

Using Component-Resolved Diagnosis to Characterize the Sensitization to Specific Cat and Dog Allergens in Patients with Allergic Respiratory Diseases in Catalonia, Spain

Albert Roger^a Carlota Lazo^a Noelia Arias^b Bibiana Quirant^b Nereida Albert^a
Mireia Gómez^a Waleska Schayman^a

^aAllergy Section, University Hospital Germans Trias Pujol, Badalona, Spain; ^bImmunology Department, University Hospital Germans Trias Pujol, Badalona, Spain

Keywords

Cat allergy · Dog allergy · Asthma · Allergic rhinitis · Component-resolved diagnosis

Abstract

Introduction: Sensitization to cat and dog allergens is common in patients with allergic respiratory diseases. The study objective was to determine the prevalence of immunoglobulin E (IgE) sensitization to specific cat and dog allergens using component-resolved diagnosis (CRD) in patients with allergic respiratory diseases plus cat and/or dog sensitization.

Methods: We included 87 patients aged 8–62 years, diagnosed with allergic asthma and/or rhinitis plus cat and/or dog sensitization, and attended at the allergy section of a tertiary hospital in Badalona (Catalonia, Spain). We used CRD to determine IgE sensitization to specific cat/dog allergens and skin prick tests (SPTs) to determine differences between diagnostic test results. **Results:** Patients were monosensitized to cats (20.7%) or dogs (3.4%) or sensitized to both (75.9%). The highest positive allergen rates were for Fel d 1 (91.7%) and Fel d 4 (41%) in patients sensitized to cat allergens and for Can f 5 (80%) and Can f 1 (70%) in those sensitized to dog allergens. CRD and SPT results differed somewhat: 16.1% and 27.6% of patients CRD positive for cat or dog sensitization, respectively, were SPT negative, and 6.9% SPT

positive for dog sensitization were CRD negative. Few statistically significant relationships were found between any allergen components and any respiratory disease characteristic or contact with furry animals. **Conclusions:** CRD may be used to determine the prevalence of IgE sensitization to specific cat and dog allergens in patients with allergic respiratory diseases plus cat and/or dog sensitization. As SPT may not correctly identify all patients sensitized to cats and dogs, our results support the use of CRD.

© 2023 The Author(s).

Published by S. Karger AG, Basel

Introduction

Allergens from furry pets, mainly cats and dogs, are an important cause of allergic rhinitis and asthma [1]. According to a 2016 global study in internet users aged >15 years, the most common pet worldwide was the dog (33% of households), followed by the cat (23%), with comparable findings in Spain, where 37% of people lived with dogs and

Some/all of the study data were presented in poster form in 2021 at the 33rd Congress of the Spanish Society of Allergy and Clinical Immunology, and at the 1st Congress of the Catalan Society of Allergy and Clinical Immunology.

Edited by: Oscar Palomares, Madrid.

23% with cats [2]. As rates of pet ownership appear to be growing, especially among young people [3], it is very likely that this will be accompanied by an increase in the incidence and prevalence of sensitization to cats and dogs.

Sensitization to cats and dogs is common in patients with allergic respiratory diseases. In a European study of adults with suspected allergy to inhalant allergens, about 26% and 27% were sensitized to cats and dogs, respectively [4]. Moreover, an estimated 6% of the Spanish population [5] and more than 30% of allergic patients [6] were sensitized to animals. An international study in adults with AR and/or asthma found differences in sensitization rates between 13 geographical areas in Europe, with 7.1–18.8% of patients being sensitized to cats and 11.1–20.8% sensitized to dogs [7]. However, the estimated prevalence of sensitization to cat and dog allergens in these and other studies has been based on the results of traditional immunoglobulin (IgE) antibody tests, such as skin prick tests (SPT) or in vitro specific IgE assays. The use of newer and more accurate methods of detecting allergen sensitization could, therefore, improve the precision of such estimates [8]. One such method is component-resolved diagnostics (CRD), also termed molecular-based allergy diagnostics (MBAD), molecular allergy diagnostics (MAD), and, more recently, precision allergy molecular diagnostic applications (PAMD@) [9, 10]. CRD detects IgE sensitization to specific allergenic proteins, including those relevant to cat and dog sensitization, and is an emerging tool for determining variations in the concentrations of allergens in different samples and improving the diagnosis of allergies [9, 10]. Sensitization to cats is mainly due to the allergenic component Fel d 1, whereas sensitization to dogs is more variable and several allergenic components may be responsible [11].

