

## Articles

## Prevalence of Essential Tremor on Arosa Island, Spain: a Community-based, Door-to-Door Survey

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### Abstract

**Background:** The prevalence of essential tremor (ET) is still not well understood and the various studies performed to date have generated highly variable results. Few epidemiologic studies on the prevalence of ET have been reported from Spain.

**Methods:** A one-stage door-to-door survey was conducted on Arosa Island, northwestern Spain, to determine the prevalence of ET in the population aged 65 years and older. The diagnostic criteria for ET were the presence of non-dystonic head tremor or moderate- to severe-amplitude tremor on at least four tests of the revised Washington Heights-Inwood Genetic Study of Essential Tremor (WHIGET) Scale.

**Results:** A total of 65 individuals with ET (28 males, 37 females) were identified, resulting in a crude prevalence of 8.63% (adjusted rate 8.42%). Prevalence increased with advancing age. There were no significant differences in prevalence between sexes in any of the age groups. Among the prevalent cases, 12.3% (n=8) had been previously diagnosed. Only 29.2% (n=19) reported functional disability caused by tremor. A family history of tremor was reported in 35.4% (n=23).

**Discussion:** The prevalence of ET was higher than that seen in similar populations in Spain and other countries. A high proportion of those with ET were previously undiagnosed. Since Arosa Island has been a relatively isolated area, these results might indicate a predominant role, at least in the elderly, for genetic factors in the development of ET.

**Keywords:** Tremor, essential tremor, elderly, epidemiology, prevalence, survey, population isolate

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### Introduction

Essential tremor (ET) is a common adult movement disorder and a frequent problem reported by individuals seeking neurologic consultation.<sup>1</sup> Although ET is often regarded as a benign condition, it can become very disabling.<sup>2</sup> The prevalence of ET is not precisely known and the various studies performed to date have reported highly variable results.<sup>3</sup> This variability might be because of several factors.<sup>4</sup> First, target populations can have different characteristics in terms of age, sex and ethnicity. Second, tremor can be a clinical manifestation of other neurologic disorders and can even be present in healthy elderly persons;

the diagnosis of ET is still based on clinical or consensus criteria.<sup>5</sup> And third, the methodologic approach is an important issue to consider. Population-based studies are mandatory for ET, since hospital- or clinic-based surveys underestimate prevalences.<sup>3</sup> Most population-based studies of ET have used a two-phase approach with initial screening questionnaires. This type of approach seems to lower the prevalence estimate since a high proportion of cases can screen negative.<sup>6</sup> The use of other screening instruments, such as handwriting samples, can improve the detection of cases, but still poses some limitations.<sup>7</sup> Perhaps the best method of estimating ET prevalence is a one-stage door-to-door

survey of the population with direct interviews and examinations<sup>8</sup> performed by neurologists.

To our knowledge, only two epidemiologic studies of prevalence of ET have been performed in Spain<sup>6,9</sup> and neither included populations from Galicia in northwest Spain. This relative lack of epidemiologic information on ET was a basic motive for the current study. Focusing on the Arosa Island community permitted a simplified methodology, as the target population resided in a well-defined area.

In the present study, we report on the prevalence of ET in individuals aged 65 years of age and older in the Arosa Island community, which is located in the province of Pontevedra, Galicia, Spain. Neurologists examined all of the residents using a standardized neurologic examination, tremor rating scale, and diagnostic protocol.<sup>10–12</sup>

## Methods

Arosa Island is located in the Arosa Fiord (*Ria de Arousa*) offshore of the mainland in Pontevedra, Galicia (northwestern Spain). It spans an area of 7 km<sup>2</sup>. The island is connected to the mainland by a 2 km bridge, which has been operative since 1985. Before construction of the bridge, transport to the mainland was by means of a ferry; previously, the islanders constituted a highly isolated population due to very limited transport to the mainland.<sup>13</sup>

### Participants

As of December 31, 2003, the total population of Arosa Island was 4,882 inhabitants (official census and national health-system list), of which 804 individuals (338 males and 466 females) were aged 65 years or older. A resident was defined as a person living on Arosa Island for at least 9 months each year. Persons who were on the list, and therefore eligible for inclusion, but who had moved away from this community (non-residents) were not traced. After excluding non-residents and deceased individuals who were still on the list, the population target was 753.

