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Death certificates data and causes of death in patients with parkinsonism

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ABSTRACT

Introduction: Assessment of variables related to mortality in Parkinson disease (PD) and other parkinsonian syndromes relies, among other sources, on accurate death certificate (DC) documentation. We assessed the documentation of the degenerative disorder on DCs and evaluated comorbidities and causes of death among parkinsonian patients.
Methods: Demographic and clinical data were systematically and prospectively collected on deceased patients followed at a tertiary movement disorder clinic. DCs data included the documentation of parkinsonism, causes, and place of death.
Results: Among 138 cases, 84 (60.9%) male, mean age 77.9 years, mean age of onset 66.7, and mean disease duration 10.9 years. Clinical diagnoses included PD (73.9%), progressive supranuclear palsy (10.9%), multiple system atrophy (7.2%), Lewy body dementia (7.2%) and corticobasal degeneration (0.7%). Psychosis occurred in 60.1% cases, dementia in 48.5%. Most PD patients died due to heterogeneous causes before reaching advanced stages. Non-PD parkinsonian patients died earlier due to causes linked to the advanced neurodegenerative process. PD was documented in 38.4% of DCs with different forms of inconsistencies. That improved, but remained significant when it was signed by a specialist.
Conclusions: More than half of PD cases died while still ambulatory and independent, after a longer disease course and due to causes commonly seen in that age group. Deaths among advanced PD patients occurred due to causes similar to what we found in non-PD cases. These findings can be useful for clinical, prognostic and counseling purposes. Underlying parkinsonian disorders are poorly documented in DCs, undermining its' use as sources of data collection.

1. Introduction

Despite its' significant relevance, data regarding cause of death and the relationship between neurodegenerative disorders and the possible terminal event have been overlooked over the years. In the case of Parkinson's disease (PD) and other parkinsonian disorders, gathering reliable sources of information is complex as mortality data of larger cohorts rely partially on conclusions derived from death certificate (DC) registries and other formal databanks [1]. One major limitation and source of bias in this context is the omission of the parkinsonian diagnosis on the DC. As death is the ultimate consequence of a mosaic of multiple sequential and often interrelated clinical events, picturing it objectively, necessary in these documents, is problematic [2]. Discrepancies may eventually lead to failure to recognize the potential downstream impact of comorbidities, their prognosis, and actions for supportive care and general health interventions.

The objectives of this study were firstly to evaluate records of deceased parkinsonian patients, assessing how the underlying degenerative disorder was documented on the DC. Secondly, to analyze the causes of death as described on the DCs, their potential correlation with the parkinsonian disorder, other demographic

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data, clinical features and comorbidities.

2. Methods

Data from deceased parkinsonian patients previously followed at a large tertiary movement disorders clinic were collected between January 2009 and January 2015. The local ethics committee approved the study protocol. All patients were regularly outpatients of the clinic prior to death, seen every three months according to a standard protocol. Clinical diagnosis was determined during their lifetime by the first or senior authors, both movement disorders specialists. To make the data analysis uniform and comparable, we restricted our population to cases with a clinical diagnosis of degenerative forms of parkinsonism. We did not include cases with secondary forms of parkinsonism (vascular, drug-induced, *etc.*) and cases with incomplete or imprecise data on clinical charts and DCs. Notification of death is performed routinely as a policy of the clinic and for the purpose of the study, family members consented to provide a copy of the DC.

Demographic and clinical variables included age, gender, disease duration, diagnosis, disease characteristics (motor and non-motor aspects), and the presence of comorbidities. Clinical data was updated on every visit, scheduled at three months intervals. Information related to clinical co-morbidities and health status was collected cumulatively on follow up and disease staging was updated from the most recent visit before death. Data regarding causes of death, citation of PD or parkinsonism in the DC, place of death, and identification of the physician who signed the document were collected directly from a copy of the formal DC. In the document, causes of death are listed as primary, secondary, or other causes. DCs are filled out by the physician who diagnoses and confirms death. The characterization of each of these items in the document is part of formal medical education during medical school. By definition, primary cause of death is the immediate event leading to death; secondary cause of death is the clinical disorder leading to the primary cause of death; and other causes of death include all other known clinical problems that may or may not have contributed to the secondary and/or primary cause of death. The vast majority of DCs were obtained without an autopsy which, according to the Brazilian Criminal Code Procedure, are mandatory in selected circumstances (violent death, unknown cause, and unidentified individual) [3].

PD was diagnosed during life using the Queen Square Brain Bank Criteria [4]. Atypical parkinsonism cases were defined according to established criteria [5–7]. Disease stage was determined using the Hoehn and Yahr (H&Y) scale [8]. Dementia and psychosis diagnoses were established using Movement Disorders Society criteria [9,10].