The main objective of the study was to determine the prevalence of IgE sensitization to component-specific cat and dog allergens in patients with allergic respiratory diseases plus cat and/or dog sensitizations in Catalonia, Spain. Secondary objectives were focused on finding a series of relationships: SPT and CRD; allergic respiratory disease and sensitization profile; symptoms elicited by contact with pets and specific component sensitization; immunotherapy; and number of sensitized components.

Materials and Methods

Patients

We conducted a prospective study of patients with allergic respiratory diseases (allergic asthma, allergic rhinitis, or both) with sensitization to cats and/or dogs. The study was performed in the

allergy section of a tertiary hospital in Catalonia, Spain, from September 2020 to April 2021. Patients were invited to participate if they had been diagnosed with allergic asthma according to the Spanish Asthma Management Guidelines (GEMA) [12] and/or allergic rhinitis according to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines [13]. Patients were also required to have a diagnosis of sensitization to cats and/or dogs confirmed by a positive IgE SPT and/or ImmunoCAP™ Whole Allergen Test (Thermo Fisher Scientific Inc., Uppsala, Sweden). Additionally, patients could be from 0 to 99 years old. No exclusion criterion was defined. When allergists in our center visited patients that met all inclusion criteria, they invited them to participate in the study. Finally, we included 87 patients with allergic respiratory diseases and sensitization to cats and/or dogs. Patients were almost equally divided between males and females, with a mean patient age of 26.4 years (range 8–62 years).

Patients who agreed to participate signed an informed consent form. Then, allergists completed a case report form for each patient at the enrollment visit, which contained the following items: age, type of respiratory disease (rhinitis and/or asthma), classification of disease (persistent, intermittent), severity of disease (mild, moderate, severe), sensitization to other allergens (mites, pollens, molds), contact with cat/dog and symptoms related to exposure to cat/dog (yes/no), characteristics of respiratory disease, presence of cat/dog and pollen/mite sensitizations, and contact with cats/dogs. Afterward, a serum sample was drawn for IgE testing.

The study was approved by the Ethical Committee of the University Hospital Germans Trias Pujol (Badalona, Spain), approval number [PI-19-259]. Before entering the study, patients or their parents/legal guardians provided written informed consent. All patients' data were anonymized by codification.

CRD and SPT

CRD (ImmunoCAP™ Whole Allergen test) was used according to the manufacturer instructions to measure specific IgE to allergenic components for cat (Fel d 1, Fel d 2, Fel d 4, and Fel d 7) and dog (Can f 1, Can f 2, Can f 3, Can f 4, Can f 5, and Can f 6) in the serum of the study participants. A cutoff point of ≥ 0.1 kUA/L was used to determine sensitization. Samples were collected by nurses from the Allergy Section. SPTs were performed according to a European guide [14], using a standard panel of local allergens (mites, molds, pets, pollens).

The primary endpoint was the proportion of patients with cat or mixed allergy with IgE sensitization to component-specific cat allergens (Fel d 1, Fel d 2, Fel d 4, and Fel d 7) and the proportion of patients with dog or mixed allergy with IgE sensitization to component-specific dog allergens (Can f 1, Can f 2, Can f 3, Can f 4, Can f 5, and Can f 6). Secondary endpoints included comparison of CRD and SPT results, agreement between sensitization profile and clinical symptoms, and association between sensitization profiles and allergen-specific immunotherapy (AIT) prescription.

Statistical Analysis

Descriptive analysis of data was performed with frequency and percentage for qualitative variables and with measures of central tendency for quantitative variables. Categorical data were compared using the Fisher's exact test, while ordinal data were analyzed with the Mann-Whitney U test for two groups and with the Kruskal-Wallis test for three or more groups. Data were analyzed using SAS System 9.4 (SAS, Cary, USA) software package.

