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Component Resolved Diagnosis (CRD): how much is it presently used by Italian allergists?

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Summary
Component resolved diagnosis (CRD) represents an innovative and revolutionary tool in allergy diagnosis. At the same time, some criticisms can be outlined. The present web survey aimed at investigating the role of CRD in daily clinical practice, according to a sample of Italian specialists who manage allergic patients. 127 physicians, mostly allergists, completed the questionnaire, mainly coming from North and Center of Italy. Most of them (80%) were allergists. One physician out of three regularly takes into consideration CRD, that is currently available about in a half of the hospitals where the specialists work. CRD is mostly prescribed in the diagnostic work-up of suspected food allergy, as it can drive risk assessment, epinephrine prescription and dietary advice. Concerning respiratory allergy, CRD is considered useful in investigating cross-reactivity and in defining the best treatment option, even if only 32% of patients treated with immunotherapy had been previously studied with CRD. The present survey points out the need for the specialists to develop a more practical know-how about CRD. Its diagnostic accuracy and its real impact on the clinical management need to be better defined. The lacking of CRD technology in many hospitals limits the possibility for many allergists to directly experience molecular diagnosis.

Introduction

The best approach for the correct diagnosis of allergy is based on information collected from a well-targeted and detailed medical history and physical examination. Nevertheless, once there are sufficient clinical grounds to suggest a diagnosis of allergy, confirmatory in vivo and in vitro tests are usually indicated. In vitro techniques have rapidly grown up in the last two decades (1). Allergen-specific IgE antibody is the most important serological marker used in the diagnosis of allergic disease to confirm sensitization in an individual who has a positive history of exposure. Thanks to Component resolved diagnosis (CRD), nowadays we are able to collect more detailed information about the sensitization profile of allergic patients (2). Third generation auto-analyzers allow accurate, reproducible and quantitative measurements of the levels of IgE antibody directed to single molecular components (ImmunoCAP) (1). Moreover, also a multiplexed, microarray-based allergy test is available (ISAC) (2). It measures IgE antibodies to multiple allergenic components in one analysis and has a high negative predictive value. Defined panels of aeroallergens and food allergens relevant to different age groups are used (3). The multi-allergen screen is a cost-effective test, especially when more than 10 components have to be tested, but produces only qualitative results (1).

At the same time, the CRD approach still represents a challenge for allergists. In the present survey we investigated allergist's opinions about the use of CRD in daily practice and looked for criticism and unmet needs, that may affect its use in daily routine.

Materials and methods

A web anonymous questionnaire was available on the website of the Association of Italian Allergists (AAITO - www.aaito.it) for 60 days, from 1st January 2012 to 28th February 2012. An invitation to participate to the survey was sent twice by e-mail to all 583 members of the Association, 30 days apart. The 23 multiple-choice questions concerned the following items: specialization and provenance of the physicians involved in the survey, CRD-related know-how, number of allergic patients visited per week, diagnostic in vivo and in vitro tools commonly used, reasons for using CRD (ImmunoCAP or ISAC) and expected information.

Results

127 physicians (21.7% of AAITO members) completed the questionnaire, mainly coming from North and Center of Italy. Most of them (80%) were allergists. Other specialists such as pediatricians (19%), pneumologists (11%) and dermatologists (1%) who manage allergic patients in their clinical practice filled the questionnaire as well. The interviewed physicians report to know and use CRD since 30 months on average. They visit 39 patients per week on average (range 6-60). In 29% of cases specific IgE evaluation is requested, in 12% of cases with molecular components. One physician out of three is used to take into consideration both single ImmunoCAP components and ISAC, depending on diagnostic work-up complexity and on the number of single molecular components needed to be tested. Six molecular components per patient are assayed on average. About half of the specialists reported that neither ImmunoCAP nor ISAC is available in the hospital where they work, and therefore 48% of patients are forced to move to another hospital to have the test done. CRD is mostly prescribed in the diagnostic work-up of suspected food allergy (> 90%). It is included also in latex allergy (61% of cases) and Hymenoptera venom allergy (45% of cases) diagnosis (**figure 1**). CRD is applied especially when patients are polysensitized to inhalant allergens, food, or both, and when clinical profile is quite severe or complex (i.e. discordance between symptoms and in vivo tests results). Concerning respiratory allergy, specialists consider CRD a useful tool in order to investigate cross-reactivity (86.3%) and to define the best treatment option (73.5%).

Nevertheless, among the patients treated with specific immunotherapy only 32% had been previously studied with CRD. In the case of food allergy, almost 90% of specialists consider CRD a useful tool in order to point out cross-reactivity phenomena. According to more than 65% of specialists, CRD also can drive risk assessment, epinephrine prescription and dietary advice (**figure 2**). Almost 90% of physicians state that their CRD-related know-how comes mostly from scientific congresses and literature (**figure 3**). Lack of CRD technology in the hospital where they work seems to explain why many specialists don't use CRD. Most of them would like to improve their knowledge about CRD through practical courses and e-mail updating (**figure 4**).

