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ORIGINAL ARTICLE

National Dyslipidemia Registry of the Spanish Arteriosclerosis Society: Current status☆

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Abstract
Introduction: Clinical registries are a very effective tool to verify the usual clinical practice, to compare clinical strategies and to improve the knowledge of diagnostic and therapeutic new procedures.
Methods: The National Registry of Dyslipemias of the Spanish Society of Arteriosclerosis (SEA) is an on-line, retrospective and prospective database where the different Spanish lipid units accredited by the SEA introduce data from patients with disorders of lipid metabolism.
Results: The registry was created in 2013, and since then clinical, analytical, genetic and evolutionary data of 4449 patients have been introduced until June 2017. In the last year the registry has given rise to a considerable number of international publications and there are several more in progress. An ambitious incentive plan for inclusion of patients has been initiated to get the SEA registry as a global reference that helps to improve the knowledge and clinical management of these patients.

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Conclusions: From the coordinating group of the registry we encourage all SEA partners to collaborate in the multiple forms that the registry allows, and to make it an international scientific reference.

PALABRAS CLAVE
Registro;
Dislipemias;
Hipercolesterolemia familiar;
Sociedad Española de Arteriosclerosis

Registro Nacional de Dislipemias de la Sociedad Española de Arteriosclerosis: situación actual

Resumen
Introducción: Los registros clínicos son una herramienta muy eficaz para comprobar la práctica clínica habitual, comparar estrategias y mejorar el conocimiento de diferentes procedimientos diagnósticos y terapéuticos.
Métodos: El Registro Nacional de Dislipemias de la Sociedad Española de Arteriosclerosis (SEA) es una base de datos *on-line*, retrospectiva y prospectiva, donde las diferentes unidades de lípidos españolas acreditadas por la SEA introducen datos de pacientes con trastornos del metabolismo lipídico.
Resultados: El registro fue creado en 2013, y desde entonces datos clínicos, analíticos, genéticos y evolutivos de 4.449 pacientes han sido introducidos hasta junio de 2017. En el último año el registro ha dado pie a un número considerable de publicaciones internacionales y existen varias más en desarrollo. Se ha iniciado un ambicioso plan de incentivación de inclusión de pacientes para conseguir que el registro de la SEA sea un referente mundial que ayude a mejorar el conocimiento y el manejo clínico de estos pacientes.
Conclusión: Desde el grupo coordinador del registro animamos a todos los socios de la SEA a colaborar en el mismo en las múltiples formas que el registro permite, y conseguir que sea una referencia científica internacional.

Introduction

The National Dyslipidaemia Registry of the Spanish Arteriosclerosis Society (Sociedad Española de Arteriosclerosis, SEA) is a national, online (http://www.rihad.es), anonymised and multi-centre registry where a significant number of lipid units throughout the different autonomous communities of Spain enter the information of patients with a lipid metabolism disorder that have been looked after in these units. All lipid units that participate in the registry have been accredited by the SEA and at least the director must be an active member of the society. The precedent to the current dyslipidaemia registry was created in 2011 with the acronym ''RIHAD'', whose aim was to create a single registry of patients with dominant, autosomal hypercholesterolaemia with a genetic study of the LDL receptor (*LDLR*). This was conceived and put in place by Prof. Miguel Pocoví, of Zaragoza, with a grant awarded by Progénika Biopharma and IT support from a specialised company called INFOZARA. In the course of 2012, the SEA took the decision to transform this registry into a broader and more dynamic platform that included other lipoprotein disorders, prospective and retrospective data and the participation of most of the units accredited by the SEA. This is how the current registry emerged, which has come to be known as the National Dyslipidaemia Registry of the Spanish Arteriosclerosis Society, where the SEA is the only data custodian. At that time, the guidelines, general aims and associated projects were established, a coordinator was appointed (Prof. Fernando Civeira), the project was approved by the Independent Ethics Committee of Aragon in September 2012 and was presented at the 26th SEA conference in May 2013, held in Zaragoza.

The purpose of this article is to inform the scientific community, and especially all SEA members, about the structure, projects, current patient enrolment situation and plans for the near future.

The registry is a scientific tool to improve knowledge of lipid metabolism disorders in Spain. It is designed to facilitate easy access to objective, quality, retrospective and prospective information with a common methodology for all projects and all lipid units. It simultaneously records a large amount of information online on behalf of the lipid units (socio-demographic data, family and personal history, analytical data with and without treatment, genetic data, lipid-lowering treatment and other patient treatments). Because the information is obtained from qualified clinical professionals from lipid units throughout the Spanish communities and it is subjected to certain quality criteria, the National Dyslipidaemia Registry of the SEA has become a tool of high scientific value.

