Original Paper



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A Simple Score to Predict Survival with Dementia in the General Population

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Key Words

Prognosis · Dementia · Cohort studies · Survival

Abstract

Background/Aims: This study was designed to develop a practical risk score for predicting 5-year survival after the diagnosis of dementia. *Methods:* Using the Paquid Study (prospective, population-based, long-term cohort study), we created a prognosis score with incident cases of dementia and validated it in another prospective, populationbased, long-term cohort study, the Three City Study. **Results:** Among the 3,777 subjects enrolled in the Paquid Study, 454 incident cases of dementia were included in this study. After a 5-year follow-up period, 319 (70.3%) were deceased. The score was constructed from three independent prognostic variables (gender, age at diagnosis and number of ADL restricted). The discriminant ability of the score was good with a c index of 0.754. Sensitivity was 64.7% and specificity 76.3%. In the validation cohort, the discriminant ability of the prognostic score with *c* statistics was 0.700. Sensitivity was 26.3% and specificity 95.4%. Conclusions: The prognostic factors selected in the predictive model are easily assessable, so this simple score could provide helpful

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E-Mail karger@karger.com www.karger.com/ned © 2013 S. Karger AG, Basel 0251–5350/13/0411–0020\$38.00/0 information for the management of dementia, particularly to identify patients with duration of the disease greater than 5 years. Copyright © 2013 S. Karger AG, Basel

Introduction

After the disclosure of a diagnosis of dementia, information on the prognosis is one of the most important issues for patients and caregivers. Knowledge of the estimated duration of the disease before death is helpful to primary care physicians and specialists, social workers, case managers and other health providers since they have to advise patients and their families about follow-up visits, the burden and cost of the pathology, and the available drug and nondrug treatment strategies. Furthermore, they have to provide information to caregivers about support and palliative care options such as entry into nursing homes. Dementia patients' survival is highly variable across individuals (depending on gender, age, cognitive function, socio-economic status, etc.) and studies (depending on design, length of follow-up, quality of diagnosis, methodology). Studies based on incident

Fleur Delva ISPED, INSERM U897, Case 11 146 rue Leo Saignat FR-33076 Bordeaux Cedex (France) E-Mail fleur.delva@isped.u-bordeaux2.fr cases of dementia diagnosed at various stages estimate survival with dementia ranging from 3 to 9 years [1-7]. Several factors are thought to predict mortality in dementia [8]. However, attempts to develop and validate statistical models to predict the survival of demented patients are still very scarce. To our knowledge, only four studies have developed a risk function to predict survival of Alzheimer's disease (AD) patients [6, 9-11]. Three of them analyzed prevalent cases consulting a specialist in a clinical setting [9–11], leading to a selection bias with a possible erroneous estimation of survival [12]. Moreover, some of the predictors reported in these studies, such as EEG [9] or biologic parameters [6, 11], are difficult to interpret or not sufficiently accessible to be included for use in clinical practice. The fourth study estimated transition probabilities between different states (nonmedical home for elderly, nursing home and death) in a small sample of incident cases of dementia from a population-based study [6].

For a pragmatic point of view, it would be useful to have a prognostic function based on a simple clinical tool that is easy for clinical practitioners to administer to patients in primary care or in social structure. The aim of our study was to develop such a practical prognostic score to predict 5-year survival after the diagnosis of dementia in a large population-based sample. This was achieved with a development cohort, the Paquid Study [13]. Thereafter, the score was validated in an independent cohort, the Three City (3C) Study [14].

Materials and Methods

The Paquid Study as Development Cohort

The predictive mortality score was derived from the Paquid cohort. The detailed methodology of the Paquid Study has been previously described [13]. This ongoing prospective cohort study addresses a representative (initially in terms of age and gender) sample of community dwellers aged 65 years and older living in the south-west of France. Its main objectives were to assess the incidence, prevalence through cumulative incidence and predictors of AD and other dementias. Initially, 3,777 subjects accepted to participate. Data collection began in 1988. Subjects were interviewed at baseline (T0), and then every 2 or 3 years (T1, 3, 5, 8, 10, 13, 15, 17, 20, 22). A wide range of environmental, social, neuropsychological and medical information was collected at home by a trained psychologist.