Official permission for the study was obtained from the local (the Mayor of the Arosa Island) and medical (Provincial Public Health) authorities. All participants gave their informed consent before participation in the study. Residents who were unable to attend an examination at the local primary health center were also included, after obtaining consent from the resident or his/her primary caregiver; these residents were examined in their homes.

### Study design

The epidemiologic approach was to use door-to-door interviews and neurologic examinations. This study was conducted in parallel with a study on parkinsonism.<sup>13</sup> A letter was sent and/or telephone call was made to each eligible person, giving an examination date at the local primary health center or at the resident's home if the person was unable to attend at the center. Four research neurologists directly examined the participants between March and December 2004. Residents living in private households and those in nursing homes were included.

For individuals who could not be clinically examined or refused an onsite examination, information was obtained from the collaborating primary-care physician who personally attended the individual and had access to medical records. None of the non-examined residents was reported to have any type of tremor.

Each individual underwent a neurologic evaluation by one of the study neurologists searching for clinical symptoms or signs of tremor. Those presenting with postural limb or kinetic tremor were re-examined in the neurology service of the Complejo Hospitalario de Pontevedra and/or Hospital do Salnés, where a complete neurologic examination with videotaping, diagnostic work-up, and reviews were performed. The workup included information on toxin or drug exposure, and family history (first-degree) of tremor or other movement disorders. All other possible causes of tremor were excluded and anti-tremor therapy was initiated if indicated.

**Diagnostic research criteria for ET.** Tremor examination and testing included one test for postural tremor and five for kinetic tremor, performed with each hand (12 tests total). The revised Washington Heights-Inwood Genetic Study of Essential Tremor (WHIGET) Scale<sup>10</sup> was used for the evaluation of tremor and to rate its severity. Two neurologists (M.S.-M. and M.C.R.) were trained to use the rating scale by reviewing a training tape that included educational and self-assessment sections.<sup>10</sup> The neurologists scored each item on the basis of the recorded examinations.

The diagnostic criteria for ET required the presence of non-dystonic head tremor or moderate- to severe-amplitude tremor on at least four tests of this scale. Based on the interviews and examinations, the neurologists independently assigned a diagnosis (ET or normal). Concordance analysis was performed. A final diagnosis was assigned when both neurologists agreed. When they disagreed, a consensus diagnosis was reached following review of the available medical information.<sup>12</sup>

### Data analysis

Crude and age-adjusted prevalence rates for ET were estimated as the number of cases per 100 population on the prevalence date of December 31, 2003. Crude prevalence rates and 95% confidence intervals (CI s) were calculated for the global sample and stratified by sex and the following age intervals: 65–74 years, 75–84 years, and 85 years and older. Adjustment for age was conducted using the 1998 European standard population. The chi-squared ( $\chi^2$ ) test was used to examine the presence of sex and age effects on ET prevalence. Statistical analyses were performed with EPIDAT version 3.1 (Consellería de Sanidade SERGAS/OPS-OMS).

## Results

### Study sample

In January 2003, letters were mailed to the 804 listed residents of the Arosa Island community aged 65 years or older, explaining the objective of this survey and inviting their participation. Twenty-nine individuals were listed in the census but died before the prevalence

**Table 1.** Prevalence of Essential Tremor, Stratified by Age and Sex

Age (Years)	Prevalence, Cases/100 population (95% Confidence Interval) (n)		
	Males	Females	Both Sexes
65–74	7.37 (3.39–11.35) (14)	7.33 (3.76–10.90) (17)	7.35 (4.74–9.95) (31)
75–84	11.34 (4.51–18.17) (11)	8.97 (3.97–13.96) (13)	9.92 (5.94–13.89) (24)
≥85	10.71 (2.27–28.23) (3)	11.47 (2.66–20.29) (7)	11.24 (4.11–18.36) (10)
Total	8.89 (5.59–12.19) (28)	8.45 (5.73–11.17) (37)	8.63 (6.56–10.70) (65)

date, and 22 individuals in the census were non-resident or were not located after multiple telephone calls, letters or other means. Thus, 753 individuals (315 males and 438 females) were considered eligible for examination. Of these, 712 individuals (94.6%) were actually examined, 13 in their homes and the rest at the primary health center. A total of 41 individuals were not examined for the following reasons: refusal to be examined by the research team ( $n=14$ ; 1.9%) or death after the prevalence date but prior to examination ( $n=27$ ; 3.6 %).