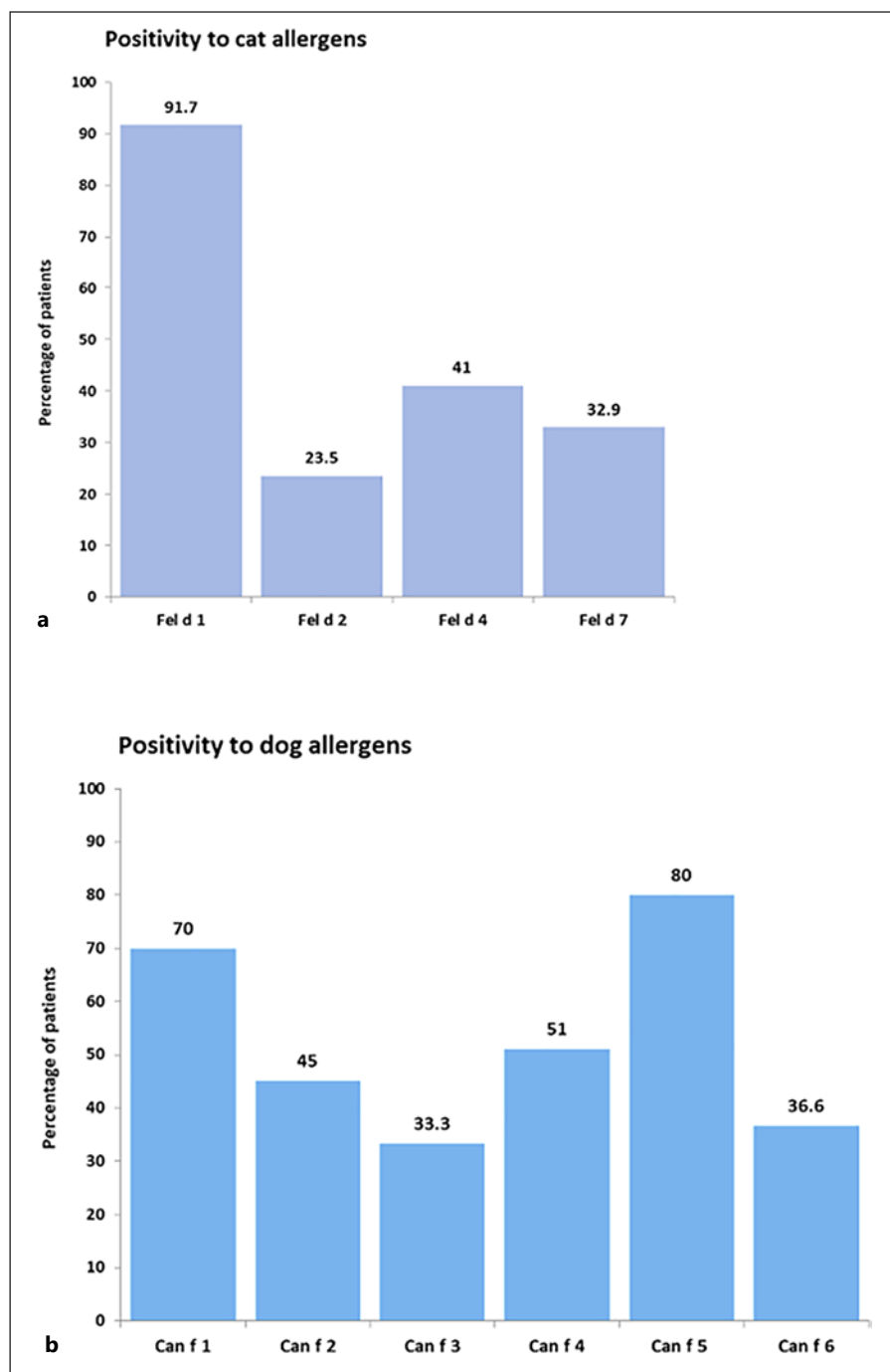


Fig. 1. Percentage of patients with sensitization to specific cat allergens ($n = 85$) (a) and dog allergens ($n = 60$) (b).

Results

Online supplementary Table S1 (for all online supplementary material, see www.karger.com/doi/10.1159/000528643) provides the demographic, respiratory disease, and allergy characteristics of the study population. The majority of patients had either mixed allergic rhinitis/asthma (44.8%)

or allergic rhinitis alone (41.4%), with an allergic respiratory disease that was persistent (69.0%) and of mild or moderate severity (90.8%).

