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Deep Spinal Infection after Outpatient Epidural Injections for Pain: A Retrospective Sample Cohort Study Using a Claims Database in South Korea

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ABSTRACT

Background: Deep spinal infection is a devastating complication after epidural injection. This study aimed to investigate the incidence of deep spinal infection primarily after outpatient single-shot epidural injection for pain. Secondarily, this study assessed the national trends of the procedure and risk factors for said infection.

Methods: Using South Korea's National Health Insurance Service sample cohort database, the 10-yr national trend of single-shot epidural injections for pain and the incidence rate of deep spinal infection after the procedure with its risk factors were determined. New-onset deep spinal infections were defined as those occurring within 90 days of the most recent outpatient single-shot epidural injection for pain, needing hospitalization for at least 1 night, and receiving at least a 4-week course of antibiotics.

Results: The number of outpatient single-shot epidural injections per 1,000 persons in pain practice doubled from 40.8 in 2006 to 84.4 in 2015 in South Korea. Among the 501,509 injections performed between 2007 and 2015, 52 cases of deep spinal infections were detected within 90 days postprocedurally (0.01% per injection). In multivariable analysis, age of 65 yr or more (odds ratio, 2.91; 95% CI, 1.62 to 5.5; $P = 0.001$), living in a rural area (odds ratio, 2.85; 95% CI, 1.57 to 5.0; $P < 0.001$), complicated diabetes (odds ratio, 3.18; 95% CI, 1.30 to 6.7; $P = 0.005$), multiple epidural injections (three times or more) within the previous 90 days (odds ratio, 2.34; 95% CI, 1.22 to 4.2; $P = 0.007$), and recent use of immunosuppressants (odds ratio, 2.90; 95% CI, 1.00 to 6.7; $P = 0.025$) were significant risk factors of the infection postprocedurally.

Conclusions: The incidence of deep spinal infection after outpatient single-shot epidural injections for pain is very rare within 90 days of the procedure (0.01%). The data identify high-risk patients and procedure characteristics that may inform healthcare provider decision-making.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Deep spinal infection after outpatient epidural injections is a rare yet devastating complication
- The incidence of and risk factors for deep spinal infection remain unclear

What This Article Tells Us That Is New

- A deep spinal infection was defined as an infection recorded in South Korea's national insurance database, occurring within 90 days of an outpatient epidural injection, and requiring 4 weeks of antibiotic therapy
- In a randomly sampled population of adults between 2007 and 2015, 501,509 injections performed in 95,551 individuals were associated with 52 deep spinal infections (1.0 infections per 10,000 injections)
- Multivariable analysis demonstrated that age of 65 yr or more, living in a rural area, complicated diabetes, repeated epidural injections (three times or more) within 90 days, and recent use of immunosuppressants or systemic steroids were associated with the diagnosis of a deep spinal infection after epidural injection

The use of epidural injection in the outpatient pain practice has been increasing,[1,2] which could result in an increase in the incidence of adverse events, such as iatrogenic or secondary spinal infections.[3] In particular, a deep spinal infection is one of the most devastating complications after epidural procedures.[4] However, secondary spinal infections are not common; thus, the evaluation of their incidence and the specific risks is challenging. Currently, case reports on spinal infections after outpatient-based, single-shot epidural injections for pain management are scarce.[5–8] In previous studies, which included thousands of cases of single-shot epidural injections, relevant risk factors for deep spinal infection were not reported.[9–11] Moreover, difficulties in determining the causal relationship in procedure-related spinal infections exist, given that infectious complications are usually delayed compared to the exposure of the pathogen.[12,13] Such rarity and latency of deep spinal infection after epidural procedures impede the adequate screening of risk factors in patients who are scheduled to undergo epidural

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injection for pain management in an outpatient setting. The comment on adverse events in the informed consent form, *i.e.*, "infection may occur after your single-shot epidural injection," appears vague and may only cause anxiety among patients before the procedure.

The National Health Insurance Service (Wonju-si, South Korea) is a single-payer national insurance system mandatory for all citizens in South Korea.[14] It possesses a broad claims database for public insurance, consisting of National Health Insurance and Medical Aid but excluding car insurance, industrial accident compensation, and uncompensated items.[15] As such, it has provided a longitudinal sample database comprising a stratified random sample of about 1 million anonymized individuals[16] that is relatively easy to access for researchers. Given the difficulties in accounting for the prevalence of and risk factors for deep spinal infections after outpatient-based epidural procedures *via* single-center observational or small randomized studies, we considered the South Korean National Health Insurance Service sample data as a relevant source for the assessment.

Although previous literature estimated that the rate of severe infection associated with spinal injections might range from 0.01 to 0.10%,[16] few studies have focused on the specific prevalence of single-shot epidural injection–related deep spinal infection in outpatient pain practice. Therefore, in this study, we hypothesized that the infection incidence after the procedure would be very rare, ranging from 0.01 to 0.10%. The primary aim of this study was to determine the incidence of deep spinal infections after single-shot epidural injections in outpatient pain practice based on the South Korean National Health Insurance Service sample cohort. The secondary aims were to determine the national trend of outpatient single-shot epidural injections in South Korea and to identify potential risk factors associated with deep spinal infection using multivariable regression analysis.

Materials and Methods

Data Source

The South Korean National Health Insurance Service sample database 2.0 was used in this retrospective cohort study. South Korea has used a single universal health insurance coverage system for all citizens since 1989, and the National Health Insurance Service has been the single insurer since 2000, comprising both National Health Insurance and Medical Aid.[14] It has provided longitudinal sample data from approximately 1 million people from 2002 to 2015, which accounted for 2.2% of the total South Korean population eligible for health insurance in 2006.[16] Individuals were stratified with proportional allocation according to age, sex, region, health insurance type (medical insurance premium or medical aid), and household income. Within each stratum, systematic stratified random sampling was conducted using the individual's total annual medical expenses as a target variable for sampling to ensure representativeness. The sample database contains information about the patients' age, sex, and type of insurance; a list of diagnoses based on the International Classification of Diseases, Tenth Revision; the medical costs claimed; prescribed medications; treatments covered by National Health Insurance, including interventions with their relevant diagnoses; hospital facility information; and socioeconomic and survival status. Data on socioeconomic status included the area of a patient's residence (a rural area or small or large cities), level of income, and information on whether medical insurance premium or medical aid was used. The cohort population is refreshed annually by adding representative samples of newborns each year as preexisting patients become ineligible by death or emigration. Since 2006, information from medical aid beneficiaries has been incorporated into a single database[17]; therefore, we used the data from 2006 to 2015 in this study. Because an anonymized public database was used, the requirement for approval for the study was waived by the Seoul National University Hospital (Seoul, South Korea) Institutional Review Board (approval No. 1901-107-1005).