The present study included all incident cases of dementia occurring between T5 and T17. We did not include incident cases at T1 and T3 because the diagnosis of dementia had changed with the approval of tacrine in 1995. We did not include incident cases at T20 and T22 so as to have at least a 5-year follow-up. To include only recent incident cases of dementia, we excluded all cases not seen at the visit preceding the visit at which the diagnosis was made.

The 3C Study as Validation Cohort

The 3C Study is also an ongoing population-based cohort conducted in three French cities (Bordeaux, Dijon, Montpellier) with a comparable methodology to that of Paquid for cognitive and functional assessments [14]. Thus, the same outcome and prognostic factors were collected with a similar design. The study began in 1999 on 9,294 elderly people aged over 65 years who were seen every 2–3 years (T2, 4, 7, 10) thereafter.

For this study, all incident cases of dementia occurring at T2 and T4 were included. We did not include incident cases at T7 and T10 so as to have at least a 5-year follow-up. We also excluded all cases not seen at the visit preceding the visit of the diagnosis.

Diagnosis of Incident Dementia in the Two Cohorts

At baseline and at each follow-up, after the neuropsychological interview, the psychologist used the Diagnostic and Statistical Manual of Mental Disorders checklist [15] to select subjects suspected of having dementia. Then, a senior neurologist interviewed and examined these subjects at home, plus all those with at least a 3-point decline on the Mini-Mental State Examination (MMSE) score since the previous visit, to confirm or rule out the diagnosis of dementia and specify the etiology of dementia. The clinical criteria were the NINCDS-ADRDA criteria [16] for AD and the Hachinski score [17] for vascular dementia. Cases were classified as probable or possible AD, vascular dementia and other types of dementia. Furthermore, in the 3C Study, the final diagnosis of dementia was made by a panel of 5 neurologists specialized in dementia, independent of the 3C Study investigators, who reviewed all accessible information for each incident case.

Primary Outcome

Survival status and date of death were systematically and regularly collected throughout the follow-up for each participant from families, physicians, civil state records and the national registry of mortality statistics.

Prognostic Factors

Sociodemographic Characteristics

Age at the diagnosis of dementia, sex, education level (having or not having the French elementary school diploma called 'Certificat d'Etudes Primaires') [13], marital status categorized as: married, living as a couple or other situations (always single, widowed, divorced, separated or other) [13], and accommodation type (living in community or in institution) were analyzed. Etiology of dementia was classified in three categories: AD, vascular dementia (VaD) and other type of dementia.

Cognitive Function

The MMSE [18] was used as an index of global cognitive status. A score ranging from 0 to 30 was obtained, lower scores indicating greater cognitive impairment.

Functional Status

The basic Activities of Daily Living (ADLs) were assessed using the French version of the Katz scale [19], which includes five basic activities: bathing, dressing, toileting, transferring and eating. As incontinence is an impairment rather than a disability, it was excluded from disability staging [20].One point was as-

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signed to subjects needing help according to the thresholds defined by the authors for each activity. A total score of five indicates 'severe functional impairment' and 0 indicates 'full function'.

The capacity to perform Instrumental Activities of Daily Living (IADL) was assessed using the French version of the Lawton-Brody scale [21]. We used four (ability to use the telephone, use of transport facilities, responsibility for taking own medication and ability to handle personal finances) out of the eight original IADLs, which are relatively independent from gender roles and are best associated with cognitive performances and short-term risk of dementia [22]. For each activity, subjects were considered to be non-restricted if they were able to perform the activity at the highest level of performance (coded 0). Otherwise, they were considered to be restricted (coded 1). An IADL score was calculated by summing the number of restricted activities (ranging from 0, full independence, to 4) [22].

Health Measures

Depressive symptomatology at the diagnosis of dementia was evaluated by the Center for Epidemiologic Studies Depression Scale [23]. Participants were classified as depressed if they scored 17 and over for men, or 23 and over for women [24].

