.

All the patients were treated with VIT from different companies, and in all cases the extracts used were aqueous. The maintenance dose was 100 µg in 81.22% of patients, with the remaining patients having a maintenance dose of between 150 and 300 µg. Median specific IgE values against *Apis*, *Vespula*, and *Polistes* fell significantly during VIT (Figure).

All patients underwent an SCT. The median time from the beginning of immunotherapy to the SCT was 35.6 months (17.4-58). A total of 372 SCT were performed in the 261 patients enrolled, as 18% of patients were challenged more than once. Among the patients who underwent repeated SCT, 83.6% were beekeepers, and the aim was to confirm the persistence of their tolerance status. One patient underwent 2 sting challenge tests owing to a positive reaction with 100 µg of bee venom and was subsequently up-dosed to 200 µg with a negative result.

Table 2. Intradermal Tests and Laboratory Values at Diagnosis.

Positive Intradermal tests at diagnosis		
<i>Apis mellifera</i>	No. (%)	113 (46.9%)
<i>Vespula</i> species	No. (%)	70 (28.9%)
<i>Polistes dominula</i>	No. (%)	133 (55%)
Laboratory values at diagnosis		
Total IgE, U/mL N=155	Median (IQR)	61 (30-203)
Tryptase, µg/L N=207	Median (IQR)	4.91 (3.69-6.79)
<i>Apis mellifera</i> –allergic patients (n=127)		
sIgE <i>Apis mellifera</i> , kU _A /L N=106	Median (IQR) Positive (>0.1), No. (%)	10.1 (3.54-27.4) 106 (100%)
sIgE Api m 1, kU _A /L N=83	Median (IQR) Positive (>0.1), No. (%)	2.7 (0.94-15) 74 (89.1%)
sIgE Api m 2, kU _A /L N=25	Median (IQR) Positive (>0.1), No. (%)	0.02 (0.01-0.11) 6 (24%)
sIgE Api m 3, kU _A /L N=13	Median (IQR) Positive (>0.1), No. (%)	0.13 (0.01-0.27) 8 (61.5%)
sIgE Api m 5, kU _A /L N=24	Median (IQR) Positive (>0.1), No. (%)	0.1 (0.02-1.26) 11 (45.8%)
sIgE Api m 10, kU _A /L N=52	Median (IQR) Positive (>0.1), No. (%)	1.28 (0.1-13.27) 38 (72%)
<i>Polistes dominula</i> –allergic patients (n=96)		
sIgE <i>Polistes dominula</i> , kU _A /L N=92	Median (IQR) Positive (>0.1), No. (%)	7.02 (3.38-21.07) 92 (100%)
sIgE Pol d 5, kU _A /L N=61	Median (IQR) Positive (>0.1), No. (%)	0.39 (0.08-3.2) 43 (70.5%)
<i>Vespula</i> species plus <i>Polistes dominula</i> –allergic patients (n=35)		
sIgE <i>Vespula</i> species, kU _A /L N=34	Median (IQR) Positive (>0.1), No. (%)	5.61 (1.78-10.23) 34 (100%)
sIgE Ves v 1, kU _A /L N=15	Median (IQR) Positive (>0.1), No. (%)	0.3 (0.1-4.77) 11 (73.3%)
sIgE Ves v 5, kU _A /L N=17	Median (IQR) Positive (>0.1), No. (%)	2.3 (0.98-9.9) 15 (88.2%)
sIgE <i>Polistes dominula</i> , kU _A /L N=34	Median (IQR) Positive (>0.1), No. (%)	3.71 (1.46-9.38) 32 (94.1%)
sIgE Pol d 5, kU _A /L N=16	Median (IQR) Positive (>0.1), No. (%)	1.71 (0.26-12.57) 13 (81.2%)

In the remaining 16.4%, repeated stings were performed with different species, as these patients were double-sensitized. Most were performed with *Vespula* and *Polistes*, and 1 was performed with *Apis* and *Polistes*. The Hymenoptera with which the challenges were performed were *A mellifera* in 61.6% of cases, *P dominula* in 34.1%, and *Vespula* in 4.3% (Table 1).

Of all the SCTs, 356 (95.7%) were negative and only 16 (4.3%) were positive (15 patients) (Table 1). Among the positive tests, 14 reactions were mild (10 were grade 1 and 4 grade 2), while 2 were moderate (grade 3). No severe reactions were reported. The challenges with *P dominula* were negative in 98.4% of cases, while with *A mellifera* and *Vespula*, 94.8% and 87.5%, respectively, were negative.