Study Design and Data Collection

This study consisted of three parts: the first part describes the 10-yr national trend of outpatient-based single-shot epidural injections in pain practice in South Korea; the second part measured the incidence of deep spinal infections after single-shot epidural injections in outpatient pain practice, which was the primary outcome of the study; and the third part assessed the risk factors for infectious complications after these injections. The data analysis and statistical plan were written after the data were accessed.

National Trend of Single-shot Epidural Injections in the Outpatient Pain Practice. We conducted a nation-specific descriptive analysis of the overall use of outpatient-based, single-shot epidural injections in pain practice from 2006 to 2015 in South Korea. The following procedures were identified as a single-shot epidural injection for the management of pain: "epidural injection (LA221)," "cervicothoracic epidural injection (LA321)," "lumbosacral epidural injection (LA322)," "spinal nerve block (LA252)," "selective nerve root block (LA354)," "dorsal root ganglion block (LA355)," and "epidurography (HA102)." The code of "epidural injection" has replaced "cervicothoracic" and "lumbosacral epidural injections" since 2008. Similarly, the code of "spinal nerve block" has been updated to "spinal nerve root block" or "ganglion block" since 2008. Various epidural procedures, such as caudal epidurography, transforaminal epidural injection, and epidural adhesiolysis, had been claimed using the same code ("epidurography"). Epidural injections for regional analgesia/anesthesia were distinguished from single-shot epidural injections for pain management; different injection codes were designated for epidural anesthesia. Additionally, inpatient and outpatient procedures were distinguished by different claim codes. Outpatient-based epidural injections could be performed repeatedly in a single patient; thus, demographics were presented only once per individual, although the characteristics of epidural injections were described per claim. Demographic data included sex, age, residential area (large city, small city, or rural area), and health insurance subscriber status (National Health Insurance or Medical Aid). The details of the epidural injection included the diagnosis relevant to the epidural injection; class of institution where the procedure was performed for managing pain (primary clinic, community hospital, secondary general hospital, or tertiary general hospital); medical department of the interventionalist who had claimed medical costs (anesthesiologist, spine surgeons [orthopedic surgeons and neurosurgeons], or others [rehabilitation doctors, internists, radiologists, and general surgeons]); type of the procedure (epidural injection, cervicothoracic epidural injection, lumbosacral epidural injection, spinal nerve block, selective nerve root block, dorsal root ganglion block, or epidurography); and use of corticosteroids for epidural injection (triamcinolone, dexamethasone, methylprednisolone, betamethasone, hydrocortisone, or none).

Incidence of Deep Spinal Infection after Single-shot Epidural Injection in the Outpatient Pain Practice as the Primary Outcome. We assessed the primary outcome of the study, which was the incidence of deep spinal infection after only outpatient-based, single-shot epidural injection in pain practice. First, we defined deep spinal infection as a new-onset infection occurring within 90 days of the most recent outpatient-based single-shot epidural injection. For classifying a "deep" spinal infection, the infectious event needed to include hospitalization for at least 1 night and oral or intravenous antibiotic therapy for at least 4 weeks.[18–20] Therefore, the primary outcome included the following three major concepts: the deep spinal infection code, at least a 4-week course of antibiotic therapy that needed hospitalization for at least 1 night, and an epidural injection within the preceding 90 days. Injections were assumed to be independent of one another. Patients who had a new-onset deep spinal infection but died during the 4-week antibiotic treatment period were still included in the analysis. To distinguish between persisting and new deep spinal infections, we reviewed the medical history up to at least 1 yr before the registered date of deep spinal infection. Because we used the sample data from 2006 to 2015, deep spinal infections newly registered from 2007 to 2015 were counted in the second part. Spinal infection was identified using the International Classification of Diseases, Tenth Revision (Supplemental Digital Content 1, http://links.lww.com/ALN/C581); some infections were defined according to codes in a previous study on postoperative and drug abuse–related spinal infection,[21] and other relevant codes were chosen by the authors. Extradural or subdural abscesses and postprocedural infections were included if they occurred in the spine. To eliminate superficial infections, codes regarding infection of muscles were excluded. Tuberculous spondylitis and *Brucella* spondylitis were excluded because their characteristics differ from those of pyogenic deep spinal infection.[22]

Risk Factors for Deep Spinal Infection after Single-shot Epidural Injection in the Outpatient Pain Practice. We analyzed the predisposing risk factors for deep spinal infection after an outpatient-based, single-shot epidural injection in pain practice. The date of the last epidural injection was set as the index date (fig. 1), and data on all explanatory variables for risk analysis were obtained based on the index date. In addition to the demographic data, such as age, sex, residential area, and income level, the Charlson Comorbidity Index[23] was estimated to investigate the predisposing comorbidity relevant to injection-related deep spinal infection. Comorbidities were reviewed up to 1 yr before the index date, which included myocardial infarction, congestive heart failure, peripheral vascular disease, hemiplegia or paraplegia, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild/moderate to severe liver disease, diabetes with/without chronic complications, renal disease, malignancy, and metastatic solid tumor.[24] Each comorbidity has a weighted score according to its potential influence on mortality, and the total score of the Charlson Comorbidity Index is the sum of these scores; a higher comorbidity score is associated with higher in-hospital mortality.[24] Additionally, we obtained data on the use of immunosuppressive agents, such as cyclosporine, tacrolimus, or methotrexate, or systemic steroids for 30 days or more within the 90 days before the index date. Moreover, the types of epidural procedures, the claims for epidural steroids, and the performance of multiple epidural injections within 90 days (three times or more) were compared between patients with deep spinal infection and those without infectious events.

Statistical Analysis

The sample size was based on the available data from the South Korean National Health Insurance Service sample database 2.0, and no statistical power calculation was conducted before the study. The data were extracted using the SAS Enterprise Guide 7.1 (SAS Institute, USA). Statistical analyses were performed using R 3.3.3 (R Core Team, Austria),[25] which included the following packages: "haven,"[26] "tidyverse,"[27] "tableone,"[28] and "MASS."[29] The data were reported as mean ± SD, median (interquartile range), and frequencies with percentages. The Shapiro–Wilk test was used to assess the normality of data. All P values presented are two-tailed, and $P < 0 < 0.05$ was considered statistically significant.

