Preplanned Studies

Evaluation of the Factors Influencing the Survival Times of Chinese Patients with Probable Creutzfeldt-Jacob Disease — China, 2020–2022

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Summary

What is already known about this topic?

The clinical durations of sporadic Creutzfeldt-Jacob disease (sCJD) patients typically do not exceed 2 years, though considerable variation exists. The factors influencing survival among Chinese sCJD patients remain incompletely characterized.

What is added by this report?

A comprehensive evaluation of 31 factors across 7 categories was conducted in a retrospective cohort of 300 probable Chinese sCJD patients. The analysis revealed that patients over 65 years of age at onset, those presenting with pyramidal or extrapyramidal dysfunction, those showing high signal intensity in caudate/putamen on magnetic resonance imaging, and those not receiving nasal feeding demonstrated significantly shorter survival times.

What are the implications for public health practice?

This study provides the first systematic documentation of potential risk factors affecting survival times in Chinese sCJD patients, establishing an evidence base for developing and implementing targeted intervention strategies.

ABSTRACT

Introduction: The clinical durations of sporadic Creutzfeldt-Jacob disease (sCJD) patients typically do not exceed 2 years, though considerable variation exists. The factors influencing survival among Chinese sCJD patients remain incompletely characterized.

Methods: We analyzed the potential elements associated with survival using the data of 300 probable sCJD cases from 2020 to 2022 by China National Surveillance for CJD. The associations of 31 factors in 7 categories with survival were estimated by univariate analysis of Kaplan-Meier and multivariate regression analysis of Cox proportional hazard model.

Results: Statistical assays figured out that the patients >65 year-old at onset, having pyramidal or extrapyramidal dysfunction, recording high signal in caudate/putamen on magnetic resonance imaging (MRI), and not receiving nasal feeding were closely associated with short survival. In the subgroup analysis of ≤65 years and >65 years at onsetage, nasal feeding was the contributor to prolonged survival for both groups. MRI high signal of caudate/putamen in the younger group and pyramidal or extrapyramidal dysfunction in older group seemed to be more associated with poor survival separately.

Conclusions: The data indicate the onsetage and nasal feeding are the most crucial factors influencing the prognosis for Chinese sCJD patients, establishing an evidence base for developing and implementing targeted intervention strategies.

Human prion diseases encompass Creutzfeldt-Jacob disease (CJD), Kuru, Gerstmann-Sträussler-Scheinker syndrome (GSS), and fatal familial insomnia (FFI). Globally, sporadic CJD (sCJD) accounts for approximately 85% of human prion diseases, while 10%–15% are genetic forms associated with mutations in the *PRNP* gene — including genetic CJD (gCJD), GSS, and FFI. The remaining 1% are acquired forms, such as Kuru, iatrogenic CJD (iCJD), and variant CJD (vCJD) (*1*). While sCJD predominantly affects individuals aged 60–70 years, onset can occur between 20–90 years. Clinical presentations vary substantially among sCJD patients, with disease durations ranging from several months to 2 years (*2*). Despite numerous clinical trials over recent decades (*3*–*4*), effective prophylactic and therapeutic interventions remain elusive. Therefore, prompt and appropriate symptomatic management, along with proper nursing

care, are crucial for improving patient outcomes.

Previous evaluations of Chinese sCJD patients revealed a median clinical duration of approximately 5.3 months (5). However, factors influencing survival time remain incompletely understood. In this retrospective cohort study, we analyzed 300 probable sCJD cases diagnosed through the China National Surveillance for CJD (CNS-CJD) from January 1, 2020, to December 31, 2022. Diagnoses were established according to the Chinese National Health Commission's CJD diagnostic criteria as previously described. The study incorporated comprehensive medical records, epidemiological information, clinical data, laboratory findings, and follow-up documentation. We examined the relationship between survival time and 31 factors across 7 categories, including demographic characteristics, clinical features, laboratory results, and post-diagnosis medical care. To ensure data integrity, cases were selected based on criteria outlined in Figure 1, with standardized questionnaires administered by trained investigators to minimize information bias. Follow-up concluded on December 31, 2023, with surviving cases classified as censored. Survival time was calculated from disease onset to death.