Most patients (66/87, 75.9%) were sensitized to both cats and dogs, with monosensitization to cats being more frequent (18/87, 20.7%) than that to dogs (3/87, 3.4%). Slightly more than half of patients were in contact with

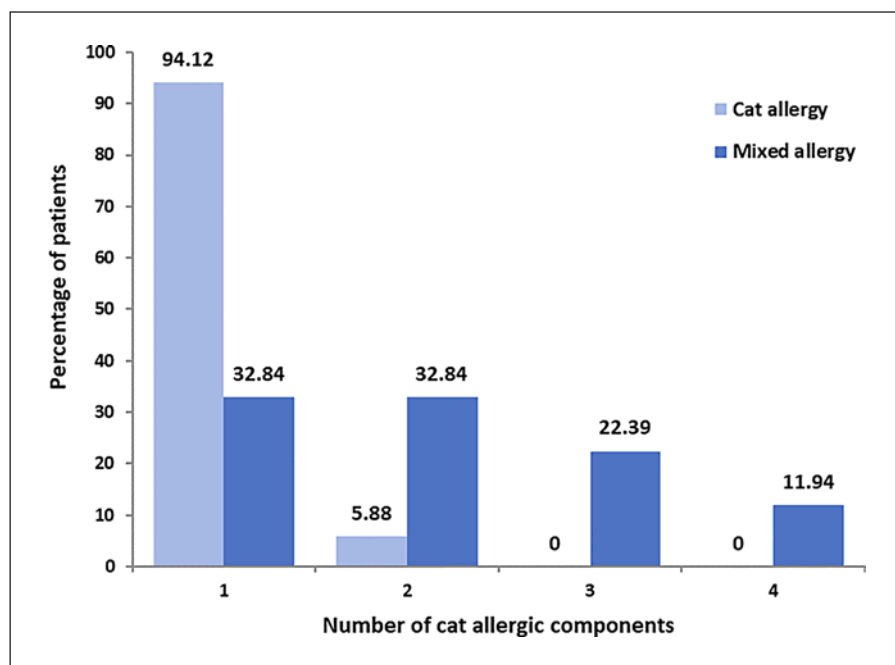


Fig. 2. Distribution of cat allergens in patients with only cat allergy ($n = 18$) or mixed allergy ($n = 66$).

cats and/or dogs (45/87, 53.6%). Almost all patients (82/87, 94.3%) were also sensitized to mites and/or pollen. One-third of patients were receiving AIT for cat and/or dog allergies.

Sensitization to Specific Cat and Dog Allergens

Based on the results of CRD, IgE sensitization to the tested cat component allergens was shown in 97.7% (85/87) of study patients, and IgE sensitization to the tested dog component allergens was shown in 69% (60/87). Of the 85 patients showing IgE sensitization to specific cat allergens, almost all were positive for Fel d 1 ($n = 78$; 91.7% of patients), more than a third were positive for Fel d 4 ($n = 35$; 41%), with fewer being positive for Fel d 7 ($n = 28$; 32.9%) and Fel d 2 ($n = 20$; 23.5%) (Fig. 1; online suppl. Table S2). In the 60 patients with CRD sensitization for specific dog allergens, more than half were positive for Can f 5 ($n = 48$; 80%) and Can f 1 ($n = 42$; 70%), with fewer patients being positive for Can f 4 ($n = 31$; 51%), Can f 2 ($n = 27$; 45%), Can f 6 ($n = 22$; 36.6%), and Can f 3 ($n = 20$; 33.3%) (Fig. 1; online suppl. Table S3). In addition, levels of specific IgE load for each allergen component are shown in online supplementary Figure S1.

Patients with sensitization to cat or dog were positive mainly to only one allergen, but patients with co-sensitization were sensitized to two or more allergens (Fig. 2, 3). Both of the patients sensitized to only Fel d 7 as a cat allergen were also sensitized to dog allergens. Of the 10

patients (16.6%) sensitized to only Can f 5 as a dog allergen, one was not sensitized to any cat allergens, and eight were sensitized to Fel d 1. All 5 of the patients sensitized to only Can f 6 as a dog allergen were also sensitized to at least 1 cat allergen. Median of positive allergens was significantly higher in patients treated with AIT than in those not treated with AIT, including total allergens (median 5.4 vs. 3.4; $p = 0.0008$), cat allergens (median 2.4 vs. 1.6; $p = 0.0018$), and dog allergens (median 3.0 vs. 1.8; $p = 0.0025$).

