Septic arthritis is a serious orthopedic disease that is associated with severe adverse effects such as osteomyelitis, joint destruction, ankylosis, sepsis and death.\(^1\)\(^2\)\(^3\) Septic arthritis can occur in people of any age group, from newborns to the senile population.\(^1\)\(^2\) In adults, the most commonly affected joint is the knee joint, and osteoarthritis also commonly occurs in the knee joint.\(^4\)\(^7\) Although some studies reported that the incidence of septic arthritis ranged from 1.6% to 9.2%, using the regional or hospital-based data,\(^4\)\(^7\) there are few studies on the nationwide incidence of septic arthritis of the knee in adults.\(^8\)

Intra-articular injections are a recommended treatment option for management of osteoarthritis according to several international guidelines.\(^9\)\(^10\)\(^11\) The use of intra-articular hyaluronic acid injections has increased in elderly patients with osteoarthritis.\(^10\) Physicians commonly use intra-articular injections in symptomatic patients with mild osteoarthritis of the knee because the superficial knee joint can be easily accessed without any assistive device such as ultrasound and fluoroscopy. Although the efficacy of hyaluronic injections has been well-documented, septic arthritis has also been a concern associated with the frequent use of hyaluronic.\(^13\) Population aging is also prominent in East Asia, reflected by a high prevalence of osteoarthritis.\(^14\) Accordingly, the use of hyaluronic for the
management of osteoarthritis is increasing in East Asia.\textsuperscript{15,16} However, an epidemiologic study on the incidence of septic knee and the utilization of hyaluronate in East Asia has not been conducted. Considering the low incidence of septic arthritis of the knees, the nationwide database appears to be useful and provides sufficient statistical power. Our hypothesis was that the trends of incidence of septic knees were similar to that of the utilization of hyaluronate in the elderly Korean population.

The purpose of this study was to evaluate trends in the incidence of septic knees and compare these with the utilization of hyaluronate in the Korean population from 2008 to 2012, using nationwide data from the Health Insurance Review and Assessment Service (HIRA).

\textbf{METHODS}

The data on the utilization of hyaluronate and the incidence of septic arthritis of the knee was retrieved from the HIRA between 2008 and 2012. In Korea, 97.0\% of the population is obliged to enroll in the Korean National Health Insurance Program. Patients pay around 30\% of the total medical costs to the clinics or hospitals; however, some medical services are not covered by insurance, such as cosmetic surgery and some unproven therapies. The clinics and hospitals then submit the claims for inpatient and outpatient care, including data on diagnoses (as determined by the International Classification of Diseases, 10 revision [ICD-10]), procedures, prescription records, and demographic information to obtain reimbursement for 70\% of the total medical costs. The remaining 3\% of the population that is uninsured by the Korean National Health Insurance Program, is either covered by another Medical Aid Program or are temporary or illegal residents. These claims are also reviewed by HIRA that was established by the Korean government, and nearly all information about the patients and their medical records can be obtained from the Korean HIRA database, which has been used in several earlier epidemiological studies.\textsuperscript{17-20}

Data regarding hyaluronate prescription and the number of prescriptions was abstracted and collated. The utilization of hyaluronate was determined from the annual number of prescriptions of hyaluronate. Patients with septic knees essentially require hospitalization for surgical intervention, and these data are recorded prospectively in nationwide cohort using ICD-10 codes, as described above. To identify septic knees in adults, selected ICD-10 codes (ICD-10 M0006 and M0016) and a minimum cut-off value of 50 years were used.\textsuperscript{21} To exclude prevalent patients who visited outpatient clinics, only hospitalizations were included in the study. To determine trends in the incidence of septic knee, the patients were categorized by age (subdivided into 5-year increments) and gender. Age-adjusted and gender-specific incidence rates (per 100,000 persons) were calculated using the respective annual population. The number of men and women above 50 years of age was obtained from the Statistics Korea web site (http://www.kosis.kr), the official web site of the Central Government Organization for Statistics.\textsuperscript{22} The changes in incidence of septic knee from 2008 to 2012 were calculated using annual percentage change for trends (Joinpoint Regression Program ver. 3.5.2, Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD, USA). To obtain age-adjusted and gender-specific incidence, the Korean population in 2011 was used as a standard population. Age-adjusted and gender-specific incidences from 2008 to

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Variable} & \textbf{No. of septic knees} & \textbf{Incidence of septic knees} & \textbf{Age-adjusted incidence of septic knees*} \\
\hline
\hline
\textbf{Man} & & & \\
2008 & 124 & 2.06 & 2.07 \\
2009 & 137 & 2.17 & 2.18 \\
2010 & 167 & 2.52 & 2.53 \\
2011 & 171 & 2.46 & 2.46 \\
2012 & 196 & 2.69 & 2.68 \\
\hline
\textbf{Woman} & & & \\
2008 & 229 & 3.24 & 3.21 \\
2009 & 252 & 3.41 & 3.39 \\
2010 & 294 & 3.81 & 3.81 \\
2011 & 310 & 3.86 & 3.86 \\
2012 & 350 & 4.18 & 4.17 \\
\hline
\textbf{Total} & & & \\
2008 & 353 & 5.30 & 5.29 \\
2009 & 389 & 5.58 & 5.57 \\
2010 & 461 & 6.34 & 6.33 \\
2011 & 481 & 6.32 & 6.32 \\
2012 & 546 & 6.87 & 6.85 \\
\hline
\end{tabular}
\caption{Table 1. Absolute No. and Age-Adjusted and Gender-Specific Incidences (per 100,000 Persons) of Septic Knees in the Korean Population above 50 Years of Age}
\end{table}

*Age-adjusted to the Korean population in 2011.
2012 were used in the analysis. Statistical results were presented as 95% confidence interval (CI). Because the data used is available to the public, only the de-identified information was used in the present study. The study protocol was approved by the HIRA Institutional Review Boards.