Statistical analysis was performed using SPSS 21.0 statistical software (IBM, Armonk, NY, USA). Survival times with 95% confidence intervals (*CI*) were calculated using the Kaplan-Meier estimator. Between-group differences in survival time were assessed using the log-rank test. Factors showing statistical significance ($P<0.05$) in univariate analysis were subsequently evaluated through multivariate analysis using the Cox proportional hazard model to determine hazard ratios (*HR*) with corresponding 95% *CI*. The complete workflow for data collection and statistical evaluation is detailed in Supplementary Figure S1 (available at https://weekly.chinacdc.cn/).

Of the 300 sCJD cases documented in CNS-CJD, 285 cases had confirmed death dates prior to the follow-up endpoint, while 15 cases were censored. The median survival time was 5 months (95% *CI*: 4.165, 5.835). The cohort demonstrated a male-to-female ratio of 1:1.14, with an average onset age of 65 years (range: 39–84 years). The majority of cases (187 cases, 62.3%) occurred in patients aged 60–74 years.

Analysis of 31 factors across 7 categories using Kaplan-Meier methodology revealed several significant associations with survival time (Table 1). Among demographic factors, onset age showed statistical significance ($P=0.035$), with patients >65 years demonstrating shorter survival times (median: 5 months, 95% *CI*: 3.644, 6.356) (Supplementary Figure S2A, available at https://weekly.chinacdc.cn/). Regarding clinical manifestations, patients without pyramidal or extrapyramidal dysfunction exhibited significantly longer survival times (median: 7 months, 95% *CI*: 2.962, 11.038, $P=0.003$) (Supplementary

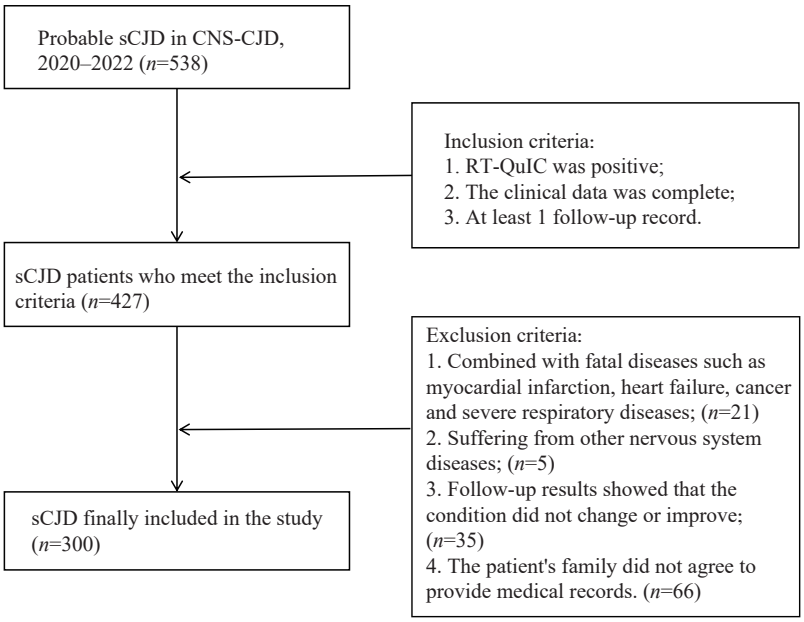

FIGURE 1. Flow chart of case selection.
Abbreviation: sCJD=sporadic Creutzfeldt-Jacob disease; CNS-CJD=China National Surveillance for CJD; RT-QuIC=Real-time Quaking-Induced Conversion.

TABLE 1. Univariate analysis of factors associated with survival in sCJD patients.