Objectives

The general objective is to provide a database to improve knowledge of lipid metabolism disorders in Spain. The secondary objectives are to improve the diagnosis and treatment of these disorders; perform clinical studies; create a collaboration structure in care and research with other scientific societies, companies or research groups; and to collaborate with other similar databases around the world.

The operational objectives are updated every year and for 2017 they are as follows:

1. Enrolment of up to 5000 patients in the registry by 31 December 2017. All types of dyslipidaemia may be included but we want to prioritise the inclusion of patients with familial hypercholesterolaemia, including children, severe hypertriglyceridaemia, diabetic dyslipidaemia or patients with hyperlipoproteinaemia (a).
2. Reconsideration of the research projects associated with the registry, its managers and updating the methodology.
3. Creation of a list of managers and members of the units that participate in the registry and their inclusion in publications derived from the registry.
4. Publication of at least three articles in international journals with data derived from the registry.
5. Hold two meetings throughout the year with the highest possible attendance of representatives from the lipid units, coinciding with the Annual Meeting of Lipid Units and the SEA National Conference.

General rules for the operation of the registry

1. The registry belongs to the SEA, which is the data custodian and is in charge of its maintenance and funding.
2. The management and exploitation of data is delegated by the SEA to a scientific committee that is currently composed of five members and who are the signatories of this report.
3. The composition of the scientific committee is established by the SEA Board of Directors, proposed by the coordinator appointed by the board.
4. All participating lipid units must be approved by the SEA and at least its director must be an active member.
5. Each unit will be responsible for entering data into the registry anonymously, for data integrity and for giving consent for their use in accordance with publication guidelines.
6. Publications derived from the exploitation of data will be regulated by the following guidelines:

a. Periodic description of new developments in the functioning of the registry: the authors will be members of the scientific committee.
b. Studies derived from the exploitation of registry data: the authors will be three investigators from the specific study, including the first and last authorship, and five more authors from among the investigators of the units according to the number of valid cases used in the study.
c. Studies using registry data and data generated independently by other studies (cooperative groups, consortiums and coordinated projects): the authors will be a member of the registry committee and a variable number of investigators from the units according to the weight of the registry data.

The distribution of authors among the investigators of the units will be according to the D'Hondt method, with separate lists for articles. The conduct of studies to be reported at conferences is also included. The same procedure will be used as the one for scientific articles but with independent lists.

7. The publications that use data from the registry will be approved by the registry's scientific committee.
8. Quality control, evaluation of information and implementation of new developments will be performed annually.

Current status of the registry

The registry has developed very positively in its almost five years of operation, both in the number of participating units as well as the number of cases entered, variety of dyslipidaemias analysed and scientific results obtained.

As of 15 June 2017, 60 units from throughout Spain are participating in the National Dyslipidaemia Registry of the SEA (Fig. 1), with a total of 4449 recorded patients. Since 2013, the recorded number of patients has been progressively increasing (Fig. 2). It is worth highlighting that during the year 2013, the increase in the number of patients recorded was very significant, with 1306 patients recorded, belonging to 15 national units. In 2014 and 2015, although significant, the number of new patients was lower, coming from 17 units. During 2016, there was a significant increase with respect to the two previous years thanks to a campaign incentivising enrolment. The number of new patients recorded in 2017 is somewhat lower than that of 2016, but it is likely that the proposed objective for the end of this year (2017) will be achieved.

Participating lipid units

Of the 60 units registered by the SEA, 37 have currently enrolled at least one patient (Fig. 3). The fact that 38.3% of our units have not yet recorded a single case must be considered as one of our current limitations and reversing this situation will be the primary objective in the immediate future. The Registry Committee has proposed a series of data inclusion incentives, which include financial compensation per valid case and the possibility of conducting doctoral theses and degree and master's dissertations with registry data following the registration of a certain number of complete cases.

Diagnoses

At least one diagnosis per case can be entered into the registry. The list of possible diagnoses is shown in Table 1. Most of the patients currently recorded have a diagnosis of familial, genetic and/or clinical hypercholesterolaemia. Other diagnoses with a significant number of patients include: familial combined hyperlipidaemia, severe hypertriglyceridaemia, familial chylomicronaemia syndrome, homozygous

Figure 1 Distribution of lipid units in the Dyslipidaemia Registry of the Spanish Arteriosclerosis Society.

