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The Dutch neuromuscular database CRAMP (Computer Registry of All Myopathies and Polyneuropathies): Development and preliminary data

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Abstract

Each of the various neuromuscular diseases is rare. Consequently, solid epidemiological data are not available and it is often difficult to find sufficient patients for studies. For this reason, the Dutch neuromuscular database, CRAMP (Computer Registry of All Myopathies and Polyneuropathies), was developed in 2004 by the Dutch Neuromuscular Research Support Centre, to store information on patient characteristics and diagnoses (based on Rowland and McLeod's classification) in a uniform and easily retrievable manner. Care was taken to preserve data confidentiality. It is envisaged that CRAMP will prove particularly useful for studies in which multicentre collaboration is needed to recruit a sufficiently large number of patients. More than 10,000 patients with neuromuscular diseases (4837 female, 5476 male) have been registered since 2004, half of whom ($n = 5059$) have peripheral nerve disorders.

Keywords: Neuromuscular diseases; Epidemiology; Database; Prevalence

1. Introduction

The WHO Global Burden of Disease report pointed out that the burden of mental and neurological disorders has been seriously underestimated by traditional epidemiological methods that took into account mortality, but not disability, rates (http://www.who.int/mental_health/neurology/en/). While mental and neurological disorders are responsible for only about 1% of deaths, they account for almost 11% of disease burden worldwide, suggesting that the burden of *neuromuscular disorders* is seriously underestimated.

CRAMP (Computer Registry of All Myopathies and Polyneuropathies) was developed in The Netherlands to

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store information on the characteristics and diagnoses of patients seen at one of the Dutch University Medical Centres or a large regional medical centre. The aim was to use this database to recruit appropriate patients for treatment trials and research, including population-based and epidemiological studies of the various neuromuscular diseases. Such a database would also make it possible to estimate the burden of neuromuscular diseases in The Netherlands.

2. Methods

2.1. CRAMP participants

The neuromuscular centres of the seven University Medical Centres and one large regional medical centre in The Netherlands provide information for the CRAMP database designed by ISNO, the Dutch Neuromuscular Research Support Centre.