To determine the statistically significant predisposing risk factors, univariable and multivariable analyses were performed and presented with the estimated odds ratio and 95% CI of covariates. Patients with missing data were excluded from the analysis. For multivariable regression analysis, we constructed three models. Model 1 (full model) included all covariates except for variables with a low frequency of less than four. Model 2 was established with significant covariates ($P < 0.05$) from univariable analysis, and model 3 (final model) included covariates chosen from a backward stepwise selection. Statistically significant covariates ($P < 0.05$), which minimized the Akaike information criterion, remained in the final model. The estimates of each

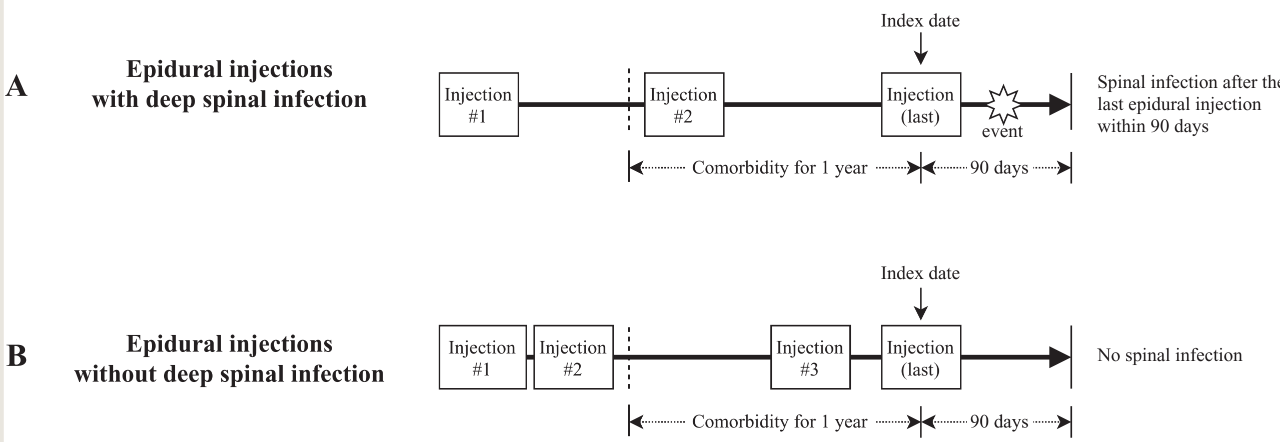

Fig. 1. Cases with deep spinal infections after outpatient-based, single-shot epidural injections and controls without deep spinal infections. (*A*) A case with a deep spinal infection within 90 days after the last epidural injection. (*B*) A control without a deep spinal infection after the last epidural injection.

model were internally validated with relative bias and root mean square difference based on 200 bootstrapped samples. In the final model, multicollinearity between the covariates was tested by the variance inflation factor. The performance of the final model was assessed using the Hosmer–Lemeshow *P* value test.[30] In addition, sensitivity analyses were conducted for the final multivariable model, using broader and more restrictive time-based definitions (antibiotics for 2 weeks or more and for 6 weeks or more) of deep spinal infection.

Results

National Trend

In South Korea, the number of individuals who underwent single-shot epidural injection in pain practice steadily increased by twofold from 2006 to 2015, and most of them were outpatients (13.1 per 1,000 persons in 2006 to 28.8 per 1,000 persons in 2015; Supplemental Digital Content 2, http://links.lww.com/ALN/C582). During the observational period, the proportion of men increased from 36.7 to 40.5%, those aged 65 yr or more increased from 38.3 to 43.5%, those covered by National Health Insurance increased from 91.6 to 94.2%, and those living in large cities increased from 52.2 to 57.8%.

The number of epidural injections in the outpatient pain practice also doubled from 40.8 injections per 1,000 persons in 2006 to 84.4 in 2015. Although the actual number of outpatients who underwent epidural injections increased over time, the number of injections per patient was relatively constant during the period (a median of two times a year with the same interquartile ranges from one to three, except for 2006). Although most procedures were performed in clinics, claims by community hospitals increased from 9.5% in 2006 to 19.0% in 2015. Only half of the claims included corticosteroids for epidural injections during the study period (42.5 to 58.1%). Among the types of corticosteroids, triamcinolone had a 95.5 to 96.6% claim rate until 2012, which rapidly dropped to 48.9% in 2013 and 15.5% in 2015. The claim rate for dexamethasone was 4.4 to 5.4% in the 2000s, which increased sharply to 43.6% in 2012 and 74.6% in 2015.

Incidence of Deep Spinal Infection

Among 1,108,361 individuals in the sample cohort between 2007 and 2015, 111,098 underwent at least one outpatient-based single-shot epidural injection in pain practice. In addition, 96,083 individuals (86.5%) who did not undergo any inpatient-based single-shot epidural injections were included in the analyses (fig. 2; Supplemental Digital Content 2, http://links.lww.com/ALN/C582). Among them, 584 patients had codes for deep spinal infection; however, only 191 met the antibiotic treatment criteria of this study. Of these 191 patients, 143 underwent invasive procedure(s) within 90 days before the occurrence of infection; 91 patients were excluded because they had surgical operations (n = 68) or paraspinal injections (n = 23) other than epidural injections. Consequently, of 95,551 individuals who underwent 501,509 outpatient-based single-shot epidural injections in pain practice, 52 patients met our criteria of the deep spinal infection after the injection (fig. 2). The incidence rate of the deep spinal injection was 5.4 (95% CI, 4.1 to 7.2) subjects per 10,000 outpatients who underwent single-shot epidural injections and 1.0 (95% CI, 0.8 to 1.4) cases per 10,000 epidural injections (0.01%) in outpatient pain practice. Incidences were scattered from just 1 case in 2007 to 9 cases in 2013 (median, 7; interquartile range, 4 to 8; table 1). Among the 52 patients, 34 (65%) underwent a surgical operation to treat the infection, 4 (8%, including 1 surgical case) died in the succeeding month, and 9 (17%, including 3 surgical cases) died 6 months from the occurrence of the infection.

