



Treatment Patterns and Health Care Costs for Age-Related Macular Degeneration in Japan

An Analysis of National Insurance Claims Data

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Purpose: To investigate changes in the proportion of patients with age-related macular degeneration (AMD) visiting hospitals and to investigate factors associated with AMD, treatments, and medical expenses, as well as the outlook for AMD in Japan using a large health insurance database.

Design: Analysis of national insurance claims data.

Participants: People 40 years of age or older who were registered in the Japan Medical Data Center database.

Methods: Patients with AMD were identified from 2005 through 2013 based on International Classification of Diseases, 10th revision, diagnosis codes. Changes in patient proportions, treatment procedures, and medical expenses were investigated during the study period. The data for each year were compared after adjustment based on the 2010 Japanese population annual census. The outlook for patients with AMD was predicted based on the combination of data in 2013 and an official future population prediction report.

Main Outcome Measures: Changes in treatment patterns and health care costs in Japan.

Results: A total of 3 401 299 participants were included in the analysis, and 3058 AMD patients were identified over the 9-year period. The proportion of patients with AMD increased significantly from 0.084% (95% confidence interval, 0.050%–0.119%) in 2005 to 0.26% (95% confidence interval, 0.24%–0.29%) in 2013 ($P = 0.0001$, Pearson correlation coefficient test). There were significantly more men than women (odds ratio, 1.25; 95% confidence interval, 1.14–1.37), and the proportion of patients with AMD increased rapidly with age. Photodynamic therapy was replaced by anti-vascular endothelial growth factor (VEGF) therapy as the predominant therapy from 2009 onward. Medical expenses per 10 000 persons increased from \$1530 to \$137 000 over the 9-year period. The proportion of AMD patients is predicted to increase in the future and will reach a maximum of 223 000 in 2035.

Conclusions: The proportion of AMD patients visiting hospitals, medical expenses, and the frequency of anti-VEGF therapy increased significantly over the 9-year period. These increasing trends are predicted to continue in Japan. *Ophthalmology* 2016;■:1–6 © 2016 by the American Academy of Ophthalmology.

Age-related macular degeneration (AMD) negatively affects vision quality^{1,2} and is a major cause of acquired blindness.^{2,3} Aging is the main risk factor for the development of AMD,^{2,4–8} suggesting that the incidence and number of patients with AMD will increase worldwide.^{6,9} A few population studies performed in Japan revealed the prevalence and risk factors for AMD. Kawasaki et al⁷ reported that the prevalences of early AMD and late AMD were 3.5% and 0.5%, respectively. Nakata et al¹⁰ reported that the prevalences of early AMD and late AMD were 22.8% and 0.58%, respectively. Both studies revealed that aging, male gender, retinal pigment abnormalities, and smoking were risk factors for AMD. However, studies of the current and future outlook⁹ of AMD are limited, particularly for Asian countries, including Japan.

Treatment strategies for AMD have changed dramatically in recent years.^{2,11} Vitrectomy, laser

photocoagulation,¹² and photodynamic therapy (PDT)^{13,14} once were considered the preferred treatments for AMD.¹¹ However, these treatments often exhibit limited effectiveness and frequently are associated with poor visual prognosis.^{2,15} By contrast, anti-vascular endothelial growth factor (VEGF) therapy successfully maintains and even improves visual function in some cases.^{15–22} Unfortunately, anti-VEGF therapy is associated with increased medical expenses because of the cost^{23,24} of the therapy and the need for repeated injections. Few studies have examined the practical implications of anti-VEGF therapy for medical expenses. The aims of this study were to investigate changes in AMD patient proportions, treatment regimens, and medical expenses over the past 9 years and to predict future trends of AMD in Japan based on the largest Japanese health insurance database.

Methods

This study was performed in accordance with the tenets of the Declaration of Helsinki and was approved by the Institutional Ethics Review Board of the University of Yamanashi. Because the data used in this study do not contain any personal information, the Institutional Ethics Review Board approved this study without requiring written informed consent from all patients.

Database

In Japan, all individuals must join one of the public insurance systems. Two main types of public insurance systems are available: National Health Insurance for retired persons, the self-employed, and their dependents and Employee Health Insurance for employees and their dependents. In this study, we used the health insurance claims database from the Japan Medical Data Center (JMDC), which contains medical data for patients with Employee Health Insurance. Established in 2002, the JMDC is the largest medical database in Japan. Its purpose is to accumulate medical data to aid epidemiologic and health service research. The details of this database have been described elsewhere.^{25,26} In brief, the database links all claims from different hospitals, clinics, and pharmacies using an anonymous linkage system applying an encryption code and combines individual medical claim information via a computer-aided standardization method after entry. This database enables the aggregation of all claims for the same patient without duplicating medical claims, including patients who change their Employee Health Insurance enrollment or visit multiple medical institutions, including hospitals, clinics, and pharmacies.