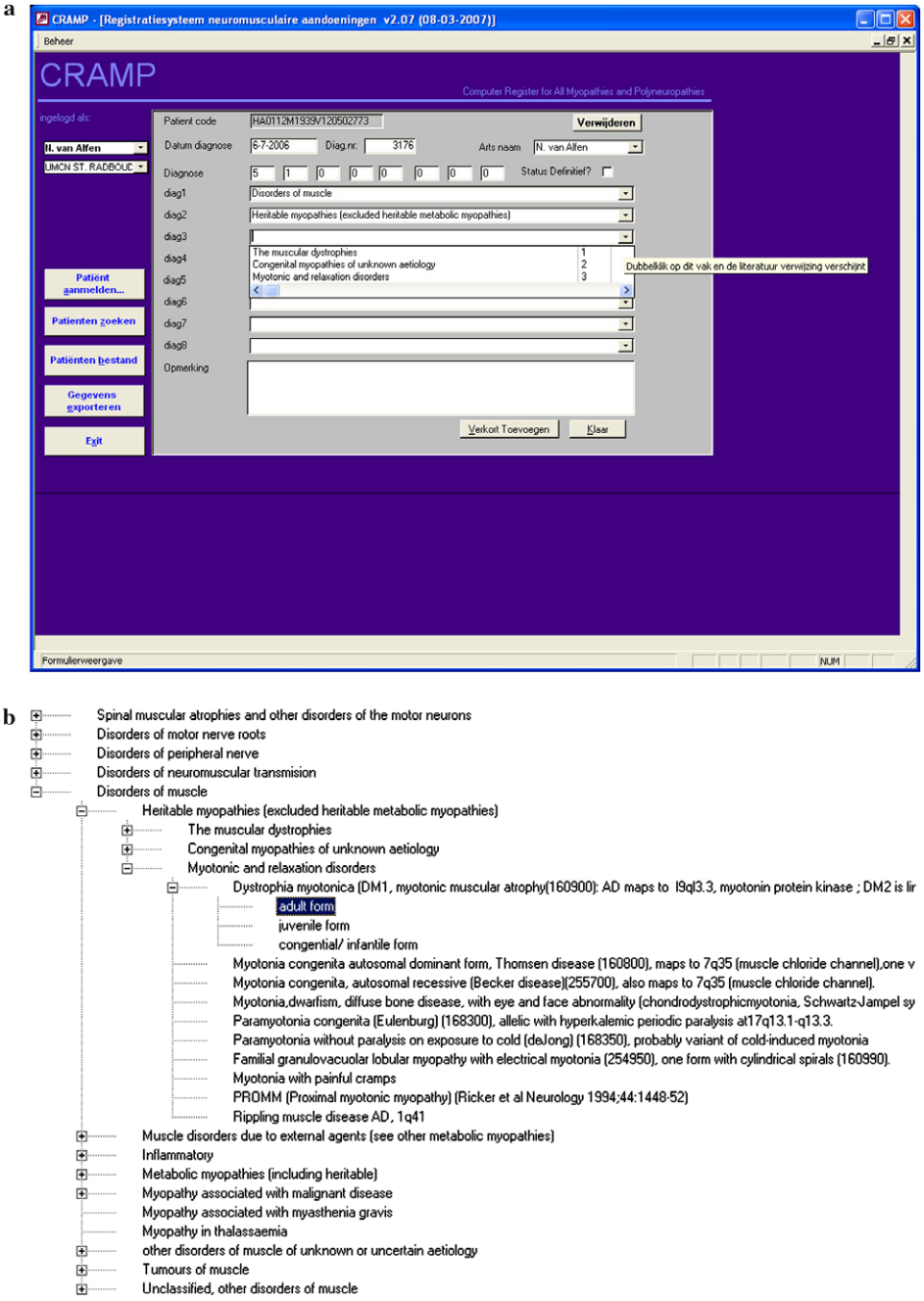

Fig. 1. (a) Entering the diagnosis *myotonic dystrophy* in CRAMP. (b) Part of the tree-like structure, highlighting the adult form of myotonic dystrophy.

Table 1
Selected neuromuscular diagnoses with number of patients in the CRAMP database

Diagnosis	Number	Diagnosis	Number	Diagnosis	Number
Disease of motor neurons	1079	Disease of motor neurons of undetermined aetiology	680	Amyotrophic lateral sclerosis	328
Disease of motor nerve roots	618	Neuralgic amyotrophy	391		
Disease of peripheral nerve	5059	Neuropathy associated with paraproteinaemia	172		
		Chronic neuropathy with no known cause	640		
Disease of neuromuscular transmission	601	Autoimmune disorders of neuromuscular transmission	552	Myasthenia gravis	494
Disease of muscle	2956	Heritable myopathies	1294	Myotonic dystrophy, adult	333
		Inflammatory myopathies	383	Sporadic inclusion body myositis	123
		Metabolic myopathies	497	Mitochondrial and lipid myopathies	227
		Unclassified, other disorders of muscle	605		

2.2. CRAMP system

CRAMP is a stand-alone system that is connected to the participating hospitals' information systems, which makes it possible to retrieve patient information by entering the patient's unique hospital number. The data contained in CRAMP includes the name of the hospital, and the patient's code number, postal code, diagnosis, date of diagnosis, date of birth, sex, date of first consult, and date of death (if applicable). Additional information can be entered, if desired. All patient information is entered in English. Great care has been taken to preserve the confidentiality of patient data, with patients being referred to by individual code numbers. Individual patient data are stored at the local hospital, and only the CRAMP code (unique for each patient) and the diagnoses are sent by email twice a year to the central CRAMP database. Thus only the local CRAMP representatives have access to the detailed data of the patients seen in their own hospital. CRAMP was developed with Microsoft Access and can be accessed through a personal computer.

2.3. Neuromuscular disorders

Neuromuscular disorders are classified according to an established international classification [1], supplemented with clinical genetic data as these become available. The database has a tree-like structure, with maximally five "branches" at each of the maximally eight levels of data entry. An additional subheading "*unclassified*" was added to "disorders of muscle" and to "disorders of peripheral nerves". Because clinical data, such as lactate and creatine kinase levels (CK; normal, elevated), EMG findings (normal, abnormal, not done), and muscle biopsy findings (normal, abnormal, not done), are also registered, it is possible to enter patients in the database who have certain features but who have not been diagnosed with a classified neuromuscular disease.