Comorbidities were evaluated by self-reporting of diseases, symptoms or impairments, elicited through a semi-structured interview investigating the following: diabetes, history of stroke or myocardial infarction, dyspnea (feeling out of breath during minor effort or everyday activities or permanent dyspnea).

Subjective health [25] was assessed by the following question: 'How would you rate your health status presently?' on a fixed 5-level scale: very good, good, fair, bad, or very bad.

Statistical Analysis

As the median survival time from onset of the disease was estimated to be 4.5 years [4], we chose to investigate prognostic factors of mortality occurring within 5 years after the diagnosis. As cumulative mortality at 5 years was the outcome, subjects were censored after 5 years of follow-up. For the analysis, the study started at the date of the visit when the diagnosis of dementia was made. Descriptive and comparative analyses were conducted using appropriate tests (t tests, χ^2 tests or Fisher exact tests). Survival probability at 5 years was calculated by the Kaplan-Meier method. Age-adjusted bivariable and multivariable analyses were carried out with a Cox regression model using a backward stepwise procedure. Hazard ratios of mortality and 95% confidence intervals (CIs) were estimated. Variables associated with survival with a p value <0.25 in the age-adjusted bivariable analysis were included in the multivariable regression. For continuous prognostic factors, the linearity of the effect on the log hazard (linearity hypothesis) was tested [26] and was not rejected. We verified the proportional hazard assumption by testing covariate-by-time interactions for each variable of the final model [27]. We found no violation for any variable.

For clinical purposes, a prediction rule was created by assigning points to each beta regression coefficient in the final model. The reference category for each prognostic factor was assigned 0 points in the scoring system; less favorable prognostic factor scores were assigned positive points, so a higher score signified a higher risk. The performance of the score was assessed in terms of calibration and discrimination by logistic regression. Calibration was tested by the Hosmer-Lemeshow test [28]. We evaluated the ability of the risk prediction model to discriminate persons who died from those who did not using an overall *c* statistic [26]. The *c* index is defined as the proportion of all usable subject pairs in which the predictions and outcome are concordant. c statistics also equals the area under a receiver-operating characteristic curve. A c index value of 0.5 indicates random prediction while higher values (up to 1) indicate increasing predictive accuracy [29]. An optimal threshold was determined using the Youden Index (sensitivity + specificity - 1) [30]. Two groups were defined as: (1) low-risk (below the cut-off obtained by the Youden Index) and (2) high-risk (equal to or greater than the cut-off obtained by the Youden Index). Sensitivity, specificity, positive predictive value (PPV; probability of death in the highrisk group) and negative predictive value (NPV; probability of survival in the low-risk group) were calculated. To ensure the relevance of this score in clinical practice because new dementia cases frequently go unrecognized in clinical practice [31], we performed these analyses in the subsample with subjects restricted to those who had reported a cognitive or memory complaint to their general practitioner.

To validate this score in the 3C Study sample, we implemented the score defined in the Paquid Study and calculated the *c* index to study its discriminant capacity in this cohort. Calibration was tested by the Hosmer-Lemeshow test for sensitivity, specificity, PPV and NPV. Then, we compared 3C subjects with a low and high risk using Kaplan-Meier plots. Statistical analyses were performed with SAS, version 9.1 (SAS Institute Inc., Cary, N.C., USA) and Stata statistical software, version 9.2.

Results

Among the initial total sample of 3,777 subjects in the Paquid cohort, 628 incident cases of dementia were diagnosed between T5 and T17 (fig. 1), including 454 who were evaluated as nondemented at the visit prior to the diagnosis of dementia. Mean age at diagnosis was 86.4 years (SD 5.5). One hundred and forty-eight subjects were male (32.6%) and 368 (81.0%) had a diagnosis of probable or possible AD. Their mean MMSE score at diagnosis was 18.8 (SD 5.6). After the 5-year follow-up, 319 subjects (70.3%) were deceased, so the survival probability was 29.7%. Sociodemographic characteristics, physical health, subjective health, functional status and cognitive performance of the participants are described in table 1, subdivided by vital status 5 years after diagnosis (table 2).

