Incidence, Cause of Death, and Survival of Amyloidosis in Korea

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Research

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Abstract

Background

We sought to assess incidence and survival for amyloidosis.

Methods

We acquired data from newly diagnosed cases related to amyloidosis from the National Health Insurance Service in Korea from 2006 through 2017 (n=2,233; male 53.5%). We calculated the age-standardized incidence rate, analyzed the survival rate (SR) using the Kaplan-Meier method, and analyzed the death risk using Cox proportional hazards methods.

Results

The mean age was 57.0 (±16.7) years in males and 56.8 (±15.6) years in females (p=non-significant). The proportion of death was 34.7%. The causes of death were endocrine, nutritional, and metabolic diseases (33.9%), malignant neoplasm (20.8%), diseases of the circulatory system (9.68%), and diseases of the genitourinary system (9.29%). The overall age-standardized incidence rate was 0.47 persons per 100,000 persons in 2017. Overall, the 10-year SR for amyloidosis was 57.7% (55.9% in males and 59.2% in females). Adjusted hazard ratios were 9.16 (95% confidence interval [CI] 2.23, 37.5) among 40-49 year-old, 16.1 (95% CI 4.00, 65.3) among 50-59 year-old, 30.3 (95% CI 7.53, 122.0) among 60-69 year-old, 48.7 (95% CI 12.1, 196.3) among 70-79 year-old, 80.1 (95% CI 19.6, 326.3) among people 80 years or older and 1.21 (95% CI 1.02, 1.44) in the medium-level socioeconomic position group.

Conclusions

The age-standardized incidence rate of amyloidosis was about 0.5 persons per 100,000 persons in 2017. The 10-year SR of amyloidosis was about 58%. The most common cause of death was endocrine, nutritional, and metabolic diseases. The risk of death from amyloidosis increased with age and medium socioeconomic position.

Introduction

Amyloidosis is a rare disease that involves multiple organs. Due to delayed diagnosis and involvement of vital organs, prognosis for amyloidosis patients is usually considered to be grave. Few studies have evaluated the incidence, survival rate, cause of death, and risk factors for mortality of amyloidosis. We have previously reported the prevalence of amyloidosis in Korea [1]. In the current study, we analyzed the age-standardized incidence, survival rate, cause of death, and risk factors for death in amyloidosis patients using Korean National Health Insurance Service data from 2006 through 2017.

Methods

Study Population

We collected data from Korean National Health Insurance benefit records from 2006 through 2017. We excluded amyloidosis patients from the years 2002 to 2005 to include only newly diagnosed amyloidosis since 2006. The data contained primary diagnoses related to amyloidosis according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). Amyloidosis (ICD-10: E85) diagnoses were extracted from the records after consideration of the data given for the primary diagnoses, which depended on initial chief complaints and symptoms. The National Health Insurance benefit records do not contain information confirming diagnoses or describing treatments at medical institutes. Therefore, the final diagnoses could differ from the diagnoses in the data. In this study, we used the death data of Korean people from 2006 through 2018.

Diagnosis

Ages were categorized as 0–9 years, 10–19 years, 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, 70–79 years, and 80 years or older. Socioeconomic factors included percentile group of income level using the National Health Insurance premium divided into 20 quartiles. Income levels were categorized as upper, medium, and lower.

Cause of death

We evaluated primary cause of death: certain infections and parasitic diseases (ICD-10: A00-B99); malignant neoplasm (ICD-10: C00-C97); benign neoplasm (ICD-10: D00-D48) & diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (ICD-10: D50-D89); endocrine, nutritional, and metabolic diseases (ICD-10: E00-E90); mental and behavioral disorders (ICD-10: F01-F99); diseases of the nervous system (ICD-10: G00-G98); diseases of the circulatory system (ICD-10: I00-I99); diseases of the respiratory system (ICD-10: J00-J98); diseases of the digestive system (ICD-10: K00-K92); diseases of the skin and subcutaneous tissue (ICD-10: L00-L99); diseases of the musculoskeletal system and connective tissue (ICD-10: M00-M99); diseases of the genitourinary system (ICD-10: N00-N99); symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified (ICD-10: R00-R99); injury, poisoning, and certain other consequences of external causes (ICD-10: S00-T98); and not provided.