CRD versus SPT

For cat allergens, 14 patients (16.1%) with positive CRD results had a negative SPT, but none of the patients with a positive SPT had a negative CRD result. For dog allergens, 24 patients (27.6%) who were CRD positive had a negative SPT, while 6 patients (6.9%) with a positive SPT were CRD negative.

Sensitization Profile versus Clinical Profile

With only two exceptions, no statistically significant differences were found between the number of allergic components and the type, severity, and classification of allergic respiratory disease in the overall study population, as well as in the disease subgroups (allergic asthma only, allergic rhinitis only, or both). However, patients with severe symptoms were significantly more likely to be sensitized to Can f 1 ($p = 0.0384$) than those with mild or moderate symptoms, and those with intermittent asthma

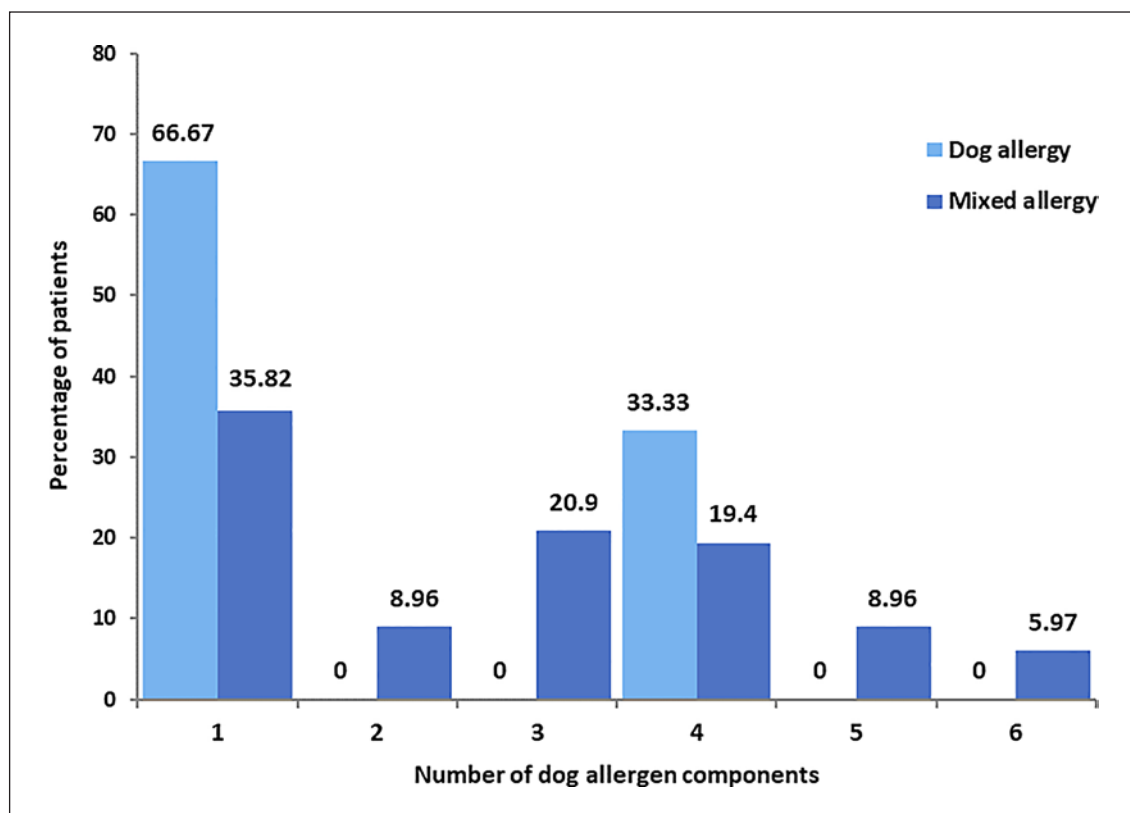


Fig. 3. Distribution of dog allergens in patients with only dog allergy ($n = 3$) or mixed allergy ($n = 66$).

were significantly more likely to be sensitized to Can f 5 than those with persistent disease ($p = 0.0454$) (online suppl. Tables S4–S17).