In age-adjusted bivariable analyses (table 3), factors collected at baseline that were associated with mortality (at $p \le 0.05$) were male gender, being in an institution, being ADL-restricted, having at least 4 IADLs restricted or a lower MMSE score. In the multivariable analysis (table 4), only three factors remained independent predic-

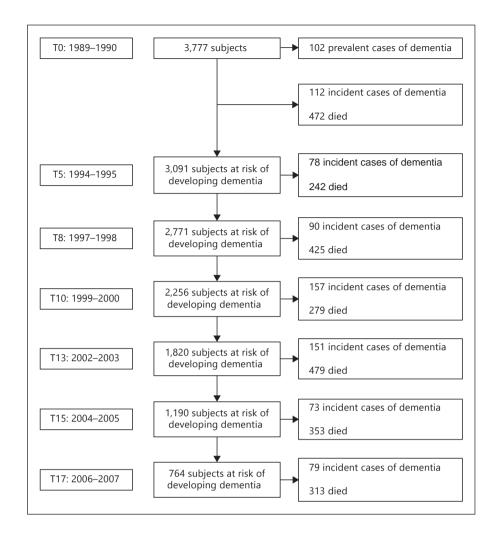


Fig. 1. Flow of study participants.

tors of death before 5 years: male gender, age at diagnosis and number of ADL restricted (at least two).

Based on the results of the final model, a prognostic score was derived (= $0.40488 \times \text{males} + 0.06494 \times \text{age} + 0.14649 \times 1$ ADL restricted + 0.53865×2 ADL restricted + 0.50662×3 ADL restricted + 0.93290×4 ADL restricted + 1.91994×5 ADL restricted) with binary variables coded 0 for no or 1 for yes. A tool for fast computation has also been developed. The Hosmer-Lemeshow score indicated good fit ($\chi^2 = 4.59$; p = 0.80). The ability of the risk prediction model to discriminate demented cases deceased before 5 years from those surviving yielded *c* statistics of 0.754.

Using the cutoff point (5.8987773306) that maximizes the Youden Index, two groups were defined: one with a low risk of death and the other with a high risk. Sensitivity was 64.7% and specificity 76.3%; the PPV (probability of death in the high-risk group) was 86.5% and the NPV (probability of survival in the low-risk group) at 5 years was 47.9%.

In the sample restricted to 125 subjects (34.4%) with cognitive or memory complaints to their practitioner, the Hosmer-Lemeshow score indicated good fit (χ^2 = 13.9; p = 0.08) and a *c* index of 0.81. Using the cutoff point defined from the whole sample, sensitivity was 53.1%, specificity was 90.9%, PPV was 91.9% and NPV was 51.2%.

In the 3C validation cohort, 267 incident cases of dementia were included, including 108 who died (40.4%) within the subsequent 5-year follow-up period. Their mean age was 80.8 years, 112 (41.9%) were male, 232 subjects had no ADL restricted (87.9%), 9 had one ADL restricted (3.4%), 19 had two ADL restricted (7.1%), 2 had three ADL restricted (0.8%), 1 had four ADL restricted (0.4%) and 1 had five ADL restricted (0.4%) (table 1). The Hosmer-Lemeshow score indicated good fit