Of the 261 patients enrolled, 146 (55.93%) experienced a field sting after the sting challenge. These patients experienced a total of 306 stings, as 68.6% of them experienced more than 1 field sting. Twenty-eight patients experienced several simultaneous field stings. The median time between the SCT and the field sting was 389 days (212-635.5).

The Hymenoptera causing the field stings were identified as a bee in 56.2% of stings and a wasp in 42.5%. The wasps involved might belong to the *Vespula* or *Polistes* genera, although patients often find it difficult to differentiate between them. In 1.3% of cases, the patients were unable to determine whether the insect was a wasp or a bee.

Among the field stings, 291 (95.1%) were negative, and 15 (4.9%) were positive. Among the positive field stings, 12 (80%) were mild (11 were grade 1 and 1 grade 2), while 2 (13.3%) were moderate (grade 3) and only 1 (6.7%) was severe (grade 4).

By comparing the SCT and field sting results, it is possible to calculate the predictive values of the SCT. Of the 146 patients who experienced a field sting, 137 had had a negative SCT result. Of these, 130 (94.9%) again had a negative field sting result. Therefore, the negative predictive value (NPV) of the SCT was 94.9% (95%CI, 89.8%-97.5%).

Furthermore, of the 146 patients who experienced a field sting, 9 had had a positive SCT result. Of these, only 3 (33.3%) subsequently had a positive field sting result, yielding a positive predictive value (PPV) of 33.3%.

The predictive value of the SCT was analyzed depending on the Hymenoptera species involved. In the case of patients allergic to bees, the NPV was 98.3%, while the PPV was 33.3%. In patients allergic to vespids, the NPV was 93.4% and the PPV 33.3% (Table 3).

Apart from calculating the predictive value of the SCT, we analyzed the variables related to a positive controlled challenge test result and found that 80% of positive SCTs were performed with honeybees. We also found a statistically significant association between the severity of the initial reaction and a positive result in the SCT, as 16% of grade 5 reactions had a positive SCT result, that is, more than for the other grades ($P=.006$). Furthermore, 46.6% of patients with a positive SCT result had experienced a grade 5 initial reaction.

Analysis of other well known risk factors showed that patients with an sIgE Api m 10 to sIgE *Apis* ratio >0.5 (n=18) had a negative SCT result in 93.3% of cases, and there was no relationship between the predominant sensitization to Api m 10