In patients with cat sensitization, no significant association was found between the appearance of symptoms as a result of contact with cats and sensitization to a specific component. However, in patients with dog sensitization, positivity to Can f 6 was significantly associated with symptoms when in contact with dogs ($p = 0.0137$). Moreover, patients in contact with cats and dogs were sensitized to more dog allergens, in particular Can f 6, than patients not in contact with cats and dogs ($p = 0.0087$). No statistically significant difference was found in the number of cat allergens (online suppl. Tables S18 and S19).

Relative to other study participants, patients with cat and/or dog sensitization who were sensitized to both pollen and mites had significantly lower rates of sensitization to Fel d 2 and Can f 3. In contrast, patients with only pollen sensitization had higher rates of sensitization to both Fel d 2 and Can f 3. Furthermore, patients with sensitization only to mites were less sensitized to Fel d 7 than the other study participants.

Sensitization Profile versus Immunotherapy

No statistically significant differences were found between sensitization to cat, dog, or both and being treated or not with immunotherapy. However, patients receiving immunotherapy were positive for a higher number of cat-, dog-, and total allergic components ($p = 0.0018$, $p = 0.0025$, and $p = 0.0008$, respectively) (online suppl. Table S20).

Discussion

We evaluated specific allergenic components in a population of patients with sensitization to cats and/or dogs and respiratory disease. CRD results showed that the more prevalent allergenic component for cat allergy was Fel d 1, found in more than 95% of patients. Fel d 1 is considered the main component of cat allergy, as shown in other studies [8, 15]. The main dog allergens are Can f 1 and Can f 5 [11]. In the present study, the most prevalent allergenic component for dog allergy was Can f 5, followed by Can f 1, whereas the latter has been the most prevalent in other studies [6]. In a study in Swedish adults,

Fel d 1 and Can f 1 were the most common allergens from furry pets, both in healthy participants and in patients with asthma [16].

Rate of monosensitization to Can f 5 (13.8%) in the study was lower than that found in previous studies in Spain, where this rate has been found of 37% [17] and even 70.5% [18]. On the contrary, from 214 patients sensitized to cat and/or dog included in a European study of animal allergy, 18 patients were sensitized only to dog, and 12 patients only to Can f 5, representing 5% of patients [15]. These differences in sensitization to dog allergens by geographical regions, even within the same country, are well recognized [19]. Furthermore, previous studies did not evaluate some allergenic components because they were not yet available. In the Swedish study, Fel d 7, Can f 4 and Can f 6 were not included in the CRD analysis [16]. In addition, we would like to point out that we are not talking about “pure” monosensitization because many allergens are still not available for in vitro testing. Therefore, we use the term “monosensitization” within the context of the allergens assessed in the study.

Dog and cat allergens can have cross-reactivity, making it difficult to identify the actual allergen [20]. As shown by the results of our study, in which some patients were monosensitized to only 1 cat or dog allergen, the use of CRD avoids such potential cross-reactivity. For example, in our study, of the 10 patients monosensitized to Can f 5, 2 patients were not sensitized to any cat allergens and 6 patients showed monosensitization to Fel d 1. Additionally, co-sensitization to cat and dog is common [20], and in the study, it was identified in more than 75% of patients.

An important finding was that SPT did not identify all sensitized patients. SPT had been negative in one in every 6 patients with cat allergy, as well as in more than one in every 4 patients with dog allergy. Therefore, new methods, in particular CRD, should be used to improve diagnosis of pet allergies. The World Allergy Organization (WAO), the ARIA initiative, and the Global Allergy and Asthma European Network (GA²LEN) provided an updated consensus document on CRD in 2020 [10], and the project VALIDA in Spain issued a number of recommendations on the best use of the different in vitro techniques for IgE determination, including CRD [21]. Of note, however, in our study, some (6.9%) patients with dog allergy were CRD negative, despite being SPT positive.

Sensitization to all tested cat and dog allergic components was associated to an increased risk of asthma and/or allergic rhinitis [22]. In our country, positivity to furry allergic components has been associated to asthma and/or

allergic rhinitis, with specific relationships between allergic components and clinical profiles [23]. However, we did not find almost any relationship between specific allergic components and respiratory disease. The only exceptions were that sensitizations to Can f 6, Can f 1, and Can f 5 were associated with symptoms in the presence of dogs, more severe symptoms, and intermittent asthma, respectively.