RESULTS

In 2012, among the population aged 50 years or older, the crude overall incidences of septic knees were 2.7 per 100,000 persons in men and 4.2 per 100,000 persons in women, respectively (Table 1). The absolute number of septic knees increased during the study period (Fig. 1). The age-adjusted incidence of septic knee increased by 6.7% per year (95% CI, 3.3 to 10.1) (Table 2 and Fig. 1). In addition, over the 5-year study period, the annual number of prescriptions of hyaluronate increased about 1.5-fold (Fig. 2).

DISCUSSION

This study showed that the incidence of septic knees significantly increased in the Korean population aged 50 years or older, while the annual utilization of hyaluronate increased approximately 1.5-fold from 2008 to 2012.

This finding concurs with the results of an epidemiologic study conducted in Iceland, where the incidence of septic arthritis increased significantly in adults over 12 years. They reported that interventions such as arthroscopy and joint injections were the main causes of increased incidence of septic arthritis in Iceland. Although the study included other joints such as the shoulder and hip joint, the knee joint was the most commonly affected joint in that study. The present study was performed over a period of 5 years because the HIRA limited the study period to a maximum of 5 years. However, this is the first epidemiologic study on the incidence of septic arthritis of the knee and the utilization of hyaluronate in East Asia.

We cannot directly compare the incidence of septic arthritis of the knee in Korea with that of other countries because the incidence of septic knee varies according to

| Gender | Annual percentage change (%) | 95% Confidence interval |
|--------|-----------------------------|-------------------------|
| Man    | 6.6                         | 2.1–11.2                |
| Woman  | 6.7                         | 4.2–9.3                 |
| Total  | 6.7                         | 3.3–10.1                |

*p < 0.05.
the definition of septic arthritis used (Table 3). 4-8,23 A previous community-based survey study in the Netherlands indicated an incidence of 5.7 per 100,000 persons among culture positive cases or cases in which microorganisms in the synovial fluid or tissue were identified. 5,24 The entire population was included in that study, but we included only the adult population above 50 years of age. We included the patients who were clinically diagnosed with septic knee by using the ICD-10 code. Generally, the incidence of culture-proven septic arthritis is lower than that of clinically-diagnosed septic arthritis because the yield of culture is below 100%. In addition, we could not exclude the possibility of duplicate case due to recurrence and readmission because we used the de-identified data from the HIRA database. These could be some of the possible reasons for the higher incidence of septic knee arthritis in Korea, as compared to those in other countries (Table 3).

Table 3. Comparison of Annual Incidence (per 100,000) of Septic Arthritis among Different Populations

| Study            | Region         | Study period | Age (yr) | Incidence |
|------------------|----------------|--------------|----------|-----------|
| Morgan et al.26  | Australia      | 1976–1994    | All ages | 9.2       |
| Kaandorp et al.  | The Netherlands| 1990–1993    | All ages | 5.7       |
| Weston et al.7   | The United Kingdom | 1982–1991  | All ages | 2.6       |
| Gupta et al.4    | Scotland       | 1997–1999    | > 16     | 1.6       |
| Geirsson et al.8 | Iceland        | 1990–2002    | All ages | 7.1       |
| Al Arfaj23       | Saudi Arabia   | 2005–2006    | All ages | 2.1       |
| Present study    | Korea          | 2012         | > 50     | 6.9*      |

*Only knee joints were included.

This study has several limitations. First, information regarding the other risk factors for septic knee (e.g., diabetes, malignancy, and immune-compromised) was not available at an individual level because this study was based on the de-identified database. Second, because we used de-identified codes and the number of prescriptions, we could not determine the amount of hyaluronate prescribed on an individual level, although the frequency of hyaluronate administration is likely to be associated with the occurrence of septic knee.3,25,26 Generally, hyaluronate was injected several times for viscosupplementation. Third, we included hyaluronate, but we did not include other injectates such as local anesthetics and corticosteroid. However, local anesthetics and corticosteroid are indicated in many other conditions. Fourth, we did not include the prescription of hyaluronate for other joints such as the shoulder and hip joints. However, the most commonly affected joint was the knee joint.4-8,23 Finally, we cannot exclude the possibility of duplicate cases because we used de-identified data. Despite of these limitations, this is the first epidemiologic study to report the nationwide incidence of septic knee and the utilization of hyaluronate in East Asia. Because of the increasing concerns of the risk of septic arthritis, we suggest a cautious aseptic technique and informing patients of the risk of septic arthritis when hyaluronate is administered for viscosupplementation.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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