Statistical Methods

The differences in age, socioeconomic position, and causes of death by sex were analyzed using the student's *t*-test for continuous variables and the χ^2-test for categorical variables. We calculated the age-standardized incidence of amyloidosis with the direct method using the beneficiaries of health insurance from the Korean National Health Insurance Statistical Yearbook from 2006 through 2017 as the subjects and the estimated Korean population in 2015 as the reference [1, 2]. The Kaplan-Meier method was also used to compare survival among patients with amyloidosis by age group and sex using log-rank tests.

Simple and multiple Cox proportional hazards analyses were carried out using the variables of age, sex, and socioeconomic position.

Ethics

This study protocol was exempted by the Institutional Review Board of Samsung Medical Center (IRB File number 2017-02-032).

Results

Table 1 shows the distribution of the patients with newly diagnosed amyloidosis (n=2,233) by sex in Korea. The mean (± standard deviation) age of amyloidosis patients was 57.0 (±16.7) years in males and 56.8 (±15.6) years in females (p=non-significant [NS]). The male proportion was 53.5%. The proportion of death in amyloidosis patients was 34.7%. The proportions of cause of death were 33.9% for endocrine, nutritional, and metabolic diseases, 20.8% for malignant neoplasm, 9.68% for diseases of the circulatory system, and 9.29% for diseases of the genitourinary system ($p<0.05$). Adjusted hazard ratios (HR) of death from amyloidosis were 9.16 (95% confidence interval [CI] 2.23, 37.5) in the 40- to 49-year age group, 16.1 (95% CI 4.00, 65.3) in the 50- to 59-year age group, 30.3 (95% CI 7.53, 122.0) in the 60- to 69-year age group, and 48.7 (95% CI 12.1, 196.3) in the 70- to 79-year age group, 80.1 (95% CI 19.6, 326.3) in the 80 years or older age group, and 1.21 (95% CI 1.02, 1.44) in medium-level socioeconomic position group (Table 2).

The overall age-standardized incidence of amyloidosis was 0.34 persons per 100,000 persons in 2006 and 0.47 persons per 100,000 persons in 2017. We also showed age-standardized incidence of amyloidosis by sex and by age group (Fig. 1 and Supplementary Table 1).

Overall, the 10-year survival rate (SR) for amyloidosis was 57.7% (55.9% in males and 59.2% in females, p=NS). The 10-year SRs for the 0- to 9-year, 10- to 19-year, 20- to 29-year, 30- to 39-year, 40- to 49-year, 50- to 59-year, 60- to 69-year, and 70- to 79-year age groups were 100%, 100%, 97.7%, 89.1%, 77.4%, 64.8%, 43.2%, and 27.8%, respectively. The 80 years or older group was censored at 9.47 years (Fig. 2 and Supplementary Table 2).

Discussion

We found that older amyloidosis patients showed a higher risk of death; adjusted HR values were higher in the age groups. A previous population-based study in Queensland, Australia from 1999 to 2013 showed higher HR with age [3]. The mean age in this study was 56.9 years (±16.2); this is similar to the mean age of 129 amyloidosis patients from a tertiary hospital in Korea from 1999 to 2011 [4]. On the other hand, 447 Australian amyloidosis patients showed a higher age of 66 years (±64) at the time of diagnosis. The 10-year SR by age group in this study showed lower SR with age. Few studies have found HR and SR by age group using population-based method; therefore, we could not compare SR by age group.

Adjusted HR for male sex was not significant in this study, similar to the Australian population-based study [3]. The 10-year SR in this study also did not differ much by sex. The proportion of males was 53.5% in this study, in close agreement with another study of 129 Korean amyloidosis patients that were 58.9% [4]. However, in the Australian study, the proportion of males was higher at 64%.

The overall 10-year SR was about 58% in this study. Our results revealed higher SRs than another study of 159 light-chain amyloidosis patients from 1996 to 2003 at 40% [5]. The Australian study showed that overall SR by age group improved over 15 years [6].

Although the age-standardized incidence increased overall and by sex during a decade in this study, the incidences of Australian amyloidosis [3] and Swedish amyloidosis [7] were higher than those found in our study. In this study, the three major causes of death for amyloidosis were endocrine, nutritional, and metabolic diseases (ICD-10: E code), malignant neoplasm (ICD-10: C code), and diseases of the circulatory system (ICD-10: I code). We did not observe more specific causes of death using ICD-10 codes due to limited data. However, in additional observation, we showed the E8 code (amyloid) had the highest proportion among the codes starting with ICD-E and the C9 code (multiple myeloma) among ICD-C codes. For socioeconomic position, we found a higher HR in the medium-level socioeconomic position group.