Only 29 patients (33.3%) were receiving AIT for cat and/or dog allergies because they were the only good candidates for AIT according to current criteria [19]. These patients were sensitized to more allergens than those not receiving AIT. Generally, the more asthma severity, the more the number of allergic components the patient is sensitized to [24]. This can be a good reason to vaccinate patients sensitized to a high number of allergens. Allergy to furry pets can be treated with AIT, but it requires an identification of allergens that is as exact as possible. CRD can help formulate the most accurate AIT according to current knowledge, thereby improving the likelihood of beneficial treatment results.

Conclusions

CRD may be used to determine the prevalence of IgE sensitization to specific cat and dog allergens in patients with an allergic respiratory disease and a cat and/or dog sensitization. Fel d 1 was, by far, the most prevalent allergenic component in patients with cat sensitization, and Can f 5 and Can f 1 were the most prevalent in patients with dog sensitization. As SPT may not correctly identify ≈ 16 and ≈ 27 of every 100 patients sensitized to cats and dogs, respectively, our results support the use of CRD when assessing potential sensitization to furry pets.

Acknowledgments

Writing and editorial assistance were provided by Carmen Acuña-Condal and Katherine A. Lyseng-Williamson, Content Ed Net, and funded by Thermo Fisher Spain through a research grant CABAL1917.

Statement of Ethics

The study was approved by the Ethical Committee of the University Hospital Germans Trias Pujol (Badalona, Spain), approval number [PI-19-259]. Before entering the study, patients provided written informed consent; for all participants aged under 18, written informed consent was obtained from parents/legal guardians. All patients' data were anonymized by codification.

Conflict of Interest Statement

The authors declare no conflict of interest.

Funding Sources

ARR received the research grant CABAL1917 from Thermo Fisher Scientific.

Author Contributions

Carlota Lazo, Noelia Arias, Bibiana Quirant, Nereida Albert, Mireia Gómez, Waleska Schayman: substantial contributions to the conception or design of the work; or the acquisition, analysis,

or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published. Albert Roger: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