### Diagnosis of ET

Of the 712 individuals who were examined, 96 (13.5 %) showed signs of postural and/or action tremor. These participants were re-examined and followed-up by the study neurologists. Of the 14 people who refused to be examined, medical information was provided for 10 individuals by their primary-care physician (researchers R.S.P. and E.T.S.) and/or through medical reports obtained from the reference hospital (Complejo Hospitalario de Pontevedra or Hospital do Salnés) with permission of the individual. None of these individuals was suspected of harboring a tremor or other neurologic disease. Formal medical information was lacking for four individuals, but none showed symptoms suggestive of tremor or movement disorder according to indirect information from the medical and nursing staff of the primary-care centre. Five individuals did not give consent for videotaping.

### Tremor results

A total of 65 participants were identified as having ET (28 males and 37 females; Table 1). Of these, eight individuals (12.3%) had been

previously diagnosed with ET by a physician and were under medical treatment. Nineteen individuals (29.2%) reported functional disability because of tremor. A family history of tremor suggestive of ET in first-degree relatives was reported by 23 individuals (35.4%). A total of 21 individuals (32.3%) reported tremor onset within the previous 5 years, eight (12.3%) between 5–10 years, and 36 (55.4%) more than 10 years before examination. No significant differences in prevalence were seen between the sexes in any of the age groups (Table 1). Concordance analysis on tremor tasks is shown in Table 2.

Three individuals presented with an isolated, non-dystonic head tremor. Of these, two participants had a first-degree family history of probable ET, including postural and action tremor affecting the upper limbs.

A 70-year-old female participant presented with isolated chin tremor since the age of 62 years. This tremor, although persistent, did not bother the participant and she had not consulted a physician; her father had experienced the same problem. There was no history of limb tremor. An 85-year-old female participant also manifested slight chin tremor, without any family history of tremor. A curious case regarded a 91-year-old female who was disabled and bedridden from a severe left hemispheric stroke with dysphasia and right hemiparesis. This individual had isolated tongue tremor, which was present with the tongue at rest and upon protrusion. These three individuals were not included as ET cases in this study.

Upper limb action tremor was present in eight individuals (12.3%) who satisfied the diagnostic criteria for ET. The tremor appeared to impact, albeit moderately, on their functional activity; however, these individuals did not complain of the tremor. They “felt adapted” to their condition and, in addition, declined anti-tremor treatment (these individuals are hereafter indicated as O+ S-).

One individual showed mixed resting, postural, and action tremor of the limbs in addition to mild limb rigidity. The diagnosis of ET was initially uncertain. Upon follow-up, parkinsonism was confidently excluded and there was consensus on the diagnosis of ET; this individual’s tremor significantly improved with anti-tremor therapy.

### Prevalence analysis

The overall crude prevalence of ET (per 100 population) for Arosan islanders aged 65 years and older was 8.63 (95% CI 6.56–10.70). When adjusted to the standard European population, the prevalence

**Table 2.** Concordance Analysis on Tremor Tasks

Task	Right Arm K	Left Arm K
Postural	0.59	0.70
Drinking	0.75	0.71
Finger–nose	0.61	0.65
Spoon	0.56	0.72
Pouring	0.81	0.70

was 8.42%. As shown in Table 1, the prevalence for ET increased from 7.33 per 100 population (95% CI 3.76–10.90) in females and decreased slightly in males in the 65–74 years age interval to 8.97 (95% CI 3.97–13.96) and 11.34 (95% CI 4.51–18.17), respectively, in the age group 75–84 years. At 85 years and older, the prevalence increased to 11.47 (95% CI 2.66–20.29) for females and decreased slightly to 10.71 (95% CI 2.27–28.23) for males.

The overall prevalences for ET were similar between the sexes (Table 1). However, considering both sexes, the prevalence increased with advancing age: from 7.35 per 100 population at 65–74 years, to 9.92 at 75–84 years and 11.24 at  $\geq 85$  years. There was a significant age effect on ET prevalence ( $\chi^2=10.552$ ;  $p=0.0003$ ); however, sex did not have an effect on ET prevalence ( $\chi^2=0.992$ ;  $p=0.321$ ).