Study Limitations

Our study has several limitations. First, we only used data from the primary amyloidosis diagnoses based on signs and symptoms, which could differ from the final diagnosis. Therefore, the incidence and SR of amyloidosis in this study might be under- or overestimated. Second, the National Health Insurance benefit records might have missed amyloidosis patients who did not use medical services or who paid for their own medical expenses [8]. Therefore, because of the increasing incidence of amyloidosis, Korea needs a well-designed hospital-based amyloidosis registry. Third, due to data limitations we did not analyze by amyloidosis subtype such as AL, which is associated with a light chain-producing plasma cell dyscrasia; AA, which is associated with longstanding inflammation; wild-type ATTR, which is associated with normal transthyretin and old age; or hereditary ATTR, which is associated with a transthyretin mutation.

Conclusions

We found that the age-standardized incidence of amyloidosis in Korea was about 0.5 persons per 100,000 persons in 2017. The SR across a decade was about 58%. Specifically, the older age groups showed lower survival rates than the younger age groups. The three major causes of death for amyloidosis were endocrine, nutritional, and metabolic disease; malignant neoplasm; and diseases of the circulatory system. The death risk for amyloidosis was higher with age and medium socioeconomic status. These patterns in incidence, survival rate, cause of death, and death risk should be considered in future research designs and policies for amyloidosis healthcare services.

List Of Abbreviations

ICD-10: the 10th revision of the International Statistical Classification of Diseases and Related Health Problems

NS: non-significant

HR: hazard ratios

CI: confidence interval

SR: survival rate

Declarations

Ethics approval and consent to participate: This study protocol was exempted by the Institutional Review Board of Samsung Medical Center (IRB File number 2017-02-032).

Consent for publication: Not applicable

Availability of data and material: Availability of result data. Result data were served from Korean National Health Insurance Benefit records from the National Health Insurance Service.

Competing interests: Not applicable

Funding: Not applicable

Authors' contributions: SYJ had made study design, analyzed statistic and discussed interpretation. DRK had discussed interpretation. JOC had discussed interpretation. ESJ had discussed interpretation and taken all responsibility for this paper. All authors read and approved the final manuscript.

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Tables

Table 1. The distribution of general characteristics, socioeconomic position, and cause of death by sex in amyloidosis (AM) and death risk for AM (n=2,233).

Variables	AM total (n=2,233)	Male (n=1,195)	Female (n=1,038)	p-value*	Crude Hazard Ratio (HR) and 95% CI	Adjusted HR and 95% CI§
	mean±SD, or number (percentage)					
Age, mean (SD)	56.9±16.2	57.0±16.7	56.8±15.6	0.795	-	-
0-9	19 (0.85)	13 (1.09)	6 (0.58)	0.052	0.00 (0.00, 999)	0.00 (0.00, 999)
10-19	31 (1.39)	17 (1.42)	14 (1.35)		0.00 (0.00, 999)	0.00 (0.00, 999)
20-29	88 (3.94)	45 (3.77)	43 (4.14)		1.0	1.0
30-39	192 (8.60)	116 (9.71)	67 (7.32)		4.01 (0.92, 17.4)	4.06 (0.93, 17.6)
40-49	323 (14.5)	160 (13.4)	166 (15.7)		8.95 (2.18, 36.6)‡	9.16 (2.23, 37.5)‡
50-59	511 (22.9)	256 (21.4)	255 (24.6)		15.9 (3.95, 64.5)†	16.1 (4.00, 65.3)†
60-69	536 (24.0)	297 (24.9)	239 (23.0)		29.5 (7.34, 118.8)†	30.3 (7.53, 122.0)†
70-79	419 (18.8)	219 (18.3)	200 (19.3)		46.2 (11.4, 186.2)†	48.7 (12.1, 196.3)†
80+	114 (5.11)	72 (6.03)	42 (4.05)		75.7 (18.6, 308.3)†	80.1 (19.6, 326.3)†
Sex, male	1195 (53.5)	1195 (100)	0 (0.00)		1.04 (0.90, 1.20)	1.00 (0.86, 1.15)
Socioeconomic position				0.248		
Upper	1079 (48.3)	596 (49.9)	483 (46.5)		1.0	1.0
Medium	585 (26.2)	299 (25.0)	286 (27.6)		0.93 (0.78, 1.11)	1.21 (1.02, 1.44)‡
Lower	569 (25.5)	300 (25.1)	269 (25.9)		1.01 (0.85, 1.20)	1.18 (0.99, 1.40)
Death	775 (34.7)	421 (35.2)	354 (34.1)	0.577	-	-
Cause of death, n=775				0.016	-	-
Certain infections and parasitic diseases (A00-B99)	18 (2.23)	7 (1.66)	11 (3.11)			
Malignant neoplasm (C00-C97)	161 (20.8)	84 (20.0)	77 (21.8)			
Benign neoplasm (D00-D48) and diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89)	11 (1.42)	7 (1.66)	4 (1.13)			
Endocrine, nutritional, and metabolic diseases (E00-E90)	263 (33.9)	140 (33.3)	123 (34.7)			
Mental and behavioral disorders (F01-F99)	1 (0.13)	1 (0.24)	0 (0.00)			
Diseases of the nervous system (G00-G98)	3 (0.39)	2 (0.48)	1 (0.28)			
Diseases of the circulatory system (I00-I99)	75 (9.68)	44 (10.5)	31 (8.76)			
Diseases of the respiratory system (J00-J98)	24 (3.10)	17 (4.04)	7 (1.98)			
Diseases of the digestive system (K00-K92)	13 (1.68)	10 (2.38)	3 (0.85)			
Diseases of the skin and subcutaneous tissue (L00-L99)	3 (0.39)	1 (0.24)	2 (0.56)			
Diseases of the musculoskeletal system and connective tissue (M00-M99)	10 (1.29)	6 (1.43)	4 (1.13)			
Diseases of the genitourinary system (N00-N99)	72 (9.29)	23 (5.46)	49 (13.8)			
Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99)	12 (1.55)	6 (1.43)	6 (1.69)			
Injury, poisoning, and certain other consequences of external causes (S00-T98)	19 (2.45)	15 (3.58)	4 (1.13)			
Not provided	90 (11.6)	58 (13.6)	32 (9.08)			