Factor	Cases (%)	Median (m) (95% *CI*)	χ^2	*P*
Demographics				
Onsetage (years)			4.441	0.035*
35–65	166 (55.3)	6 (4.356, 7.644)		
≥66	134 (44.7)	5 (3.644, 6.356)		
Gender			0.127	0.721
Male	140 (46.7)	5 (3.762, 6.238)		
Female	160 (53.3)	6 (4.229, 7.771)		
Geographic area			4.543	0.604
Northeastern	21 (7.0)	6 (1.514, 10.486)		
Eastern	86 (28.7)	6 (4.403, 7.597)		
Northern	43 (14.3)	4 (2.847, 5.153)		
Central	56 (18.7)	7 (4.340, 9.660)		
Southern	10 (3.3)	3 (1.482, 4.518)		
Southwestern	66 (22.0)	5 (3.508, 6.492)		
Northwestern	18 (6.0)	5 (0, 11.237)		
Residence			0.821	0.365
Urban	121 (40.3)	5 (4.600, 7.400)		
Rural	179 (59.7)	6 (3.690, 6.310)		
Initial symptom				
Rapid dementia			0.001	0.971
Yes	236 (78.7)	5 (3.950, 6.050)		
No	64 (21.3)	6 (3.060, 8.940)		
Slow dementia			1.833	0.176
Yes	17 (5.7)	10 (3.277, 16.723)		
No	283 (94.3)	5 (4.162, 5.838)		
Mental problems			0.210	0.647
Yes	109 (36.3)	6 (4.198, 7.802)		
No	191 (63.7)	5 (4.010, 5.990)		
Cortical blindness			1.297	0.255
Yes	31 (10.3)	4 (2.205, 5.795)		
No	269 (89.7)	6 (4.934, 7.066)		
Cerebellar disturbance			2.821	0.093
Yes	105 (35.0)	4 (3.163, 4.837)		
No	195 (65.0)	6 (4.632, 7.368)		
Pyramidal or extrapyramidal dysfunction			3.318	0.069
Yes	100 (33.3)	5 (3.726, 6.274)		
No	200 (66.7)	6 (4.570, 7.430)		
Clinical manifestation				
Myoclonus			1.073	0.300
Yes	200 (66.7)	5 (4.012, 5.988)		
No	100 (33.3)	6 (4.272, 7.728)		
Visual or cerebellar disturbance			2.162	0.141

Continued

Factor	Cases (%)	Median (m) (95% *CI*)	χ^2	*P*
Yes	222 (74.0)	5 (4.071, 5.929)		
No	78 (26.0)	7 (5.569, 8.431)		
Pyramidal or extrapyramidal dysfunction			9.043	0.003**
Yes	248 (82.7)	5 (4.095, 5.905)		
No	52 (17.3)	7 (2.962, 11.038)		
Akinetic mutism			2.316	0.128
Yes	238 (79.3)	6 (4.839, 7.161)		
No	62 (20.7)	4 (2.980, 5.020)		
Clinical examination				
EEG (PSWC)			<0.001	0.985
Yes	82 (27.3)	5 (2.953, 7.047)		
No	218 (72.7)	5 (3.842, 6.158)		
MRI				
High signal in caudate/putamen			8.084	0.004**
Yes	101 (33.7)	5 (3.972, 6.028)		
No	199 (66.3)	6 (4.467, 7.533)		
‘‘Ribbon’’ signs			0.233	0.629
Yes	233 (77.7)	5 (4.103, 5.897)		
No	67 (22.3)	7 (4.824, 9.176)		
High signal in posterior tuberosity of thalamus			0.007	0.935
Yes	29 (9.7)	6 (4.688, 7.312)		
No	271 (90.3)	5 (4.121, 5.879)		
Laboratory test				
CSF 14-3-3			1.903	0.168
pos	213 (71.0)	5 (4.022, 5.998)		
neg	87 (29.0)	6 (4.481, 7.519)		
PRNP seq				
Codon 129			0.611	0.737
MM	295 (98.3)	5 (4.172, 5.828)		
MV	4 (1.3)	2		
VV	1 (0.3)	9		
Codon 219			–	–
EE	300 (100)	5 (4.165, 5.835)		
EK	0 (0.0)	–		
Nursing and care				
Place			3.739	0.154
Professional unit	150 (50.0)	6 (4.588, 7.412)		
At home	106 (35.3)	4 (2.739, 5.261)		
Both	44 (14.7)	4 (2.561, 5.439)		
Personnel			1.362	0.506
Registered nurse	63 (21.0)	6 (2.667, 9.333)		
Care worker	182 (60.7)	5 (4.009, 5.991)		
Both	55 (18.3)	6 (3.587, 8.413)		