2.4. CRAMP input

It usually takes less than a minute to enter the relevant information. The patient's hospital number is entered first and then the programme automatically obtains the patient data (name, date of birth, sex) from the local hospital information system. The neurologist then adds information about the neuromuscular diagnosis (Fig. 1a and b). The first level offers five possible choices, reflecting the anatomy of the peripheral nervous system: (1) 'spinal muscular atrophies and other disorders of the motor neurons', (2) 'disorders of motor nerve roots', (3) 'disorders of peripheral nerves', (4) 'disorders of neuromuscular transmission', or (5) 'disorders of muscle' (Table 1). The choices available at the next level depend on the choice made at the first level. These include further anatomical subdivisions such as axonal versus demyelinating, or a subdivision based on pathogenesis, such as toxic, infectious, or degenerative. Although the diagnostic tree has a maximum of eight levels, or divisions, in practice a disease can be described in fewer steps. For example (Fig. 1b) adult myotonic dystrophy is a disorder of muscle (code 5), heritable (code 5.1), belongs to the group of myotonic and relaxation disorders (code 5.1.3), myotonic dystrophy (code 5.1.3.1), adult form (code 5.1.3.1.1).

3. Results

Data collection started in 2004. The eight neuromuscular centres function as referral centres for the whole of The Netherlands (population 16.3 million). To date,

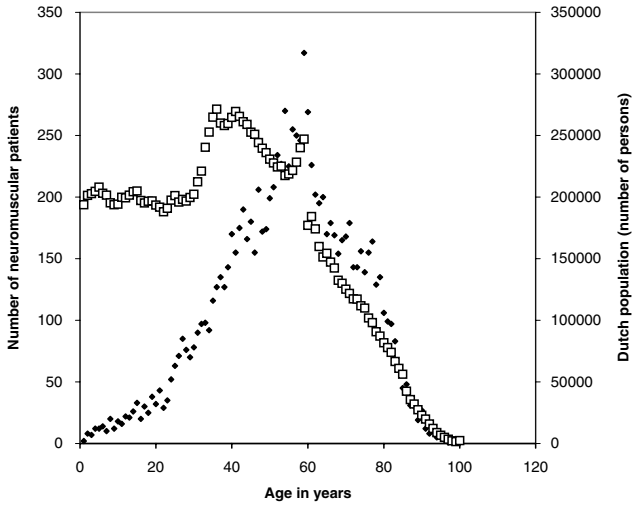

Fig. 2. Age distribution of 10,313 Dutch patients with neuromuscular diseases (♦) and the general Dutch population (□).

10,313 patients with neuromuscular diseases have been entered in the registry, 5476 males (53%) and 4837 females (47%). The numbers of patients from the individual centres ranges from 404 to 3628 patients. Of the three centres with the highest number of patients, two have connected the CRAMP database to the hospital diagnosis–treatment registration system. Two of these centres also have the most neurologists specialized in neuromuscular diseases.

Unlike the age distribution of the Dutch population, the ages of the patients with neuromuscular diseases show a normal distribution (Fig. 2). This may be because until now few child neurologists participate in CRAMP, or the prevalence of neuromuscular diseases is indeed lower in these age groups. Information about the patients' postal code has made it possible to study the regional distribution of neuromuscular diseases, with the number of patients with neuromuscular disorders being corrected for the number of inhabitants of each region (Fig. 3).

The number of patients in the database with specific neuromuscular diagnoses is given in Table 1. The manner in which data are entered makes it possible to identify various diseases affecting more than a certain number of patients. For example, more than 100 patients have been diagnosed with the following diseases: amyotrophic lateral sclerosis ($n = 328$), progressive