*student's *t*-test or χ^2-test, †p<0.001, ‡p<0.005, §Estimated by Cox proportional hazard model analysis using the variables indicated in the table

Figures

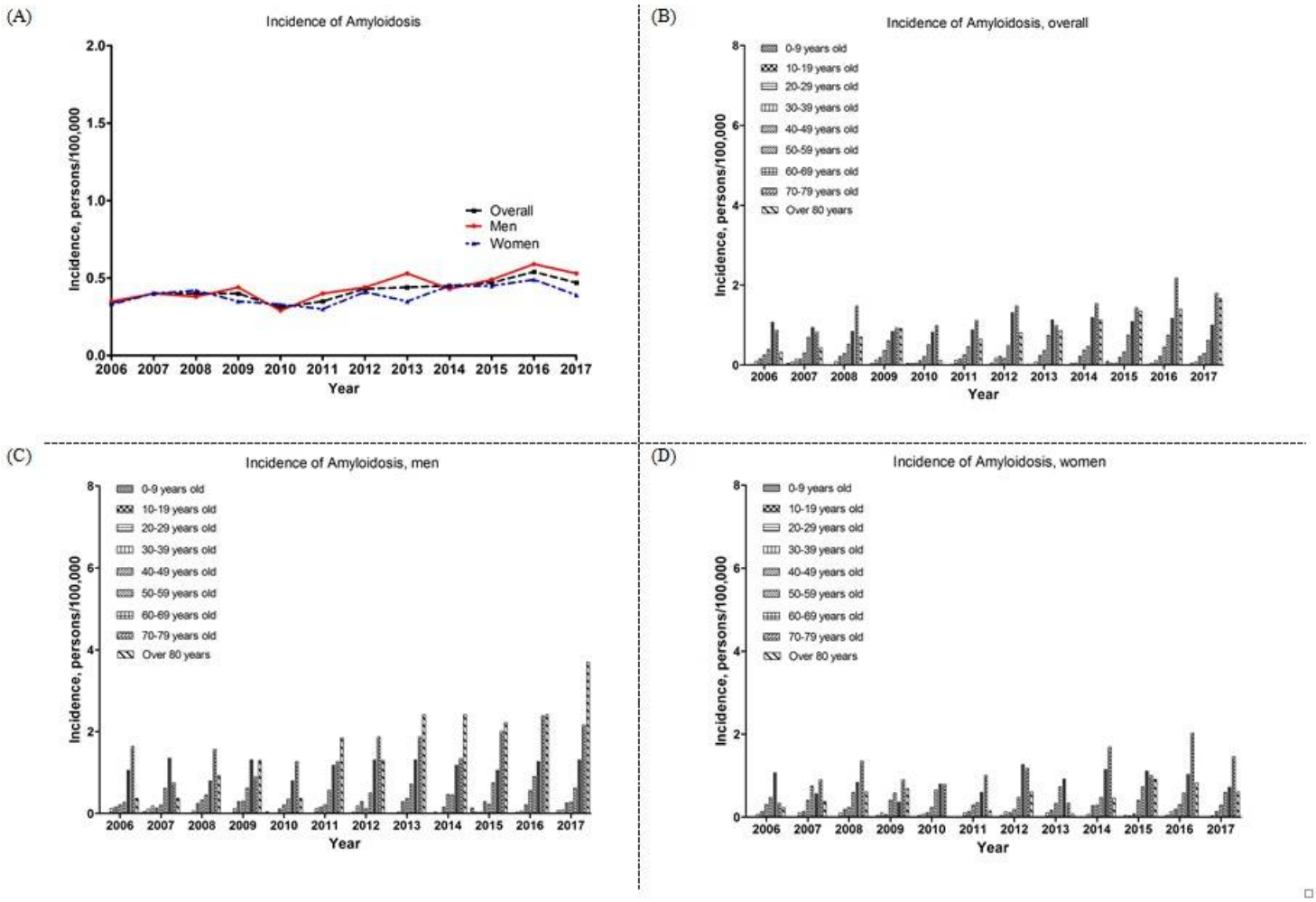

Figure 1

The age-standardized incidence of amyloidosis overall, by age group, sex, and year per 100, 000 persons between 2006 and 2017. (A) The age-standardized incidence of amyloidosis overall (middle), by sex (male: upper; female: lower), and by year per 100,000 persons between 2006 and 2017, (B) the