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	Paquid Study	3C Study
	$(n = 454^*)$	(n = 267*)
Gender male	148 (32.6)	112 (41.9)
Age at diagnosis of dementia, years	86.4±5.5	80.8±5.8
Primary education level ¹	283 (62.3)	221 (83.1)
Etiology ²		()
Probable AD/possible AD/		
mixed dementia	368 (81.1)	200 (80.0)
VaD	38 (8.4)	26 (10.4)
Others dementia	48 (12.2)	24 (9.6)
Marital status ³		
Married or living as a couple	144 (31.7)	135 (51.1)
Others (widowed, single,		
divorcee, separated)	310 (68.3)	129 (48.9)
Accommodation type ⁴		
Living in community	325 (71.9)	251 (95.1)
Living in institution	127 (28.1)	13 (4.2)
MMSE score ⁵	18.8±5.6	22.4±3.0
Number of restricted ADLs ⁶		
0	280 (61.9)	232 (87.9)
1	25 (5.5)	9 (3.4)
2	37 (8.2)	19 (7.2)
3	26 (5.8)	2 (0.8)
4	65 (14.4)	1(0.4)
5	19 (4.2)	1(0.4)
Number of restricted IADL ⁷		
0	34 (7.7)	106 (40.9)
1	49 (11.1)	56 (31.6)
2	58 (13.1)	27 (10.4)
3	86 (19.4)	33 (12.7)
4	216 (48.8)	37 (14.3)
Depressive symptomatology ⁸	67 (20.1)	64 (26.0)
Diabetes ⁹	33 (8.6)	32 (12.1)
History of stroke ¹⁰	67 (15.8)	15 (5.7)
History of myocardial infarction ¹¹	56 (13.0)	21 (7.9)
Dyspnea ¹²	144 (35.4)	55 (21.6)
Subjective health ¹³		
Poor, very poor	59 (14.0)	40 (15.5)
Fair to very good	361 (86.0)	219 (84.5)

Table 1. Sociodemographic and clinical characteristics in thePaquid Study and 3C Study

Values are means \pm SD or n (%).

* Data is missing for certain indicators from the two studies:

 1 3C Study, n = 266; 2 3C Study, n = 250; 3 3C Study, n = 264; 4 Paquid Study, n = 452; 3C study, n = 264; 5 Paquid Study, n = 442; 3C Study, n = 257; 6 Paquid Study, n = 453; 3C Study, n = 264; 7 Paquid Study, n = 443; 3C Study, n = 259; 8 Paquid Study, n = 333; 3C Study, n = 246; 9 Paquid Study, n = 383; 3C Study, n = 264; 10 Paquid Study, n = 31; 3C Study, n = 265; 11 Paquid Study, n = 432; 3C Study, n = 265; 12 Paquid Study, n = 407; 3C Study, n = 255; 13 Paquid Study, n = 420; 3C Study, n = 259.

(χ^2 = 9.27; p = 0.32). The discriminant power of the predetermined risk score measured by the *c* index was 0.700. Two hundred and eighteen subjects were included in the low-risk group as previously defined including 115 who died after 5 years of follow-up. In the high-risk

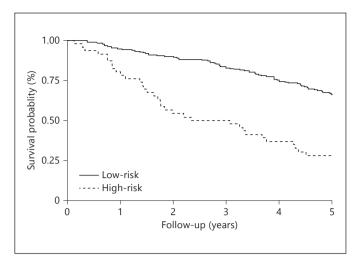


Fig. 2. Survival in cohort 3C from date of diagnosis of dementia depending on the high- and low-risk group obtained in the Paquid Study.

group, there were 46 subjects, including 41 who died after 5 years of follow-up. Sensitivity was 26.3% and specificity 95.4%, PPV was 89.1% and NPV was 47.3%. Figure 2 shows the survival probability across the groups (low vs. high risk).

Discussion

Using the Paquid follow-up data, we computed a simple score to predict survival of dementia after the time of diagnosis for new dementia patients. This simple score is based on easily obtainable variables in clinical or social practice: sex, age at diagnosis and number of ADL restricted. The score has a good predictive capability (*c* index = 0.754). The validation in an independent sample composed of incident dementia cases in another younger cohort (3C Study) gave fair confirmatory results (*c* index = 0.700). Apart from age and gender (nonmodifiable independent variables), only ADL remained independently related to survival. The number of ADL restricted represents the most serious consequences of dementia on the probability of being alive at 5 years. The strong predictive value of this factor is probably explained by the fact that restricted ADL reflected not only the state of the patient at the time of diagnosis, but also the initial rate of progression of degradation, since dementia was not present at the preceding visit. Thus, beyond the stage of the disease, these measures may also represent its initial aggressiveness, which is known to be a predictor of short-term mortality