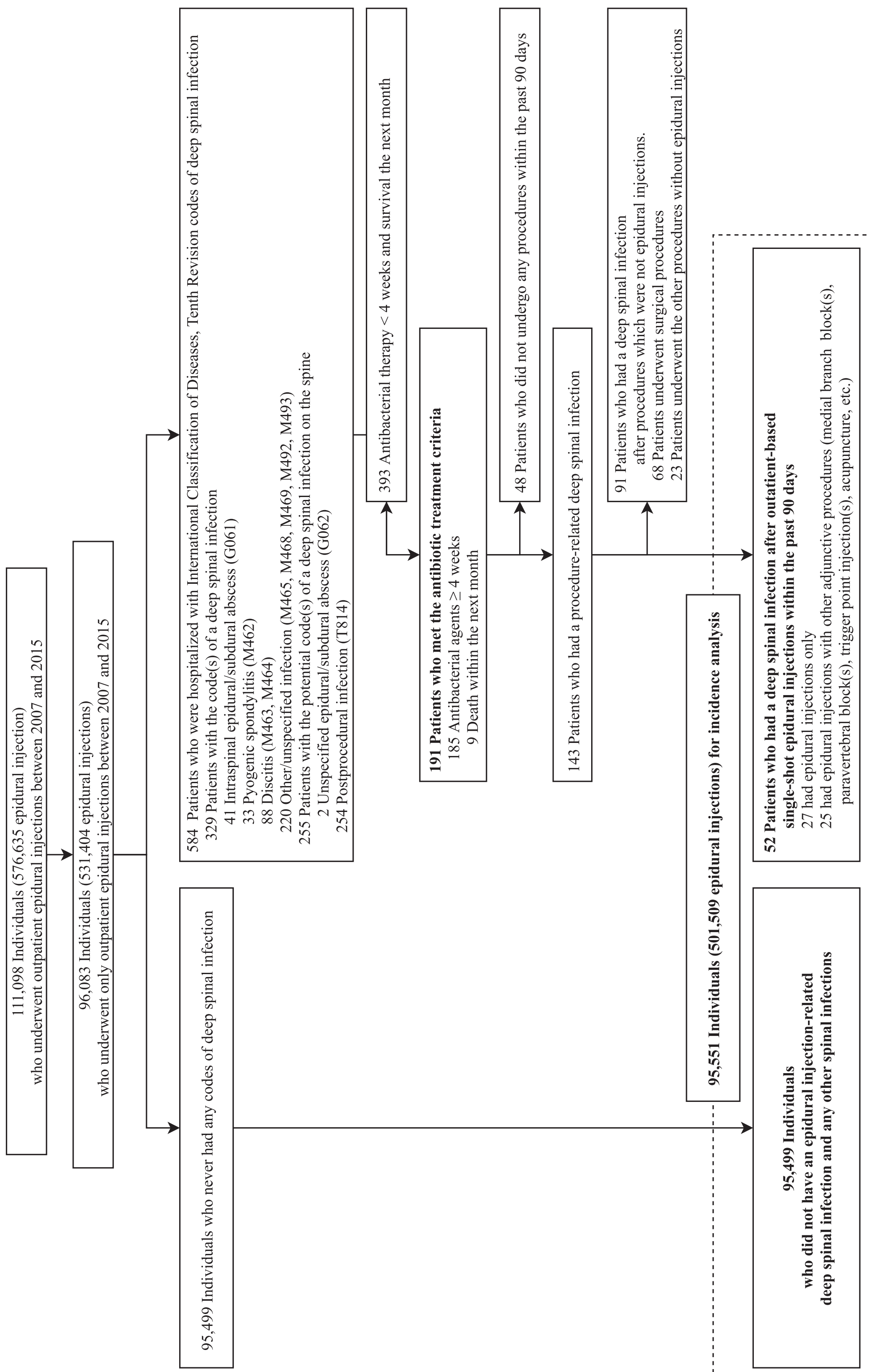

Fig. 2. Flow diagram to evaluate the incidence of deep spinal infection after outpatient-based, single-shot epidural injections in pain practice.

Risk Factors for Deep Spinal Infection

Univariable associations with deep spinal infection are presented in table 2, where age of 65 yr or more, living in a rural area, Charlson Comorbidity Index of 3 or higher, peripheral vascular disease, chronic pulmonary disease, mild liver disease, complicated diabetes, the use of immunosuppressive agents or systemic steroids, and frequent epidural injections (three times or more) within 90 days were significant variables ($P < 0.05$). There were no missing data in patients with deep spinal infection, whereas a small portion of data was missing in the control group (table 2).

In the multivariable analysis, three models, including model 1 (full model), model 2 (model with significant variables from univariate analysis), and model 3 (final model), were established (table 3). In the final model, age of 65 yr or more (odds ratio, 2.91; 95% CI, 1.62 to 5.5; $P = 0.001$), living in a rural area (odds ratio, 2.85; 95% CI, 1.57 to 5.0; $P < 0.001$), complicated diabetes (odds ratio, 3.18; 95% CI, 1.30 to 6.7; $P = 0.005$), repeated epidural injections (three times or more) within 90 days (odds ratio, 2.34; 95% CI, 1.22 to 4.2; $P = 0.007$), and recent use of immunosuppressants or systemic steroids (odds ratio, 2.90; 95% CI, 1.00 to 6.7; $P = 0.025$) remained statistically significant risk factors, with low multicollinearity among covariates (all variance inflation factors less than 2). In models 1 and 2, these factors were also statistically significant in association with the infectious complication after the procedure. The final multivariable model was well calibrated according to the Hosmer–Lemeshow goodness-of-fit test ($P = 0.610$). In the bootstrap adjustment, the relative biases of estimates on the final multivariable model were low (3.1% for advanced age, 0.7% for living in a rural area, −4.3% for complicated diabetes, and −3.3% for recent multiple epidural injections) or moderate (−7.1% for the recent use of immunosuppressants or systemic steroids).

Table 1. Incidence of Deep Spinal Infection after Outpatient-based Single-shot Epidural Injections in Pain Practice

Year	Deep Spinal Infection (No.)*	Epidural Injection (No.)†	Incidence/10,000 Epidural Injections (95% CI)†
2007	1	38,465	0.3 (0.0–1.7)
2008	5	40,569	1.2 (0.5–3.1)
2009	3	43,241	0.7 (0.2–2.2)
2010	4	48,087	0.8 (0.3–2.3)
2011	7	55,742	1.3 (0.6–2.7)
2012	7	64,830	1.1 (0.5–2.3)
2013	9	67,911	1.3 (0.7–2.6)
2014	8	69,250	1.2 (0.5–2.4)
2015	8	73,414	1.1 (0.5–2.2)
Total	52	501,509	1.0 (0.8–1.4)

*Deep spinal infection was defined as a new-onset infection occurring within 90 days of the most recent outpatient-based single-shot epidural injection and needing hospitalization for at least 1 night and oral or intravenous antibiotic therapy for at least 4 weeks. †The procedure was an outpatient-based single-shot epidural injection in pain practice.