Continued

Factor	Cases (%)	Median (m) (95% *CI*)	χ^2	*P*
Symptomatic care			0.741	0.389
Yes	280 (93.3)	6 (4.913, 7.087)		
No	20 (6.7)	4 (0.000, 8.361)		
Medical supporting and therapeutics				
Nasal feeding			20.795	<0.001***
Yes	146 (48.7)	8 (6.137, 9.863)		
No	154 (51.3)	4 (3.330, 4.670)		
Nutrition injection i.v.			1.620	0.203
Yes	114 (38.0)	5 (3.573, 6.427)		
No	186 (62.0)	5 (3.972, 6.028)		
Nutrition oral			0.044	0.833
Yes	29 (9.7)	7 (4.890, 9.110)		
No	271 (90.3)	5 (4.136, 5.864)		
Respiratory support			0.105	0.746
Yes	95 (31.7)	5 (3.322, 6.678)		
No	205 (68.3)	6 (4.885, 7.115)		
Symptomatic treatment			1.952	0.162
Yes	88 (29.3)	6 (4.471, 7.529)		
No	212 (70.7)	5 (3.876, 6.124)		
Antibiotic therapy			0.896	0.344
Yes	35 (11.7)	7 (3.688, 10.312)		
No	265 (88.3)	5 (4.097, 5.903)		
Antiviral therapy			0.243	0.622
Yes	53 (17.7)	5 (3.714, 6.286)		
No	247 (82.3)	6 (4.941, 7.059)		

Abbreviation: sCJD=sporadic Creutzfeldt-Jakob disease; m=months; *CI*=confidence intervals; PSWC=periodic sharp wave complexes; EEG=electroencephalogram; MRI=magnetic resonance imaging; CSF=cerebrospinal fluid; seq=sequence; i.v.=intravenous.
* *P*<0.05;
** *P*<0.01;
*** *P*<0.001.

Figure S2B). Clinical examinations revealed that cases with high signal intensity in caudate/putamen on magnetic resonance imaging (MRI) had shorter survival times (median: 4 months, 95% *CI*: 3.972, 6.028, *P*=0.004) (Supplementary Figure S2C). In the category of medical support and therapeutics, nasal feeding demonstrated significant impact on survival (*P*<0.001), with patients receiving nasal feeding showing longer duration (median: 8 months, 95% *CI*: 6.137, 9.863) (Supplementary Figure S2D). Further analysis of survival based on the frequency of four sCJD-associated symptoms (visual or cerebellar disturbance, myoclonus, pyramidal and extrapyramidal symptoms, mutism) or three MRI abnormalities (symmetrical or asymmetrical cortical "ribbon" signs on diffusion weighted imaging (DWI), high signal in caudate/putamen, or high signal in bilateral posterior thalamic tuberosity in the proton density phase) showed no statistical significance, although patients with more symptoms or MRI abnormalities tended toward shorter survival durations (Supplementary Table S1, available at https://weekly.chinacdc.cn/).

The factors demonstrating statistical significance in the univariate analysis were further evaluated using multivariate regression with Cox proportional hazard modeling. As shown in Table 2, all four factors maintained statistical significance. Analysis of *HR* values revealed significantly elevated hazard risks in patients who were >65 years at onset (*HR*: 1.379, 95% *CI*: 1.088, 1.748), presented with pyramidal or extrapyramidal dysfunction (*HR*: 1.476, 95% *CI*: 1.060, 2.054), demonstrated high signal intensity in

TABLE 2. Multivariate regression analysis of the factors associated with survival in sCJD.