2.1. Statistical analysis

Comparisons of study findings among different parameters used two-tailed *t*-test for means and *chi* square test with Yates correction for continuity or Fisher exact test for categorical and ordinal data. Differences were considered significant for $p < 0.05$.

3. Results

During the six years of the study period, the cumulative number of patients with parkinsonism followed regularly at the clinic was 1028. The cumulative number of deaths reported to the institution reached 207 (20.1%) during this time. Mean follow-up time was 35.3 ± 27.9 (range 7–117, median 29) months. Complete data was obtained from 138 cases. Eighty-four (60.9%) were male; mean age was 77.9 ± 7.9 years (44–95), mean age of onset of parkinsonism was 66.7 ± 9.8 years (35–92), and mean disease duration was 10.9 ± 6.3 years (2–41). The final diagnosis was PD in 102 (73.9%) cases, progressive supranuclear palsy (PSP) in 15 (10.9%), multiple system atrophy (MSA) in 10 (7.2%), Lewy body dementia (LBD) in 10 (7.2%) and corticobasal degeneration in 1 (0.7%). Mean H&Y score was 3.6 ± 0.8 (2–5). Psychosis was diagnosed in 83 (60.1%) cases, dementia in 67 (48.5%), and depression in 19 (13.8%). Most deaths took place in a hospital (100; 72.2%), but also in patients' houses (29; 21%), in nursing homes (5; 3.6%) or other (4; 2.9%).

The complete list of co-morbidities, primary, secondary and other causes of death are shown in Table 1. Forty-nine (35.5%) patients had no known co-morbidities.

In the whole sample, PD was mentioned in 50 (36.2%) DCs as a primary (1), secondary (11) and other (38) cause of death. In 16 (30.2%) of these cases, PD was documented in cases of PSP (7), MSA (6), and LBD (3). Alzheimer's disease (AD) was documented in 16 (11.6%) DCs signed by non-neurologists. Twelve of them had, in fact, a clinical diagnosis of dementia in the setting of PD established before death, while two others had dementia due to LBD and PSP, respectively. The two remaining were not demented based on the latest clinical assessment (less than three months before death). As we did not diagnose any of these cases as AD in life, the possible reasons for these discrepancies are analyzed in the Discussion section of this manuscript. Among the 38 DCs that reported PD as the final diagnosis, 25 (65.8%) represented cases in which the primary cause of death was either sepsis or respiratory failure. Finally, 19 (13.7%) of the DCs were filled out by a neurologist, 9 (47.4%) of them mentioned PD, always as an “other cause of death”.

The comparison of data from patients with clinical diagnosis of PD versus other forms of parkinsonism is shown in Table 2. Fig. 1 show the proportion of cases in each H&Y stage for PD and non-PD diagnoses. Cases of PD died more commonly at stages of the disease that are not considered advanced (H&Y $\leq$ 3) while for cases with non-PD parkinsonism, all except 1 (a case of PSP with probable myocardial infarction) died at the more advanced disease stages. Finally, we compared primary cause of death among cases of PD in more (H&Y 4 or 5) and less (H&Y $\leq$ 3) advanced stages, as shown in Table 3. Among 41 (40.2%) cases at more advanced stages, sepsis (15 patients; 36.6%) and respiratory insufficiency (11 patients; 26.8%) were the most common causes. This scenario was different among the other 61 (59.8%) who died at less advanced stages in which the primary causes of death were more diverse with myocardial infarction (9 cases; 14.8%) and cardiac arrest (8 cases; 13.1%) been the most commonly cited in the DCs. Differences were statistically significant.

4. Discussion

Our data shows that PD is under-recorded on DCs, consistent with previous studies [1,2,11–13]. PD was mentioned in 36.2% DCs, more commonly as an “other cause of death”. Death in chronic disorders portray the net effect of a number of concurrent conditions [14], therefore, the multiple items of a document such as the DC may include a seemingly open and incohesive list of diseases, events and co-morbidities. In any event, the chronic degenerative underlying disorder should ideally be listed as a secondary or “other” cause of death. Interestingly, our finding that only 36.2% of DCs listed PD among any of its' sections is not unique as previous studies using the same source of post mortem information showed similar figures, ranging from 30% to 50% [1,2,12,13]. The reasons behind this discrepancy are unclear and possibly not singular depending on different variables. For instance, despite the fact that DCs conventionally and with minimal lexical variations require the objective description of causes of death and any other diseases, in various countries and under certain circumstances it may be signed not only by any physician, but also by a nurse practitioner,

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