References

- 1 Kalayci O, Miligkos M, Pozo Beltrán CF, El-Sayed ZA, Gómez RM, Hossny E, et al. The role of environmental allergen control in the management of asthma. *World Allergy Organ J.* 2022;15(3):100634.
- 2 Man's best friend: global pet ownership and feeding trends [Internet]. [cited 2022 Jun 3]. Available from: <https://www.gfk.com/insights/mans-best-friend-global-pet-owner-ship-and-feeding-trends>.
- 3 PFMA confirms dramatic rise in pet acquisition among Millennials | PFMA News [Internet]. [cited 2022 Jun 6]. Available from: <https://www.pfma.org.uk/news/pfma-confirms-dramatic-rise-in-pet-acquisition-among-millennials>.
- 4 Heinzerling LM, Burbach GJ, Edenharter G, Bachert C, Bindeslev-Jensen C, Bonini S, et al. GA 2 LEN skin test study I: GA2LEN harmonization of skin prick testing: novel sensitization patterns for inhalant allergens in Europe. *Allergy.* 2009;64(10):1498–506.
- 5 de Moral Gregorio A, Carretero Aníbarro P, Mateo Borrega M, Zapata Yébenes J. [Chapter 20. Main indoor allergens]. In: Dávila gonzález I, Jáuregui presa I, olaguibel rivera J, zubeldia ortuño J, editors. *Tratado alergia*. 2nd ed. Tome 1. Madrid, Spain: Ergon; 2015. p. 287–310.
- 6 Pereira C, Valero A, Loureiro C, Dávila I, Martínez-Cócera C, Murio C, et al. Iberian study of aeroallergens sensitisation in allergic rhinitis. *Eur Ann Allergy Clin Immunol.* 2006;38(6):186–94.
- 7 Newson RB, van Ree R, Forsberg B, Janson C, Lötval J, Dahlén S-E, et al. Geographical variation in the prevalence of sensitization to common aeroallergens in adults: the GA 2 LEN survey. *Allergy.* 2014;69(5):643–51.
- 8 Konradsen JR, Fujisawa T, van Hage M, Hedlin G, Hilger C, Kleine-Tebbe J, et al. Allergy to furry animals: new insights, diagnostic approaches, and challenges. *J Allergy Clin Immunol.* 2015;135(3):616–25.
- 9 Chan SK, Leung DYM. Dog and cat allergies: current state of diagnostic approaches and challenges. *Allergy Asthma Immunol Res.* 2018;10(2):97–105.
- 10 Steering Committee Authors; Review Panel Members; Canonica GW, Gómez RM, Jensen-Jarolim E, Ebisawa M. A WAO-ARIA-GA2LEN consensus document on molecular-based allergy diagnosis (PAMD@): update 2020. *World Allergy Organ J.* 2020;13(2):100091.
- 11 Nilsson OB, Van Hage M, Grönlund H. Mammalian-derived respiratory allergens – implications for diagnosis and therapy of individuals allergic to furry animals. *Methods.* 2014;66(1):86–95.
- 12 Plaza V, Alobid I, Alvarez C, Blanco M, Ferreira J, García G, et al. [Translated article] Spanish asthma management guidelines (GEMA) v.5.1. Highlights and controversies. *Arch Bronconeumol.* 2022;58(2):T150–8.
- 13 Brožek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic rhinitis and its Impact on asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol.* 2017;140(4):950–8.
- 14 Bousquet J, Heinzerling L, Bachert C, Papadopoulos NG, Bousquet PJ, Burney PG, et al. Practical guide to skin prick tests in allergy to aeroallergens. *Allergy.* 2012;67(1):18–24.
- 15 Hemmer W, Sestak-Greinecker G, Braunsteiner T, Wantke F, Wöhl S. Molecular sensitization patterns in animal allergy: relationship with clinical relevance and pet ownership. *Allergy.* 2021;76(12):3687–96.
- 16 Suzuki S, Nwaru BI, Ekerljung L, Sjölander S, Mincheva R, Rönmark EP, et al. Characterization of sensitization to furry animal allergen components in an adult population. *Clin Exp Allergy.* 2019;49(4):495–505.
- 17 Basagaña M, Luengo O, Labrador M, Garriga T, Mattsson L, Lidholm J, et al. Component-resolved diagnosis of dog allergy. *J Investig Allergol Clin Immunol.* 2017;27(3):185–7.
- 18 Dávila I, Isidoro-García M. Perfiles clínicos y de sensibilización molecular en la alergia al epitelio de perro. In: *AlergoAragón SA de A-Debates sobre Alergol.* Zaragoza, Spain: Ibérica de Gestión Editorial, S.L.; 2017. p. 105–16.
- 19 Dávila I, Domínguez-Ortega J, Navarro-Pulido A, Alonso A, Antolín-Amerigo D, González-Mancebo E, et al. Consensus document on dog and cat allergy. *Allergy.* 2018; 73(6):1206–22.
- 20 Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, et al. EAACI molecular allergology user's guide. *Pediatr Allergy Immunol.* 2016;27(Suppl 23):1–250.
- 21 Casas ML, Esteban Á, González-Muñoz M, Labrador-Horrillo M, Pascal M, Teniente-Serra A. Proyecto VALIDA: validation of allergy in vitro diagnostics assays (Herramientas y recomendaciones para la valoración de las pruebas in vitro en el diagnóstico de la alergia). *Adv Lab Med/Av en Med Lab.* 2020; 1:20200022.
- 22 Nwaru BI, Suzuki S, Ekerljung L, Sjölander S, Mincheva R, Rönmark EP, et al. Furry animal allergen component sensitization and clinical outcomes in adult asthma and rhinitis. *J Allergy Clin Immunol Pract.* 2019;7(4):1230–8. e4.
- 23 Uriarte SA, Sastre J. Clinical relevance of molecular diagnosis in pet allergy. *Allergy.* 2016; 71(7):1066–8.
- 24 Bjerg A, Winberg A, Berthold M, Mattsson L, Borres MP, Rönmark E. A population-based study of animal component sensitization, asthma, and rhinitis in schoolchildren. *Pediatr Allergy Immunol.* 2015;26(6):557–63.