Factor	β	SE	Wald χ^2	*P*	*HR* (95% *CI*)
Onset age (years)					
35–65					1.000
≥66	0.321	0.121	7.039	0.008**	1.379 (1.088, 1.748)
Pyramidal or extrapyramidal dysfunction					
No					1.000
Yes	0.389	0.169	5.319	0.021*	1.476 (1.060, 2.054)
High signal in caudate/putamen					
No					1.000
Yes	0.297	0.129	5.278	0.022*	1.346 (1.045, 1.733)
Nasal feeding					
Yes					1.000
No	0.537	0.121	19.642	<0.001***	1.711 (1.349, 2.169)

Abbreviation: sCJD=sporadic Creutzfeldt-Jacob disease; *HR*=hazard ratio; *CI*=confidence intervals.
* *P*<0.05;
** *P*<0.01;
*** *P*<0.001.

caudate/putamen on MRI (*HR*: 1.346, 95% *CI*: 1.045, 1.733), or did not receive nasal feeding (*HR*: 1.711, 95% *CI*: 1.349, 2.169).

Further stratified analyses were conducted by dividing cases into age groups (≤65 years and >65 years) for both univariate and multivariate regression analyses (Table 3). In the ≤65 years group, univariate analysis identified five significant factors associated with survival time: cortical blindness as an initial symptom (*P*=0.037), cerebellar disturbance (*P*=0.032), pyramidal or extrapyramidal dysfunction (*P*=0.028), high signal in caudate/putamen on MRI (*P*=0.004), and nasal feeding (*P*=0.019). Subsequent multivariate Cox regression analysis revealed two significant factors: high signal in caudate/putamen (*HR*: 1.556, 95% *CI*: 1.111, 2.178, *P*=0.010) and absence of nasal feeding (*HR*: 1.476, 95% *CI*: 1.072, 2.033, *P*=0.017) In the group of >65 years group, four factors showed statistical significances in the univariate assay, including care place (*P*=0.022), akinetic mutism (*P*=0.016), pyramidal or extrapyramidal dysfunction (*P*=0.027), nasal feeding (*P*=0.019). Multivariate Cox regression analysis indicated 1.695-fold increased death risk (95% *CI*: 1.056, 2.721, *P*=0.025) in the patients with pyramidal or extrapyramidal dysfunction, and 2.386-fold increased death risk (95% *CI*: 1.605, 3.548, *P*<0.001).

DISCUSSION

Human prion diseases, including sCJD, remain universally fatal with significantly shorter clinical durations compared to other neurodegenerative disorders such as Alzheimer disease (AD) and Parkinson disease (PD) (*1*). Through analysis of 300 probable sCJD cases reported to the China National Surveillance for CJD between January 2020 and December 2022, we identified four key factors associated with shortened survival times: age greater than 65 years at onset, presence of pyramidal or extrapyramidal dysfunction, high signal intensity in caudate/putamen on MRI, and absence of nasal feeding.

Our findings demonstrate that patient age at disease onset significantly influences survival duration in Chinese sCJD patients. Elderly patients exhibited a 1.379-fold increased mortality risk compared to younger patients, consistent with previous studies documenting age-dependent decreased survival in sCJD (*6*–*7*). This association may be attributed to compromised health status and increased comorbidities in older populations, although some studies have failed to establish a clear correlation between onset age and clinical duration (*8*–*9*). Pyramidal or extrapyramidal dysfunction emerged as a negative prognostic factor, particularly in patients over 65 years at onset. These movement disorders, which encompass tremors, postural and gait abnormalities, limb ataxia, and dystonic spasms, are common in sCJD patients and may increase the risk of falls while complicating daily care management.

The prognostic significance of MRI for sCJD

TABLE 3. Univariate and multivariate regression analysis of factors associated with survival in two groups ≤65 and >65 years.