	Not deceased $(n = 135)^*$	Deceased $(n = 319)^*$	p value
	$(II = 155)^{+}$	$(11 = 519)^{-1}$	
Gender male	37 (27.4)	111 (34.8)	0.12
Age at diagnosis of dementia, years	84.2 ± 4.8	87.3±5.5	< 0.0001
Primary education level	80 (59.3)	203 (63.6)	0.38
Etiology			0.77
Probable AD/possible AD/mixed dementia	109 (80.7)	259 (81.2)	
VaD	10 (7.4)	28 (8.8)	
Other dementia	16 (11.9)	32 (10.0)	
Marital status			0.04
Married or living as a couple	52 (38.5)	92 (28.8)	
Others (widowed, single, divorcee, separated)	83 (61.5)	227 (71.2)	
Accommodation type ¹			< 0.0001
Living in community	115 (85.8)	210 (66.0)	
Living in institution	19 (14.2)	108 (34.0)	
MMSE score ²	20.6±4.2	18.1±6.0	< 0.0001
Number of restricted ADLs ³			< 0.0001
0	114 (84.4)	166 (52.4)	
1	6 (4.4)	19 (6.0)	
2	5 (3.7)	32 (10.1)	
3	3 (2.2)	23 (7.3)	
4	6 (4.4)	59 (18.6)	
5	1(0.7)	18 (5.7)	
Number of restricted IADL ⁴			< 0.0001
0	15 (11.4)	19 (6.1)	
1	21 (15.9)	28 (9.0)	
2	29 (22.0)	29 (9.3)	
3	30 (22.7)	56 (18.0)	
4	37 (28.0)	179 (57.6)	
Depressive symptomatology ⁵	26 (22.0)	41 (19.1)	0.52
Diabetes ⁶	9 (8.1)	24 (8.8)	0.82
History of stroke ⁷	16 (12.4)	51 (17.4)	0.20
History of myocardial infarction ⁸	16 (12.2)	40 (13.3)	0.76
Dyspnea ⁹	40 (31.2)	104 (37.3)	0.24
Subjective health ¹⁰			0.44
Poor, very poor	16 (12.1)	43 (14.9)	
Fair to very good	116 (87.9)	245 (85.1)	

Table 2. Sociodemographic and clinical characteristics by death status 5 years after diagnosis of dementia in thePaquid Study

Values are means \pm SD or n (%).

* Data is missing for certain indicators:

¹ n = 452, missing data for 2 subjects; ² n = 442, missing data for 12 subjects; ³ n = 453, missing data for 1 subject; ⁴ n = 443, missing data for 11 subjects; ⁵ n = 333, missing data for 121 subjects; ⁶ n = 383, missing data for 71 subjects; ⁷ n = 31, missing data for 31 subjects; ⁸ n = 432, missing data for 22 subjects; ⁹ n = 407, missing data for 47 subjects; ¹⁰ n = 420, missing data for 34 subjects.

in dementia [32, 33]. In addition, ADL limitations reflect a more severe degree of the disablement process, combining cognitive as well as physical components and comorbidities [34].

On the basis of this score, we defined a subgroup among newly demented cases with a higher risk of midterm death (with a probability of death at 5 years of 86.5%). These patients seem to have a more aggressive disease and may therefore require particular attention since the diagnosis, with intensive medical and social follow-up assessments and appropriate adjustments to their treatment and support of the patient and the caregiver. On the contrary, in the other group, the probability of survival was near 50%. In this group, determinants of short-term mortality were probably numerous and not related to dementia.

^{6).} These patients seem to have a more aggressiv

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Table 3. Bivariate Cox proportional hazards analyses adjusted on age at diagnosis for effects of prognostic factors at diagnosis of dementia on death at 5 years (Paquid Study, n = 454)