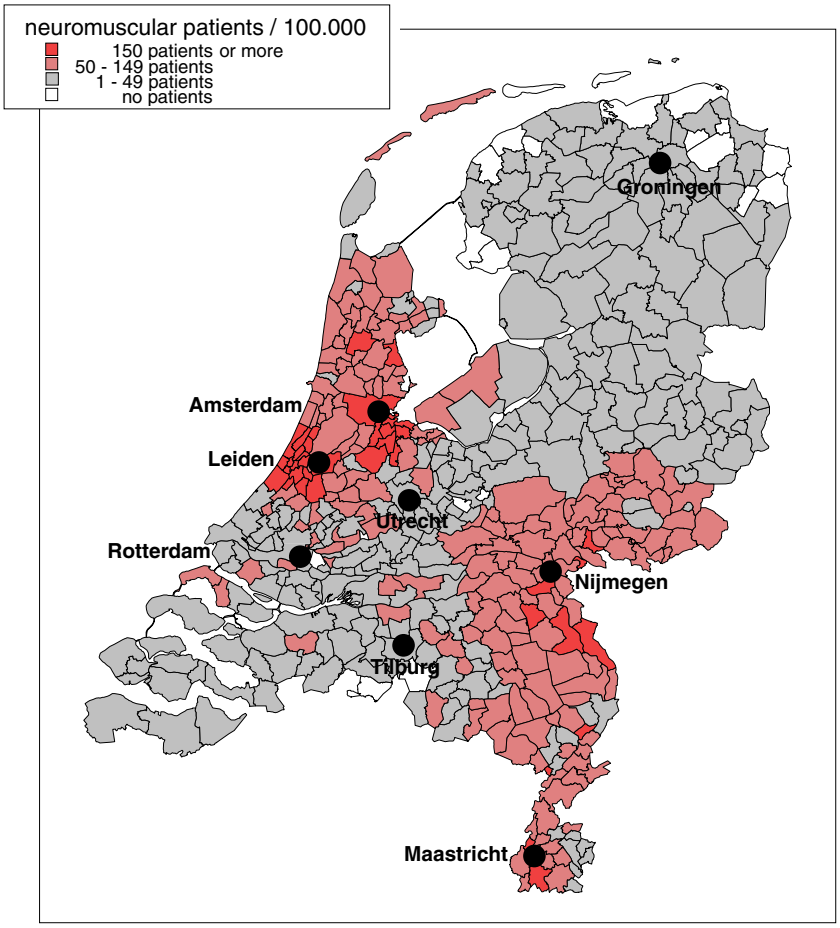

Fig. 3. Regional distribution of the 10,313 patients with neuromuscular diseases in The Netherlands, expressed as the number of affected patients per 100,000 inhabitants.

spinal muscular atrophy ($n = 140$), post-polio syndrome ($n = 132$), CMT1 ($n = 238$), CMT2 ($n = 182$), neuralgic amyotrophy ($n = 391$), chronic inflammatory demyelinating neuropathy ($n = 161$), Guillain-Barré syndrome ($n = 115$), neuropathy associated with paraproteinaemia ($n = 172$), carpal tunnel syndrome ($n = 916$), vasculitic neuropathy ($n = 104$), neuropathy associated with endocrine disorders ($n = 253$), chronic neuropathy with no known cause ($n = 640$), myasthenia gravis ($n = 494$), Duchenne and Becker muscular dystrophies ($n = 114$), facioscapulohumeral dystrophy ($n = 231$), limb girdle muscular dystrophy ($n = 161$), myotonic dystrophy ($n = 391$), glycogen storage myopathies ($n = 108$), mitochondrial and lipid myopathies ($n = 227$), inflammatory myopathies ($n = 383$), inclusion body myositis ($n = 123$), unclassified weakness ($n = 119$), unclassified cramps ($n = 147$), unclassified muscle pain ($n = 163$).

4. Discussion

We report on the development of the Dutch national database of neuromuscular diseases, CRAMP. The software is user-friendly and fast. We have taken great care to preserve patient and data confidentiality. The data of a large number of patients ($n = 10{,}313$) have been entered in the CRAMP database in a relatively short time. We believe that this success is because only a minimal amount of data needs to be entered; more detailed patient information for research purposes (e.g., special features of facioscapulohumeral dystrophy) can be retrieved from the patient records. We conclude that this is a better approach than including a large amount of detailed information in the database, because it is difficult to determine in advance which patient information will be relevant for a given future research project.

While CRAMP can be used in individual centres to identify patients with neuromuscular diseases, it is intended to facilitate the recruitment of patients for multicentre research and clinical trials, and provides the opportunity to extract epidemiological data on neuromuscular disorders in The Netherlands. In addition, the structured way in which data are entered in the database may facilitate diagnosis by providing clinicians with a differential diagnostic decision tree (Fig. 1a and b).

Epidemiological data on neuromuscular disorders are sparse, yet these data are important to alert health, community, and political decision-makers to the possible underestimation of the burden of neuromuscular disorders when emphasis is put on mortality, rather than on the prevalence of chronic diseases and disability rates.

Some factors concerning the content of the database have to be addressed. The present CRAMP data are partly retrospective because patients who were diagnosed with a neuromuscular disease in the past and who are still attending a neuromuscular centre have also been entered in the database. The patients entered in the database may be biased by the research or clinical interest of the participating neuromuscular departments of the university hospitals. For example, CRAMP includes more patients with myasthenia than patients with diabetic neuropathy. This bias will be resolved if more non-university centres participate and if more centres integrate CRAMP into their hospital registration system. Despite these shortcomings, we are able to study changes in incidence of neuromuscular disorders on the basis of the information that is collected twice a year.

In conclusion, CRAMP is the first nationwide database for neuromuscular disorders. It can serve several purposes, from patient recruitment for trials to estimation of the burden of neuromuscular disorders. Now that diagnostic criteria for most neuromuscular disorders have been established [2], the next step is to collect information on patient diagnoses in a database system, such as CRAMP, at a European level.

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