Factor	Univariate analysis			Multivariate analysis		
	Cases (%)	Median of survival (m) (95% *CI*)	*P*	χ^2	*P*	*HR* (95% *CI*)
sCJD cases ≤65 years (*n*=166)						
Cortical blindness in initial symptoms			0.037*	2.301	0.129	
Yes	8 (4.8)	4 (1.288, 6.772)				1.000
No	158 (95.2)	6 (4.241, 7.759)				0.568 (0.274, 1.180)
Cerebellar disturbance in initial symptoms			0.032*	2.919	0.088	
Yes	56 (33.7)	4 (3.025, 4.975)				1.000
No	110 (66.3)	7 (4.944, 9.056)				0.746 (0.533, 1.044)
Pyramidal or extrapyramidal dysfunction			0.028*	1.871	0.171	
Yes	139 (83.7)	5 (3.641, 6.359)				1.000
No	27 (16.3)	10 (6.183, 13.817)				0.723 (0.454, 1.151)
High signal in caudate/putamen			0.004**	6.628	0.010*	
No	66 (39.8)	7 (4.550, 9.450)				1.000
Yes	100 (60.2)	5 (3.513, 6.487)				1.556 (1.111, 2.178)
Nasal feeding			0.019*	5.686	0.017*	
Yes	84 (50.6)	8 (4.777, 11.223)				1.000
No	82 (49.4)	4 (2.622, 5.378)				1.476 (1.072, 2.033)
sCJD cases >65 years (*n*=134)						
Place of care			0.022*	2.713	0.258	
Professional unit	70 (52.2)	6 (4.366, 7.634)				1.000
At home	54 (40.3)	4 (3.105, 4.895)				1.359 (0.942, 1.961)
Both	10 (7.5)	3 (2.290, 3.710)				1.163 (0.771, 1.755)
Akinetic mutism			0.016*	0.207	0.649	
Yes	107 (79.9)	5 (3.311, 6.689)				1.000
No	27 (20.1)	3 (1.728, 4.272)				1.114 (0.610, 1.372)
Pyramidal or extrapyramidal dysfunction			0.027*	5.031	0.025*	
Yes	109 (81.3)	6 (3.062, 8.938)				1.000
No	25 (18.7)	4 (2.636, 5.364)				1.695 (1.056, 2.721)
Nasal feeding			0.019*	18.464	<0.001***	
Yes	64 (47.8.)	7 (5.041, 8.959)				1.000
No	70 (52.2)	4 (3.154, 4.845)				2.386(1.605, 3.548)

Abbreviaiton: sCJD=sporadic Creutzfeldt-Jakob disease; m=months; *HR*=hazard ratio; *CI*=confidence intervals.
* *P*<0.05;
** *P*<0.01;
*** *P*<0.001.

remains incompletely understood. A recent Korean study demonstrated that caudate nucleus and putamen involvement on diffusion-weighted imaging (DWI) correlates with poor prognosis (*7*). Our findings align with this observation, revealing high signal intensity in the caudate nucleus and putamen as a negative prognostic factor for sCJD survival, particularly in patients ≤65 years at onset. MRI lesion patterns in sCJD cases appear to demonstrate age-dependent characteristics. Previous research indicates that typical cortical and basal ganglia hyperintensities predominate in younger patients, while unilateral hemispheric or isolated cortical lesions occur more frequently in older individuals (*10*). Furthermore, extensive DWI abnormalities, particularly those involving three or more lobes with moderate to extensive cortical and striatal involvement, correlate with notably shortened median survival of approximately 1.7 months (*7*).

Importantly, most sCJD patients in our cohort underwent single evaluations of MRI, electroencephalogram (EEG), and CSF 14-3-3 testing post-onset. Serial examinations, combined with clinical features, would enable more precise stratification and prognostication of sCJD cases.

Nasal feeding demonstrates significant survival benefits for sCJD patients. Japanese research has similarly shown that tube-fed patients experience significantly extended survival compared to non-tube-fed patients, regardless of whether feeding was administered via nasogastric tube or gastrostomy (*7*). Additionally, enteral nutrition through percutaneous endoscopic gastrostomy or radiologically inserted gastrostomy correlates with markedly improved survival across sCJD, gCJD, and acquired CJD patients (*11*). We posit that nasal feeding represents a crucial intervention in the advanced-stage care of CJD patients. While dysphagia frequently compromises nutritional intake in CJD patients, nasal feeding offers a less invasive alternative to gastrostomy that can be readily implemented in small clinical settings or home environments.