Sensitivity Analysis

Sensitivity analysis was performed to assess the multivariable model, which used the modified definition of deep spinal infection. When the lenient definition was used (the use of antibiotics for 2 weeks or more), 356 patients with deep spinal infection were identified. Among them, 64 were related to an outpatient-based epidural injection (1.3 [95% CI, 1.0 to 1.6] cases per 10,000 epidural injections). Age of 65 yr or more (odds ratio, 2.46; 95% CI, 1.47 to 4.3; $P = 0.001$), living in a rural area (odds ratio, 2.50; 95% CI, 1.44 to 4.2; $P = 0.001$), complicated diabetes (odds ratio, 3.45; 95% CI, 1.58 to 6.7; $P = 0.001$), repeated epidural injections (three times or more) within 90 days (odds ratio, 2.71; 95% CI, 1.55 to 4.6; $P < 0.001$), and recent use of immunosuppressants or systemic steroids (odds ratio, 2.88; 95% CI, 1.10 to 6.2; $P = 0.015$) remained in the model derived from patients with a 2-week period of antibiotic treatment. When we adopted a stricter definition of deep spinal infection (use of antibiotics for 6 weeks or more), 117 patients with deep spinal infection were identified. Among them, 37 were related to an outpatient-based epidural injection (0.7 [95% CI, 0.5 to 1.0] cases per 10,000 injections). Age of 65 yr or more (odds ratio, 2.98; 95% CI, 1.48 to 6.5; $P = 0.003$), living in a rural area (odds ratio, 2.57; 95% CI, 1.24 to 5.1; $P = 0.008$), complicated diabetes (odds ratio, 3.91; 95% CI, 1.45 to 8.8; $P = 0.003$), and repeated epidural injections (three times or more) within 90 days (odds ratio, 2.67; 95% CI, 1.26 to 5.3; $P = 0.007$) remained in the model focused on the primary outcome definition requiring 6 weeks of antibiotics. Recent use of immunosuppressive agents or systemic steroids was excluded in the 6-week model (odds ratio, 3.25; 95% CI, 0.96 to 8.3; $P = 0.027$).

Discussion

Based on the South Korean National Health Insurance Service sample cohort, the number of outpatient-based, single-shot epidural injections per 1,000 persons in pain practice doubled from 40.8 in 2006 to 84.4 in 2015 in South Korea, which was twofold more than that in the United States (21.2 in 2000 and 42.3 in 2014 based on Medicare data).[31] The incidence of deep spinal infection after the procedure was 5.4 (95% CI, 4.1 to 7.2) per 10,000 persons and 1.0 (95% CI, 0.8 to 1.4) cases per 10,000 injections (0.01%), representing 1 deep spinal infection per 10,000 outpatient single-shot epidural injections. Age of 65 yr or more (odds ratio, 2.91), living in a rural area (odds ratio, 2.85), complicated diabetes (odds ratio, 3.18), the use of immunosuppressants or systemic steroids (odds ratio, 2.90), and epidural injections three times or more within 90 days (odds ratio, 2.34) increased the risk of deep spinal infection after epidural injections in the outpatient pain practice by two- to threefold.

The increase in epidural injections performed in the outpatient pain practice may be explained by the increased

Table 2. Univariable Analysis of Risk Factors of Deep Spinal Infection after an Outpatient-based Single-shot Epidural Injection for Pain Management

	Controls without Deep Spinal Infection (N = 95,499)	Cases with Deep Spinal Infection (N = 52)	Crude Odds Ratio (95% CI)	*P* Value
Sex (female)	55,091 (57.7)	27 (52)	0.79 (0.46–1.37)	0.401
Missing value	3 (0.0)			
Age of 65 yr or more	35,297 (37.0)	36 (69)	3.84 (2.17–7.1)	< 0.001
Missing value	3 (0.0)			
Residential area				
Large city	55,346 (58.0)	23 (44)	Reference	
Small city	27,293 (28.6)	11 (21)	0.97 (0.46–1.95)	0.933
Rural area	12,857 (13.5)	18 (35)	3.37 (1.80–6.2)	< 0.001
Missing value	3 (0.0)			
Income level				
Upper	37,321 (39.4)	18 (35)	Reference	
Middle	32,390 (34.2)	19 (37)	1.22 (0.64–2.34)	0.552
Lower	25,005 (26.4)	14 (28)	1.16 (0.57–2.33)	0.676
Missing value	783 (0.8)			
Charlson Comorbidity Index				
0	70,104 (73.4)	28 (53)	Reference	
1–2	20,081 (21.0)	14 (27)	1.75 (0.89–3.30)	0.089
3 or higher	5,314 (5.6)	10 (20)	4.7 (2.18–9.4)	< 0.001
Comorbidities				
Myocardial infarction	434 (0.4)	1 (2)	4.3 (0.242–19.6)	0.149
Congestive heart failure	2,406 (2.5)	2 (4)	1.55 (0.253–5.0)	0.545
Peripheral vascular disease	9,103 (9.5)	10 (20)	2.26 (1.08–4.3)	0.021
Cerebrovascular disease	6,251 (6.5)	7 (14)	2.22 (0.91–4.6)	0.050
Dementia	599 (0.6)	1 (2)	3.11 (0.175–14.1)	0.262
Chronic pulmonary disease	13,455 (14.1)	15 (30)	2.47 (1.32–4.4)	0.003
Rheumatologic disease	1114 (1.2)	0 (0)	Not applicable	
Peptic ulcer disease	16,346 (17.1)	13 (25)	1.61 (0.83–2.94)	0.135
Liver disease				
Mild	8,168 (8.6)	9 (17)	2.24 (1.02–4.4)	0.028
Moderate to severe	194 (0.2)	0 (0)	Not applicable	
Diabetes				
Uncomplicated	11,332 (11.9)	10 (19)	1.77 (0.84–3.38)	0.106
Complicated	3,173 (3.3)	7 (14)	4.5 (1.86–9.4)	< 0.001
Hemiplegia or paraplegia	315 (0.3)	0 (0)	Not applicable	
Renal disease	737 (0.8)	1 (2)	2.52 (0.142–11.5)	0.360
Malignancy				
Primary	2,520 (2.7)	3 (6)	2.60 (0.55–6.2)	0.171
Metastatic	267 (0.3)	1 (2)	7.0 (0.394–32.0)	0.055
Immunosuppressants within 90 days*	2,475 (2.6)	5 (10)	4.0 (1.39–9.1)	0.003
Epidural injections three times or more within 90 days	11,653 (12.2)	14 (27)	2.65 (1.39–4.8)	0.002
Type of epidural injection				
Epidural	4,431 (4.6)	1 (2)	0.40 (0.023–1.83)	0.368
Lumbosacral	64,215 (67.3)	39 (75)	1.46 (0.80–2.85)	0.236
Cervicothoracic	9,121 (9.6)	3 (6)	0.58 (0.141–1.58)	0.359
Spinal nerve†	529 (0.6)	0 (0)	Not applicable	
Selective nerve root	10,520 (11.0)	7 (14)	1.26 (0.52–2.61)	0.574
Dorsal root ganglion	2,530 (2.6)	0 (0)	Not applicable	
Epidurography	4,431 (4.6)	3 (6)	0.93 (0.226–2.54)	0.905

The data are shown as frequencies (%) or odds ratios (95% CIs).