The database includes data on age and gender. If medical records are available, then the following data are disclosed: International Classification of Diseases, 10th revision, diagnosis codes, prescribed drugs, medical examinations, treatment, and the medical institution size. In this study, those 40 years of age or older who were registered in the JMDC database between 2005 and 2013 were included. All registered data belonging to the database were subject to the analysis. Subjects whose insurance system could not be identified after they quit Employee Health Insurance were excluded.

Definition of Age-Related Macular Degeneration

Patients with AMD were identified based on the following International Classification of Diseases, 10th revision, diagnosis codes: age-related macular degeneration (H353), polypoidal choroidal vasculopathy (H353), exudative age-related macular degeneration (H353), idiopathic choroidal neovascularization (H353), and atrophic age-related macular degeneration (H353).

Data Analysis

The proportion of patients in each year was defined as the number of patients divided by the total number of subjects in the JMDC database in each year. Treatment procedures for AMD were limited exclusively to PDT and anti-VEGF therapy because the number of AMD patients who underwent vitrectomy was too small for statistical analysis. The treating frequency in each year was defined as the number of treated patients divided by the number of patients in each year. For the medical expense analysis, the exchange rate was calculated based on \$1 United States dollar equaling ¥120 Japanese yen.

The proportion of patients with AMD in each study year was adjusted based on the 2010 Japanese census to compare proportions among years during the study period. Because the number of AMD patients in each age group was small, the effect of age on AMD was investigated in 5-year age groups. Future numbers and

proportions of patients with AMD were estimated based on a combination of data in 2013 and official prediction data from the National Institute of Population and Social Security Research based on birth and mortality rates in January 2012.

Statistical Analysis

For the statistical analysis, a chi-square test for onset-related factors and the Pearson correlation coefficient test for changes over time were used. The odds ratio was calculated by Poisson regression analysis. Probability values less than 0.05 were considered significant.

Results

The total number of cumulative subjects registered in the database from 2005 to 2013 was 9 851 083. Of these subjects, 3 401 299 (men, 1 824 849; women, 1 576 450) were 40 years of age or older. After eliminating subjects counted multiple times by a computer-aided standardization after entry, 3058 patients with AMD were included in the study, including 1953 men and 1105 women.

Changes in the Proportion of Age-Related Macular Degeneration Patients

Figure 1 indicates that the proportion of AMD patients increased significantly, by approximately 300%, from 0.084% (95% confidence interval, 0.050%–0.119%) in 2005 to 0.26% (95% confidence interval, 0.24%–0.29%) in 2013 ($P = 0.0001$, Pearson correlation coefficient test). The annual rate of increase was 0.022% over 9 years. The proportion of AMD patients increased until 2009 and seemed to plateau thereafter.

Effects of Gender and Age on the Proportion of Age-Related Macular Degeneration Patients

Figure 2A shows that the effects of gender and age were investigated exclusively using the 2013 data set. The proportion of AMD patients differed significantly between men and women at 0.29% and 0.24%, respectively (odds ratio, 1.25; 95% confidence interval, 1.14–1.37; $P < 0.0001$). The proportion of patients with AMD increased significantly with age ($P = 0.0035$, Pearson correlation coefficient test); the odds ratio per unit was 1.82 for every 5 years. The proportion of AMD patients

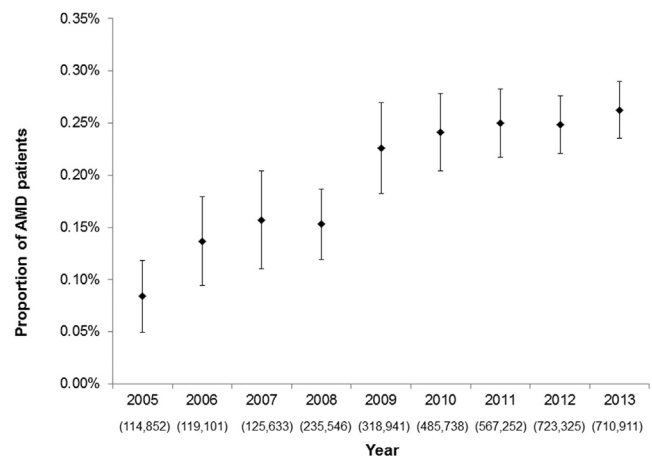


Figure 1. Graph showing changes in the proportion of age-related macular degeneration (AMD) patients. The numbers in parentheses indicate registered subjects in each year. Error bars = 95% confidential intervals.

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