Several limitations should be acknowledged in this study. First, all cases were classified as probable sCJD without neuropathological confirmation or PrP^{Sc} detection, which may introduce diagnostic bias. Second, the relatively modest sample size necessitates further validation through expanded cohort studies to confirm the stability of our findings. Third, the implementation of nasogastric feeding is influenced by multiple factors, including family support, patient end-of-life preferences, and physician judgment, which may confound the observed associations. Continued evaluation of these identified survival factors through ongoing CJD surveillance will be crucial for optimizing medical interventions and care strategies for Chinese CJD patients.

Conflicts of interest: No conflicts of interest.

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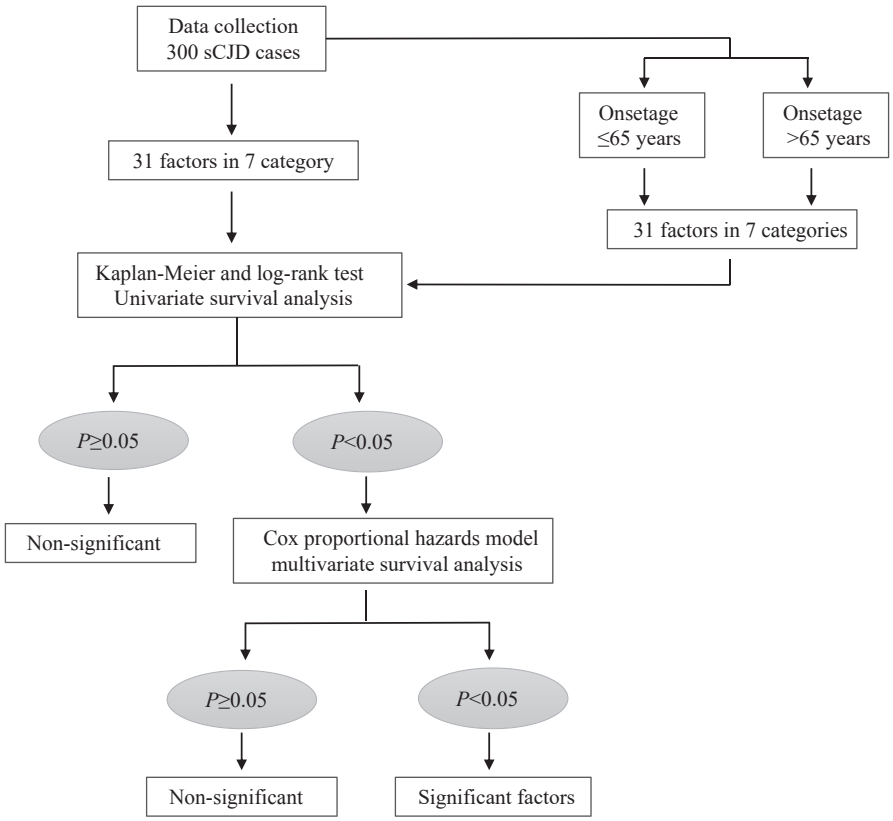
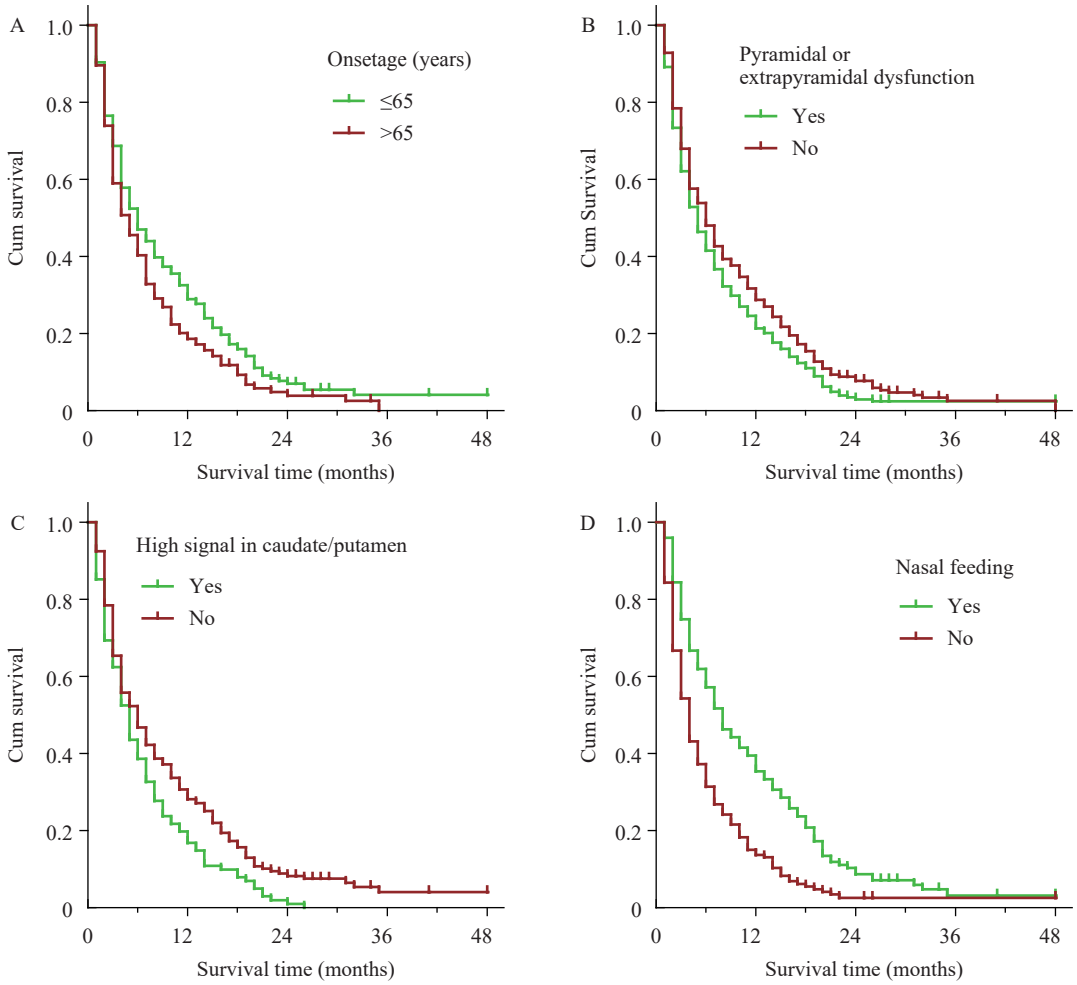
Supplementary Material