*Oral immunosuppressants or systemic steroids for 30 days or more within the past 90 days. †Spinal nerve plexus, root, or ganglion block.

supply and demand for specialized spinal pain management in South Korea. The recent aging trend in South Korea[32] has led to the rapidly increasing prevalence of degenerative spinal pain disorders,[33,34] potentially resulting in the increasing use of epidural injections in an outpatient setting. Pain management to improve the quality of life, which has become a global trend,[35] possibly steered the marked increase in the number of procedures and expenses of the National Health Insurance in South Korea.[36] Moreover, economic growth and a broad application of the National Health Insurance Service have allowed more South Koreans to have access to specialized pain interventions.[37] Although health disparity might exist in individuals between living areas (rural *vs.* cities), the increasing proportion of hospital-based epidural injections since early 2010 suggests that a growing number of specialty hospitals providing spinal interventions have

Table 3. Coefficients and Bootstrap Validation of the Multivariable Model of Deep Spinal Infection after a Single-shot Epidural Injection in Outpatient Pain Practice

	Adjusted Odds Ratio (95% CI)	*P* Value	Bootstrap Adjusted Odds Ratio (95% CI)	Relative Bias (%)*	Root Mean Square Deviation Ratio†
Model 1					
Female	0.66 (0.390–1.19)	0.174	0.67 (0.393–1.15)	3.5	0.28
Age of 65 yr or more	2.65 (1.41–5.2)	0.003	2.71 (1.34–5.4)	2.4	0.36
Rural area‡	2.63 (1.43–4.7)	0.001	2.63 (1.46–4.6)	0.2	0.29
Income level (middle *vs.* upper)	1.46 (0.76–2.83)	0.252	1.47 (0.91–2.81)	0.6	0.31
Income level (lower *vs.* upper)	1.21 (0.59–2.43)	0.598	1.19 (0.51–2.52)	−8.5	0.40
Charlson Comorbidity Index (1–2 *vs.* 0)	0.72 (0.252–1.85)	0.508	0.66 (0.307–1.40)	22.6	0.43
Charlson Comorbidity Index (3 or higher *vs.* 0)	1.08 (0.205–4.4)	0.920	0.95 (0.174–3.32)	−167.8	0.76
Peripheral vascular disease	1.22 (0.57–2.41)	0.582	1.16 (0.51–2.20)	−25.6	0.37
Cerebrovascular disease	1.11 (0.44–2.21)	0.805	1.06 (0.46–2.24)	−46.7	0.41
Chronic pulmonary disease	1.68 (0.67–4.5)	0.280	1.76 (0.72–3.94)	8.3	0.44
Peptic ulcer disease	0.98 (0.49–1.84)	0.942	0.96 (0.47–1.70)	87.8	0.32
Liver disease, mild	1.42 (0.50–4.1)	0.510	1.40 (0.40–3.48)	−3.9	0.55
Diabetes, uncomplicated	1.34 (0.61–2.70)	0.439	1.39 (0.68–3.48)	−0.6	0.38
Diabetes, complicated	3.26 (1.13–8.7)	0.022	3.29 (1.23–8.9)	0.69	0.52
Immunosuppressants within 90 days§	2.66 (0.90–6.2)	0.043	2.48 (0.87–5.6)	−6.9	0.52
Epidural injections three times or more within 90 days	2.31 (1.20–4.2)	0.008	2.25 (1.12–4.1)	−3.0	0.33
Type of epidural injection, lumbosacral	1.56 (0.73–3.85)	0.292	1.63 (0.85–4.4)	10.6	0.43
Type of epidural injection, selective nerve root	1.86 (0.64–5.3)	0.242	1.74 (0.50–5.3)	−10.5	0.60
Model 2					
Age of 65 yr or more	2.69 (1.47–5.1)	0.002	2.78 (1.53–5.8)	3.2	0.33
Rural area‡	2.82 (1.55–5.0)	< 0.001	2.84 (1.62–4.9)	0.7	0.29
Charlson comorbidity index (1–2 *vs.* 0)	0.71 (0.252–1.81)	0.492	0.66 (0.282–1.36)	21.6	0.43
Charlson comorbidity index (3 or higher *vs.* 0)	1.11 (0.214–4.4)	0.890	0.98 (0.175–3.34)	−121.8	0.75
Peripheral vascular disease	1.23 (0.57–2.41)	0.577	1.16 (0.50–2.20)	−25.2	0.37
Chronic pulmonary disease	1.67 (0.66–4.4)	0.287	1.74 (0.72–3.91)	7.9	0.43
Liver disease, mild	1.50 (0.53–4.4)	0.449	1.48 (0.41–3.50)	−3.0	0.55
Diabetes, complicated	2.96 (1.06–7.5)	0.028	2.94 (1.14–7.6)	−0.6	0.49
Immunosuppressants within 90 days§	2.61 (0.89–6.1)	0.047	2.43 (0.85–5.5)	−7.1	0.51
Epidural injections three times or more within 90 days	2.30 (1.20–4.2)	0.008	2.24 (1.11–4.1)	−3.3	0.33
Model 3					
Age of 65 yr or more	2.91 (1.62–5.5)	0.001	3.00 (1.61–6.0)	3.1	0.34
Rural area‡	2.85 (1.57–5.0)	< 0.001	2.87 (1.57–4.9)	0.7	0.29
Diabetes, complicated	3.18 (1.30–6.7)	0.005	3.02 (1.17–6.3)	−4.3	0.44
Immunosuppressants within 90 days§	2.90 (1.00–6.7)	0.025	2.69 (1.00–6.5)	−7.1	0.52
Epidural injections three times or more within 90 days	2.34 (1.22–4.2)	0.007	2.28 (1.12–4.1)	−3.3	0.34

Model 1 (full model) contained all covariates with a frequency count of four or more. Model 2 contained covariates from univariable analysis with a significance ($P < 0.05$). Model 3 (final model) contained covariates chosen from a backward stepwise section.