Figure 1 - *Prescription of components in different allergy suspicions.*

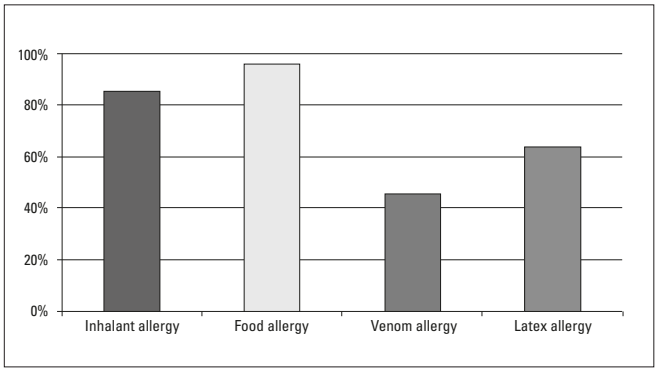


Figure 2 - *Benefits of CRD in Food Allergy.*

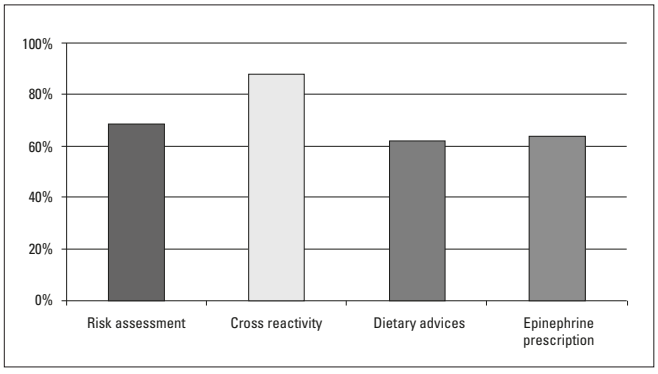


Figure 3 - *Sources of CRD know-how.*

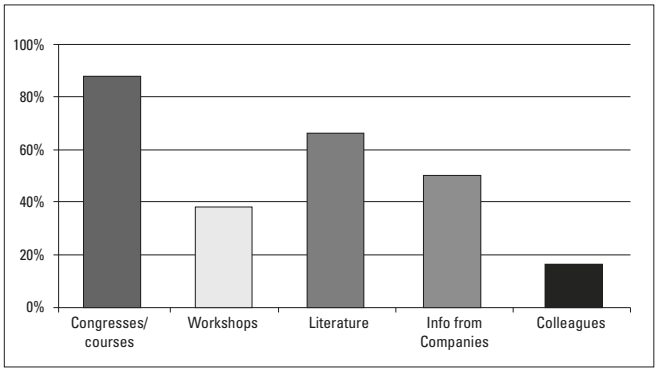
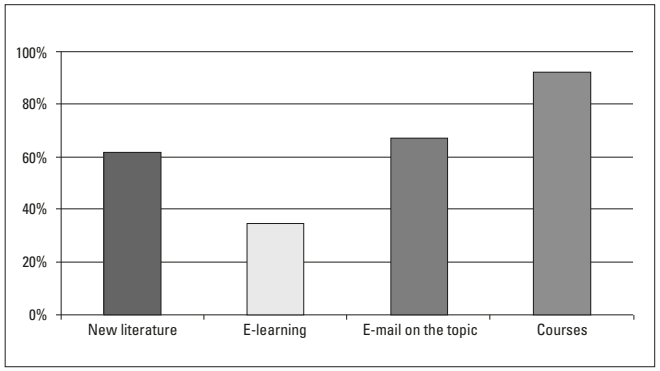


Figure 4 - *Tools needed to increase knowledge on CRD.*



Discussion

During the last two decades, the major and minor IgE binding proteins of the most prevalent allergenic natural sources have been characterized at a molecular level, and many of them are available as recombinant or highly purified proteins. Diagnostic tests based on single recombinant (or natural) allergens, both in classical and in microarray format, have been developed allowing to better define the sensitization profile of allergic patients. The CRD represents an innovative and revolutionary concept in allergy diagnosis. It allows to discriminate between cross and co-sensitization (4), to help in selecting the most appropriate immunotherapy (5,6,7) and to estimate the risk of severity of the clinical manifestations in food allergy (8). According to our survey, Italian specialists who manage allergic patients show great interest and awareness of CRD, even if it could be defined more as a theoretical knowledge than as a real know-how. In fact, few specialists report to include the use of CRD in their daily clinical practice. On one hand it may reflect one of the limits of new molecular diagnostic tools. In fact, before the CRD tests and in particular the microarray-based tests become a standard diagnostic tool in clinical laboratory, clinicians and pathologists have to better define their diagnostic accuracy and their real impact on the clinical outcome (7). On the other hand, according to our data a fully spread knowledge about CRD is still lacking. Another problem is the lack of CRD technology in many hospitals. It limits the possibility for many allergists to directly experience molecular diagnosis.

In conclusion, the present survey points out the need for allergists and other specialists who treat allergic patients to develop a practical know-how through courses and constant updating concerning the use of molecular tools. Moreover, an easy-access network involving specialists and referral centers for CRD diagnosis should be created. Finally, it has to be stressed that specialists visit 39 patients per week on average. Considering the burden of allergic disease from an epidemiological point of view, it means that less than 15% of allergic patients is visited by a specialist and therefore an easier access to allergists has also to be improved for a better management of allergic diseases.

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