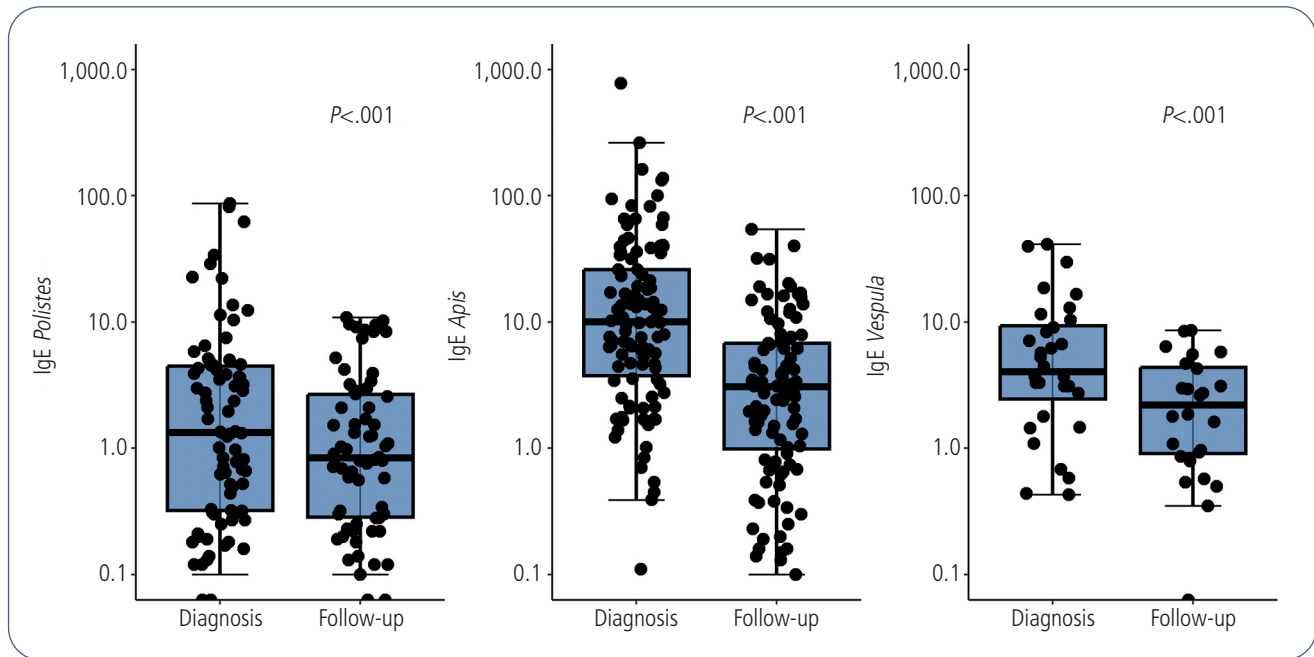


Figure. Changes in specific IgE values for *Polistes*, *Apis*, and *Vespula* species during venom immunotherapy.

and a higher percentage of positive SCTs. However, in this group of patients, the results may have been affected by the finding that 77.8% had a maintenance dose over 100 μ g.

In the study, we included 20 patients with systemic mastocytosis, in all of whom the SCT was negative. In these patients, 95% had a maintenance dose of 100 μ g, and 35% were allergic to honeybees.

Discussion

The SCT is considered the most reliable tool for monitoring the efficacy of immunotherapy with Hymenoptera venom [6]. One of its advantages is that a negative challenge test result improves patient quality of life, as it reduces anxiety regarding the risks involved in a new sting [18-21]. Furthermore, a negative SCT result allows adrenaline to be withdrawn in patients not at risk of relapse. Additionally, a positive SCT result allows the dose of immunotherapy to be increased, thus improving the efficacy of the treatment [17,26].

The SCT is a safe test for patients receiving VIT, as no fatal reactions have been reported [17,27]. In our study, a third of the patients had previously had severe reactions to stings. Nevertheless, all the SRs following the SCT were mild or moderate, thus confirming the safety of the technique.

Studies from decades ago on the natural history of Hymenoptera allergy analyzed the predictive value of the SCT in patients not receiving VIT, revealing the NPV of the test to be 85.4% in the case of bees and 89.9% in the case of vespids. An NPV of 95% has been reported [17,27-31].

The predictive value of the SCT in patients receiving VIT was previously unknown. The fact that the SCT was performed in a controlled environment, with no cofactors such as heat or physical activity, which can both affect field stings, casts doubt

Table 3. Contingency Table: Results of Sting Challenge Tests and Field Stings Based on the Hymenoptera Species Involved (Honeybee or Vespids).

		Field Sting, No. (%)		
		Negative	Positive	Total
Honeybee				
Sting challenge test, No (%)	Negative	59 (98.3)	1 (1.7)	60
	Positive	4 (66.7)	2 (33.3)	6
Vespids				
Sting challenge test, No (%)	Negative	71 (93.4)	5 (6.6)	76
	Positive	2 (66.6%)	1 (33.3)	3

on the reproducibility of the test. Furthermore, the amount of venom administered during the SCT is unknown and may vary in the case of vespids [32,33]. Doubts were also raised as to whether the result of a negative SCT could be replicated in the case of several simultaneous field stings [17].

We demonstrated the NPV of the SCT to be very high (94.9%), thus reinforcing the usefulness of the test. Twenty-eight patients experienced several simultaneous field stings, all of them had had a negative sting challenge test result, and 27 also tolerated multiple field stings. Therefore, the high NPV of the SCT is maintained, even in a scenario involving multiple field stings.

Furthermore, we found the PPV to be low (33.3%), that is, only one-third of positive sting challenges have a positive reaction in field stings. In the case of vespids, this may be because a different species was involved in the SCT and field sting, as it can be difficult for the patient to distinguish between *Vespula* and *Polistes*. However, more than 50% of such cases

were allergic to bees, whose stings are normally identified correctly. Another possible explanation is that the result of the SCT is more reliable, as it is performed under controlled conditions for 30 seconds and ensures clear exposure to the venom, conditions that are not present in field stings. Thus, a negative result from a field sting does not always ensure that the VIT is effective, as reported by other authors [34].

When we analyzed the predictive value of the test depending on the Hymenoptera species involved, we found a higher NPV in the case of SCT with bees. This may be because, in the challenge with bees, the entire amount of venom in the venom sac is delivered when the bee anchors the sting in the skin.

The effectiveness of VIT is very high, reaching 84% in bee-allergic patients and 96% in vespid-allergic patients [7]. This study was not designed to prove the effectiveness of VIT, as only patients suitable for the SCT were included, with the result that patients who experienced a systemic reaction from field stings or from VIT were excluded. Therefore, the efficacy of VIT as shown by challenge tests was 95.7%. Furthermore, in the case of VIT with *P dominula*, this effectiveness reached 98.4%.