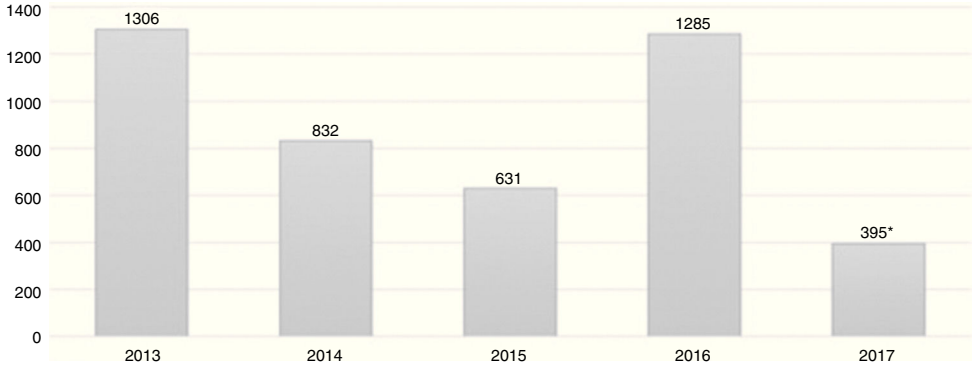

Figure 2 Total number of patients registered annually.

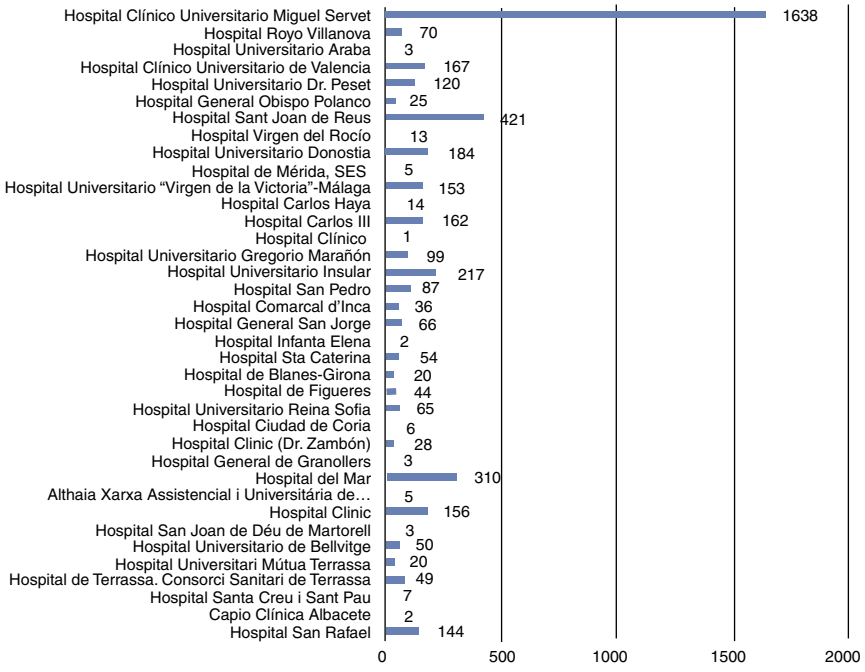

Figure 3 Number of patients registered by lipid units.

Table 1 List of potential diagnoses from the National Dyslipidaemia Registry of the Spanish Arteriosclerosis Society.

Diagnoses
Familial hypercholesterolaemia
LDLR, *ApoB*, *PCSK9* and *ApoE* receptor-dependent familial hypercholesterolaemia
Non-*LDLR*, *ApoB*, *PCSK9* and *ApoE*-receptor familial hypercholesterolaemia
Familial hypercholesterolaemia without genetic diagnosis (unknown or pending)
Homozygous familial hypercholesterolaemia (National Registry)
Polygenic hypercholesterolaemia
Familial combined hyperlipidaemia
Dysbetalipoproteinaemia
Hypoalphalipoproteinaemia
Hypobetalipoproteinaemia
Hypertriglyceridaemia
Familial hypertriglyceridaemia
Sporadic hypertriglyceridaemia
Familial chylomicronaemia syndrome
Rare diseases
Abetalipoproteinaemia
Apo A1 deficiency
Hepatic lipase deficiency
LAL deficiency
LCAT deficiency
LPL, Apo CII and LPL inhibitor deficiency
Tangier disease
Cerebrotendinous xanthomatosis
Sitosterolaemia
Secondary dyslipidaemia
Others

familial hypercholesterolaemia, dysbetalipoproteinaemia and diabetic dyslipidaemia. The variety of diagnoses makes the registry a useful and valid tool for any unit, irrespective of the number of patients and common diagnoses that are treated by the various lipid units, facilitating collaboration in one or more lines of research.