*Relative bias was calculated as the difference between the mean bootstrapped regression coefficient estimates and the final multivariable model estimates divided by the final multivariable model estimates. †Root mean squared differences of the bootstrapped estimates compared to the final multivariable model estimates were divided by the standard error of the final model estimates. ‡Rural area *versus* large and small city. §Oral immunosuppressants or systemic steroids for 30 days or more within the past 90 days.

been established in South Korea.[38] The rising number of epidural injections in outpatient pain practice could reduce disability and socioeconomic loss caused by spinal pain.[32] However, concerns about the unnecessary usage of epidural injection and increasing exposure to devastating complications, such as spinal infections, have been raised.[4]

Previously, Windsor *et al.*[16] suggested that the severe infection rate associated with spinal injections ranged from 0.01 to 0.10%. In our study, the incidence of deep spinal infection after outpatient-based single-shot epidural injection for pain management (0.01%) was that of the lower value reported by Windsor *et al.* (0.01%).[16] Defining deep spinal infections after epidural injections was the most challenging aspect of this study because a strict definition could omit true positives, whereas a lenient definition may include false positives. We assume that the definition of the infection in our study was closer to the strict one. It led us to perform sensitivity analyses using broader (antibiotics use for 2 weeks or more) and strict definitions (antibiotics use for 6 weeks or more), which did not substantially differ from our definition (antibiotics use for 4 weeks or more). Despite their rarity, deep spinal infections after epidural injections are catastrophic complications, which required surgical operation in most patients (n = 34, 65%) and led to death within 6 months in 27% (n = 13) of patients in this study. Moreover, the incidence of deep spinal infection caused by outpatient single-shot epidural injections in our study seems to be 10-fold higher than that reported in obstetric patients treated with epidural analgesia/anesthesia, which was 7 to 9 cases per million.[39] This could be attributed to the different characteristics of the subjects, such as advanced age with a high frequency of comorbidities in our study, compared to relatively young and healthy pregnant women in the previous study.[39] Concurrent administration of steroids may have also contributed to the difference between the studies. Therefore, healthcare providers must pay attention to high-risk patients who are scheduled for single-shot epidural injections in outpatient pain practice.

Regardless of the exogenic infectious source, predisposing comorbidities including diabetes mellitus, chronic renal disease, malignancy, and substance abuse are known risk factors for spinal infections, such as pyogenic osteomyelitis, epidural abscess, or discitis.[13,40] Our univariable analysis suggests that advanced age, Charlson Comorbidity Index of 3 or higher, complicated diabetes, chronic pulmonary disease, peripheral vascular disease, liver disease, and recent use of immunosuppressants are associated with epidural injection–related deep spinal infection. Although the exact reasons are unknown,[41] the higher risk of deep spinal infection after epidural injection in patients with the aforementioned diseases could be attributed to immunosuppressive conditions in such diseases[42] or the effects of treatment, such as corticosteroid use in chronic pulmonary disease[43] or peripheral vascular disease.[44] In our multivariable analysis, patients with complicated diabetes had a more than threefold higher risk of deep spinal infection after the procedure in the outpatient pain practice than those without complicated diabetes. However, chronic pulmonary disease and peripheral vascular disease showed no statistical significance after adjusting for the recent administration of immunosuppressants. Furthermore, frequent epidural injections were associated with an increased risk of infectious complications, and those living in rural areas were more exposed to the risk of procedure-related deep spinal infection even after adjusting for age and several comorbidities in the multivariable regression. Although this could be explained by several assumptions, the main reason could be the health disparity between rural and urban populations in South Korea, including the relatively low accessibility to pain experts, low income levels, and insufficient social support in rural areas.[45]

Another trend was noted in the use of corticosteroids in South Korea, wherein only half of the claims included corticosteroids (Supplemental Digital Content 3, http://links.lww.com/ALN/C583). Epidural injections may not always include corticosteroids for diagnostic purposes. The other assumption would arise from a new regulation by the Ministry of Food and Drug Safety (Cheongju-si, South Korea), which prohibits epidural injection of triamcinolone since the change in the indications of particulate steroids for epidural use.[46,47] Although the World Institute of Pain (Winston-Salem, NC) has recently insisted that dexamethasone is only safe for transforaminal injections, with little information on its long-term safety,[48] a dramatic change from triamcinolone to dexamethasone for epidural administration occurred between 2012 and 2013 in South Korea.[2] Claims for epidural triamcinolone after the implementation of this national regulation may not be reimbursed by the Health Insurance Review & Assessment Service (Wonju-si, South Korea). They could be classified into unclaimed corticosteroids, reflecting a limitation of using this sample database. During lumbar surgical operations, epidural injections of corticosteroids have been suggested to increase postoperative infection rates.[49,50] Therefore, future studies are necessary to investigate whether the infection risk increases similarly during single-shot epidural injections with corticosteroids in pain practice.

This study has several limitations. First, our sample database contains the general shortcomings of a claims database, such as discrepancies in actual performances caused by limited access to patients' medical records. Some valuable information, including patients' symptoms and signs, is not included in the data. In addition, all causal relationships between invasive procedures and deep spinal infection were decided on the basis of the chronological registration to the health service system in this study; hence, there might be some ambiguous cases in which it was difficult to determine the causal relationship between invasive procedures and deep spinal infection. Additionally, the South Korean National Health Insurance Service database depends only on claimed medical benefits, which means that data on treatment paid out-of-pocket were missing. Moreover, despite the fine stratification, the sample database may still have a selection bias and may not be sufficient to assess the risk of rare complications. Second, patients who received adjunctive injections (*e.g.*, acupuncture and trigger point injections) simultaneously with epidural injections and had deep spinal infection were included (n = 25 of 52, 48%); thus, the primary cause of the spinal infection may be confusing given the multiple interventions. Furthermore, the inclusion of the codes "selective nerve root block" and "dorsal root ganglion block" as epidural injections in this study may be an issue. These terms are interchangeably used with epidural injections in pain practice. However, they are technically not epidural injections, although epidural spreads of the injectates are frequently observed during the procedures. Another debate lies in defining "epidurography." In South Korea, there is no claim code for transforaminal epidural injection, but "epidurography" is used for the procedure, which mainly accompanies epidural injection with local anesthetics and/or corticosteroids. Therefore, we included all these codes as epidural injections so as to not make an overly parsimonious process in identifying this rare complication. Third, in this study, we investigated deep spinal infection after outpatient-based, single-shot epidural injection, which is only one of the several critical adverse events after the procedure. Other complications resulting in catastrophic neurologic sequelae, such as spinal cord infarct or stroke, were not analyzed in this study; therefore, these complications require future investigation.[51]

In conclusion, the incidence of deep spinal infection after single-shot epidural injection in the outpatient pain practice in South Korea was very low (0.01% per injection). Advanced age, living in a rural area, complicated diabetes, use of immunosuppressants or systemic steroids, and multiple epidural injections within 90 days were associated with a two- to threefold risk of deep spinal infection after the procedure.