In our study, the worst results in the SCTs performed were obtained with *Vespula*, where 87.5% of results were negative, possibly owing to a study limitation, that is, only 16 patients challenged with *Vespula* were included, and the 2 who had a positive SCT result had initially had grade 5 reactions. Therefore, the effectiveness rate of VIT in the *Vespula* group should be interpreted with caution. The low number of patients challenged with *Vespula* is due to the difficulty in obtaining the insect for the challenge test, as it is much less accessible than either *Polistes* or *Apis*. This does not reflect the real prevalence of patients allergic to *Vespula* in Spain.

Several risk factors have been associated with the lack of efficacy of VIT, especially immunotherapy with bee venom [35], the presence of high tryptase levels, a diagnosis of mastocytosis [36-42], and the presence of SRs associated with VIT [6,10]. Our study confirms the association between immunotherapy with bee venom and the lower efficacy of immunotherapy, as most positive SCTs were caused by bees.

The effectiveness of VIT in patients with mastocytosis lies between 74% and 86%, somewhat lower than in the general population [40], although a recent study reports an effectiveness of 96.7% [43]. Precisely for this reason, it is important to perform SCTs in patients with mastocytosis. Moreover, the safety of VIT in patients with mastocytosis was recently demonstrated [43]. We included 20 patients with mastocytosis, all of whom tolerated the SCT, thus reinforcing the notion that this technique is safe for these patients. Therefore, in our study, a diagnosis of mastocytosis was not a risk factor for the lack of effectiveness of VIT.

The severity of the initial reaction has been associated with a reduction in the effectiveness of VIT [10,44] and the risk of relapse after immunotherapy, although data on this issue are contradictory [6]. We found a clear association between the severity of the initial reaction and the risk of a positive SCT result.

High levels of Api m 10, especially sIgE Api m 10 to sIgE *Apis* ratios over 0.5, have been associated with reduced efficacy

of immunotherapy, although this issue has been a matter of some debate [35,45-47]. In our study, an Api m 10 ratio over 0.5 was recorded in 18 patients, 93.3% of whom tolerated the SCT. Of these patients, 77.8% were receiving maintenance doses over 100 µg, which may have affected the results. In any case, we found no association between predominant sensitization to Api m 10 and reduced efficacy of VIT.

Our study is subject to limitations. Its retrospective design can potentially lead to bias in data collection typically associated with this type of research. While some data suggest the vespid species involved in field stings (eg, environmental factors, the presence of nests, or food sources [48]), it is difficult to definitively determine which specific vespids (*Vespula* or *Polistes*) caused the field stings. The limited number of *Vespula* sting challenges has also been noted as a limitation. Additionally, the small number of patients exhibiting positive sting reactions is a limitation, although this outcome was expected owing to the high effectiveness of VIT.

Conclusions

Ours is the first study to show that the SCT has a high NPV in patients treated with VIT and emphasizes the usefulness of this tool for monitoring the effectiveness of immunotherapy.

Furthermore, in our population, this test could be safely performed in patients with mastocytosis, a group in which VIT may be less effective and, therefore, where it is essential to confirm that the patient is protected.

Our findings also demonstrate that the SCT is safe for patients receiving VIT who have had severe initial reactions to Hymenoptera stings.

All in all, we show that in order to optimize management, it would be advisable to have the SCT available in allergology units that treat patients allergic to Hymenoptera venom.

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Conflicts of Interest

- Teresa Alfaya Arias declares receipt of payment or honoraria for lectures, presentations, speaker bureaus, manuscript writing, and educational events from Roxall and ALK.
- Arantza Vega Castro declares receipt of consulting fees from ALK, Allergy Therapeutics, Immunotek; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, and educational events from Leti SL, Roxall, Novartis, and Allergy Therapeutics; and support for attending meetings and/or travel from GSK.
- Arantza Vega Castro is a Member of the EAACI Executive Committee and Elected President of the SEAIC.
- Jesús Macías Iglesias declares receipt of payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, and educational events from Roxall Group.
- Lluís Marquès declares receipt of grants or contracts from Roxall Medicina España SA and Allergy Therapeutics

Iberica SLU; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, and educational events from Roxall Medicina España SA; and participation on data safety monitoring boards and advisory boards from ALK.

- The remaining authors declare that they have no conflicts of interest.

Previous Presentation

This study was presented as an oral communication at the Allergy School on Insect Venom Hypersensitivity and Mastocytosis (EAACI), which took place in Bilbao, Spain, in September 2024.

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