Research projects

The registry aims to increase knowledge of all types of dyslipidaemia in Spain. This is achieved through 12 research projects on different lipid metabolism disorders (Table 2). These 12 projects (lines of work) have been in progress since the end of 2014 and have the backing and leadership of investigators and co-investigators of recognised prestige, charged with carrying out both the realisation and export of data and results. There are three projects on familial hypercholesterolaemia, which already have 2855 cases. The projects on familial combined hyperlipidaemia, atherogenic dyslipidaemia in diabetes (PREDISAT study) and severe hypertriglyceridaemia, with 810, 391 and 245 patients, respectively, are projects of special scientific interest for 2017–2018. Other ongoing projects include: intolerance to statins, dysbetalipoproteinaemia, hypoalphalipoproteinaemia and dyslipidaemia in very premature cardiovascular disease. Due to the dynamism in the design and development of new projects, we can generate and continue with projects in the future and be a benchmark in the study of lipid diseases on a national level or even globally.

Registry publications

Publications conducted with data derived from the exploitation of the familial hypercholesterolaemia study may be consulted in the recommended reading, available at the end of this article. Furthermore, there is a series of articles currently being prepared that include: autosomal

Table 2 Ongoing research projects by the National Dyslipidaemia Registry of the Spanish Arteriosclerosis Society.

Projects	Investigator	Co-investigator(s)
Cardiovascular disease in heterozygous familial hypercholesterolaemia	Dr. Fernando Civeira	Dr. José Puzo
Prevalence of cardiovascular disease in familial combined hyperlipidaemia	Dr. Juan F. Ascaso	Dr. Luis Álvarez
Lipid objectives in heterozygous familial hypercholesterolaemia Level of dyslipidaemia control and drugs used	Dr. Emilio Ros	Dr. Fátima Almagro
Risk stratification in familial hypercholesterolaemia. Independent factors associated with the development of clinical or subclinical disease	Dr. Núria Plana	Dr. Clotilde Morales
Intolerance to statins. Prevalence, clinical manifestations, level of dyslipidaemia control and baseline risk	Dr. José Mostaza	Dr. Ángel Brea
Atherogenic dyslipidaemia in diabetes. PREDISAT study	Dr. Jesús Millán	Dr. Antonio Hernández Mijares
Severe hypertriglyceridaemia	Dr. Pedro Valdivielso	Dr. Emilio Ruíz
Dysbetalipoproteinaemia	Dr. Francisco Pérez Fuentes	Dr. Juan Ferrando
Dyslipidaemia in very premature cardiovascular disease	Dr. Xavier Pintó	Dr. Manuel SuárezDr. Marta Mauri
Rare dyslipidaemia	Dr. Leonardo Reinares	Dr. Juan de Dios García
Homozygous familial hypercholesterolaemia. National Registry	Dr. Rosa M. Sánchez-Hernández	Dr. Francisco Javier Novoa
Hypoalphalipoproteinaemia	Dr. Juan Pedro-Botet	Dr. Jacinto Fernández

recessive hypercholesterolaemia in Spain; genotype of severe hypertriglyceridaemia and the impact of statins on cardiovascular disease in familial hypercholesterolaemia. All these are expected to be sent for publication during 2017.

Conclusions and final reflections

The National Dyslipidaemia Registry of the SEA is positioning itself as one of the most important databases on lipid metabolism disorders in the world. Our excellent healthcare system, which uniformly covers almost the entire population, the leadership of the SEA in the field of dyslipidaemia and the role of lipid units as units of excellence are making this possible. The registry is designed to facilitate the participation of all members of the SEA, whether they belong to lipid units or not. They can contribute by leading projects, entering cases, proposing ideas, supervising students, writing articles, etc. The Registry Committee encourages everyone to work in it to help make it grow and improve, with the main objective of improving our knowledge and providing even better care to our patients.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols implemented in their place of work regarding the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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