SUPPLEMENTARY FIGURE S1. Flowchart showing the data collection of the enrolled 300 sCJD cases and statistical analytic processes for the selected factors potentially associated with the survival of disease.
Abbreviation: sCJD=sporadic Creutzfeldt-Jakob disease.



SUPPLEMENTARY FIGURE S2. Comparative survival curves of sCJD patients (A) between the groups ≤65 years and >65 years at onset, (B) with or without pyramidal or extrapyramidal dysfunction, (C) high signal of caudate nucleus/putamen, (D) with or without nasal feeding.

SUPPLEMENTARY TABLE S1. Univariate analysis of the associations of the frequencies of clinical manifestations and MRI abnormalities with survival.

Factor	Cases	Median of survival time (m) (95% *CI*)	χ^2	*P*
Clinical manifestations			5.756	0.124
Dementia plus 1	17	7 (0.950, 13.050)		
Dementia plus 2	53	6 (3.808, 8.192)		
Dementia plus 3	134	6 (4.586, 7.414)		
Dementia plus 4	96	4 (2.800, 5.200)		
Abnormalities on MRI			4.669	0.198
0	41	6 (3.719, 8.281)		
1	164	6 (4.369, 7.613)		
2	85	5 (3.877, 6.123)		
3	10	4 (0.901, 7.099)		

Abbreviation: MRI=magnetic resonance imaging; m=months; *CI*=confidence intervals.