### Discussion

The gold standard for population prevalence studies of ET remains a one-stage survey with direct neurologic examinations performed by trained and experienced neurologists. However, this approach is costly and time-consuming, and is usually only feasible with small populations. We are aware of various studies performed with elderly populations.<sup>12,14,15</sup> Among the residents aged older than 65 years living in a retirement community in Arizona, 73 of the 356 individuals examined (20.5%) were found to have ET.<sup>14</sup> However, the method for diagnosing ET was not clear. A prevalence of 6.7% has been reported from a sample population from Turkey.<sup>12</sup> A prevalence of 1.9% has been reported from 444 consecutive elderly individuals examined in northern Israel.<sup>15</sup>

We calculated a crude prevalence of ET of 8.63% (adjusted rate: 8.42%) among elderly Arosans. This rate is higher than that reported for similar populations in Spain<sup>9</sup> and other European countries.<sup>3,12,16,17</sup> Considering both sexes, the prevalence of ET increased with advancing age. However, after the age of 84 years the prevalence increased for females and decreased slightly for males (Table 1). This tendency is of interest, but has obvious limitations considering the sample size.

Various results from this study deserve comment. Of the 65 participants with ET, only 19 (29.2%) reported functional disability. In addition, eight individuals (12.3%) showed tremor that was not reported to impact their usual activities. These individuals were examined on various occasions. They appeared to have some functional limitations on performing various tasks, but felt they adapted to the tremor in their usual daily activities. These individuals felt that the tremor was tolerable and did not have any interest in receiving anti-tremor treatment. This phenomenon has been reported in previous studies.<sup>1,9</sup>

Eight individuals (12.3%) had been previously diagnosed by a neurologist. This reinforces the notion that ET might be an underdiagnosed condition.<sup>9,12,16</sup> Patients with ET seem to seek medical attention only when the tremor impacts them functionally or becomes disabling. This reinforces the importance of population-based studies in obtaining reliable information on the prevalence of this condition.

ET is highly heterogeneous and lacks specific diagnostic biomarkers. This issue is of major importance when planning epidemiologic studies. We selected similar diagnostic criteria for ET to those used in other surveys.<sup>4,12,18</sup> The availability of complete population lists, the high response rate and participation (94.6%), and the contribution of local primary-care physicians are factors that led to comprehensive screening of the elderly population of Arosa island.

Prevalence increased with advancing age, in line with the perception of ET as an age-related disorder.<sup>11,14</sup> Although the prevalence of ET generally increases with advancing age,<sup>19</sup> some studies have reported conflicting results in the most elderly individuals.<sup>9</sup> As in other epidemiologic studies targeting the elderly Spanish population, the male casualties of the Spanish Civil War and its demographic impact may have influenced our results. In this study, the prevalence of ET was similar in males and females.

ET has a well-known familial and genetic predisposition. To date, no gene or gene product has been identified as being associated with ET, although a relationship with LINGO polymorphisms might exist.<sup>20</sup> Some studies have found ethnic differences in ET prevalence.<sup>8,15</sup> Although these remain to be confirmed, the possibility ET clusters in the Arosa Island population could imply a founder/inbreeding effect or point to a local environmental exposure. In the current study, the prevalence of ET was both higher than expected and higher than reported in other studies from Spain<sup>6,9</sup> and other populations.<sup>8,12,18,21</sup> Arosa Island was a relatively isolated area until its connection to the mainland in 1985. The geographic and demographic isolation of this community favored many consanguineous marriages. Given the high likelihood of shared genetic factors among the study individuals, the finding of prevalences higher than in other populations might indicate a predominant role, at least in the elderly, of genetic factors in the development of ET.

Epidemiologic studies contribute to the planning and organization of health systems. Although most cases of ET reported in this study were not regarded as disabling by the individuals involved, only 12.3% of ET cases had been previously diagnosed. The Spanish public health system is free and universal, and thus potential attendance barriers to medical services are not a likely explanation for the undiagnosed cases. It is possible that lack of information regarding this entity among the population might influence the high prevalence and makes ET a cause for medical concern.

We acknowledge various limitations and considerations of our study. Because we targeted the survey to a small community and population, the extrapolation of our results to wider populations in Galicia and Spain should be made with caution. In addition, as mentioned, the past geographic isolation of Arosa Island, and the possibility of consanguinity, might preclude the generalization of the present results. Further epidemiologic surveys of ET in northwestern Spain will be of interest.

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