age-standardized incidence of amyloidosis overall, (C) in males, and (D) in females by age group and by year per 100,000 persons between 2006 and 2017.

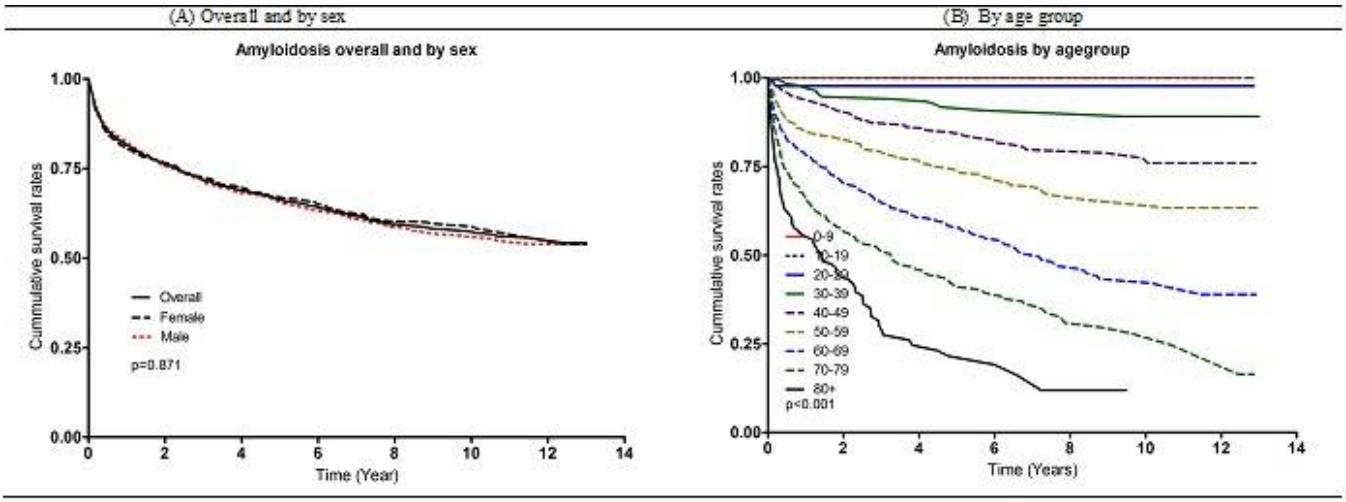

Figure 2

Survival curve for amyloidosis in Korean from 2006 through 2018 (A) Amyloidosis survival rates overall and by sex (p=non-significant); overall (middle), by sex (male: lower; female: upper) and (B) by age group (p<0.001)

Supplementary Files

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