Prognostic factor	Hazard ratio (95% CI)	p <value< th=""></value<>
Male gender	1.40 (1.10-1.78)	0.006
Primary education level	1.21 (0.96-1.52)	0.10
Etiology of dementia		0.19
Vascular dementia	1.44 (0.97-2.14)	
Others dementia	1.02 (0.71-1.48)	
Marital status (widowed, single,		
divorcee, separated, other)	1.01 (0.78-1.32)	0.92
Living in institution	1.60 (1.26-2.03)	0.0001
MMSE score (for one point)	0.95 (0.93-0.96)	< 0.0001
Number of restricted ADL		< 0.0001
1	1.10 (0.67-1.78)	
2	1.77 (1.20-2.60)	
3	1.70 (1.09-2.65)	
4	2.43 (1.79-3.30)	
5	6.33 (3.84–10.42)	
Number of restricted IADL	· · · · · ·	< 0.0001
1	1.00 (0.58-1.68)	
2	0.79 (0.47-1.34)	
3	1.17 (0.74-1.86)	
4	1.92 (1.28-2.89)	
Depressive symptomatology	0.87 (0.62–1.23)	0.43
Diabetes	1.34 (0.87-2.04)	0.18
History of stroke	1.19 (0.88-1.61)	0.25
History of myocardial infarction	1.00 (0.71-1.39)	0.98
Dyspnea	1.15 (0.90-1.47)	0.27
Subjective health: fair to very good	0.88 (0.64–1.22)	0.45

Table 4. Multivariate Cox proportional hazards analysis for predicting mortality (n = 428; deceased = 299)

Prognostic factor	Parameter estimate	Hazard ratio (95% CI)	p value
Male gender Age at diagnosis	0.40488	1.50 (1.17–1.91)	0.001
(for 1 year)	0.06494	1.07 (1.04-1.09)	< 0.0001
Number of restricted	ADL		< 0.0001
1	0.14679	1.16 (0.71-1.89)	
2	0.53865	1.71 (1.16-2.52)	
3	0.50662	1.66 (1.06-2.59)	
4	0.93290	2.54 (1.87-3.45)	
5	1.91994	6.82 (4.13–11.27)	

Strengths and Limitations

The strengths of this study are its unique prospective population-based design in two independent but very similar cohorts, the very large number of subjects at baseline and relevant outcome events, the comprehensive and systematic collection of potential (independent) predictive variables, a comprehensive clinical diagnosis of dementia and death and frequent visits during follow-up with accurate and thorough data on survival status. As only incident cases of dementia were included, the two samples contained the complete spectrum of newly diagnosed cases, while studies with prevalent cases exclude those who died quickly from aggressive disease (survival bias) [35].

The study also has limitations. First, subjects in the Paquid Study were visited every 2 or 3 years, so the 'actual date' of dementia onset, which is intrinsically difficult to determine as it is not a critical event, cannot be precisely known. Thus, when a subject was diagnosed, he/ she could have been clinically demented for from a few months to more than 2 or 3 years. However, in clinical practice, subjects are rarely diagnosed at 'the onset of dementia'.

It should to be kept in mind that our incident cases of dementia had a mean MMSE at 18.8 (which is rather low) at the time of diagnosis, and 40% had at least one ADL restricted, which occurred at a rather old age (mean: 86.4 years). The mean MMSE score of these incident cases at the time of diagnosis was very close to that observed in a randomized trial conducted on new cases of dementia in primary care practices in France [36]. Therefore, the incident cases in our population-based cohort may well be comparable to new cases of dementia diagnosed in primary care practice. However, in the validation cohort, incident cases were different, younger, less dependent on ADL, and probably diagnosed earlier. Thus, at the diagnosis, dementia is at an earlier stage of the disease and subjects die of comorbidities other than dementia [37]. Therefore, our score lacks sensitivity. For that reason, it will be important to work on other major endpoints, such as loss of independence, which would be a useful clinical endpoint for patients, caregivers and health care planners. However, this important issue is much more difficult to conceptualize as a model and requires additional studies.

Second, and surprisingly, self-reported comorbidities and the presumed etiology of dementia did not contribute to the predictive score. This could be due to the lack of precision of self-reported questionnaires, to the relatively large volume of missing data for comorbidities (depressive symptomatology, diabetes) or to the limits of precision of the clinical diagnosis of the etiology of dementia without biomarkers, brain imaging or neuropathologic assessment. However, the predictive values of this information still remains a matter of controversy [8, 12, 38–41] and the practical application would be comparable to the data collection of our population-based studies.

Conclusion

In conclusion, in spite of a low sensitivity, this score could be useful for primary care practitioner, case manager or social workers, particularly to identify patients with a duration of the disease greater than 5 years.

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