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Competing Interests

The authors declare no competing interests.

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References

1. Leem JG: Epidural steroid injection: A need for a new clinical practice guideline. Korean J Pain 2014; 27:197–9
2. Kim EJ, Moon JY, Park KS, Yoo DH, Kim YC, Sim WS, Lee CJ, Shin HY, Kim JH, Kim YD, Lee SJ: Epidural steroid injection in Korean pain physicians: A national survey. Korean J Pain 2014; 27:35–42
3. Noh SH, Zhang HY, Lee SH, Choi JK, Chin DK: Changes in trends of spondylitis in Korea based on a nationwide database. Yonsei Med J 2019; 60:487–9
4. Bicket MC, Chakravarthy K, Chang D, Cohen SP: Epidural steroid injections: An updated review on recent trends in safety and complications. Pain Manag 2015; 5:129–46
5. Hooten WM, Kinney MO, Huntoon MA: Epidural abscess and meningitis after epidural corticosteroid injection. Mayo Clin Proc 2004; 79:682–6
6. Hooten WM, Mizerak A, Carns PE, Huntoon MA: Discitis after lumbar epidural corticosteroid injection: A case report and analysis of the case report literature. Pain Med 2006; 7:46–51
7. Hanaoka N, Kawasaki Y, Sakai T, Nakamura T, Nanamori K, Nakamura E, Uchida K, Yamada H: Percutaneous drainage and continuous irrigation in patients with severe pyogenic spondylitis, abscess formation, and marked bone destruction. J Neurosurg Spine 2006; 4:374–9
8. Smith RM, Schaefer MK, Kainer MA, Wise M, Finks J, Duwve J, Fontaine E, Chu A, Carothers B, Reilly A, Fiedler J, Wiese AD, Feaster C, Gibson L, Griese S, Purfield A, Cleveland AA, Benedict K, Harris JR, Brandt ME, Blau D, Jernigan J, Weber JT, Park BJ; Multistate Fungal Infection Outbreak Response Team: Fungal infections associated with contaminated methylprednisolone injections. N Engl J Med 2013; 369:1598–609
9. McGrath JM, Schaefer MP, Malkamaki DM: Incidence and characteristics of complications from epidural steroid injections. Pain Med 2011; 12:726–31
10. Manchikanti L, Malla Y, Wargo BW, Cash KA, Pampati V, Fellows B: A prospective evaluation of complications of 10,000 fluoroscopically directed epidural injections. Pain Physician 2012; 15:131–40
11. Lee JW, Lee E, Lee GY, Kang Y, Ahn JM, Kang HS: Epidural steroid injection-related events requiring hospitalisation or emergency room visits among 52,935 procedures performed at a single centre. Eur Radiol 2018; 28:418–27
12. Cheung WY, Luk KD: Pyogenic spondylitis. Int Orthop 2012; 36:397–404
13. Zimmerer SM, Conen A, Müller AA, Sailer M, Taub E, Flückiger U, Schwenzer-Zimmerer KC: Spinal epidural abscess: Aetiology, predisponent factors and clinical outcomes in a 4-year prospective study. Eur Spine J 2011; 20:2228–34
14. Song YJ: The South Korean health care system. Jpn Med Assoc J 2009; 52:206–9
15. Song SO, Jung CH, Song YD, Park CY, Kwon HS, Cha BS, Park JY, Lee KU, Ko KS, Lee BW: Background and data configuration process of a nationwide population-based study using the Korean National Health Insurance System. Diabetes Metab J 2014; 38:395–403
16. Windsor RE, Storm S, Sugar R: Prevention and management of complications resulting from common spinal injections. Pain Physician 2003; 6:473–83
17. Lee YH, Han K, Ko SH, Ko KS, Lee KU; Taskforce Team of Diabetes Fact Sheet of the Korean Diabetes Association: Data analytic process of a nationwide population-based study using national health information database established by National Health Insurance Service. Diabetes Metab J 2016; 40:79–82
18. Jaramillo-de la Torre JJ, Bohinski RJ, Kuntz C: Vertebral osteomyelitis. Neurosurg Clin N Am 2006; 17:339–51
19. Dowdell J, Brochin R, Kim J, Overley S, Oren J, Freedman B, Cho S: Postoperative spine infection: Diagnosis and management. Global Spine J 2018; 8(4 suppl):37S–43S
20. Waheed G, Soliman MAR, Ali AM, Aly MH: Spontaneous spondylodiscitis: Review, incidence, management, and clinical outcome in 44 patients. Neurosurg Focus 2019; 46:E10
21. Alhourani A, Dietz N, Sharma M, Ugiliweneza B, Wang D, Nuño M, Drazin D, Boakye M: Health care utilization and payments of postoperative and drug abuse–related spinal infections. Spine (Phila Pa 1976) 2019; 44:1449–55

22. Perronne C, Saba J, Behloul Z, Salmon-Céron D, Leport C, Vildé JL, Kahn MF: Pyogenic and tuberculous spondylodiskitis (vertebral osteomyelitis) in 80 adult patients. Clin Infect Dis 1994; 19:746–50
23. Kim KH: Comparative study on three algorithms of the ICD-10 Charlson Comorbidity Index with myocardial infarction patients. J Prev Med Pub Health 2010; 43:42–9
24. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, Januel JM, Sundararajan V: Updating and validating the Charlson Comorbidity Index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol 2011; 173:676–82
25. R Core Team: R: A Language and Environment for Statistical Computing. Vienna, Austria, R Foundation for Statistical Computing, 2017. Available at: https://www.R-project.org/. Accessed October 24, 2019.
26. Wickham H, Miller E: haven: Import and export “SPSS”, “Stata” and “SAS” Files. 2018. Available at: https://CRAN.R-project.org/package=haven. Accessed October 24, 2019.
27. Wickham H: Tidyverse: Easily install and load the “Tidyverse.” 2017. Available at: https://CRAN.R-project.org/package=tidyverse. Accessed October 24, 2019.
28. Yoshida K: tableone: Create “Table 1” to describe baseline characteristics. 2018. Available at: https://CRAN.R-project.org/package=tableone. Accessed October 24, 2019.
29. Venables WN, Ripley BD: Modern Applied Statistics with S, 4th edition. New York, Springer, 2002. Available at: http://www.stats.ox.ac.uk/pub/MASS4. Accessed October 24, 2019.
30. Hosmer DW, Hosmer T, Le Cessie S, Lemeshow S: A comparison of goodness-of-fit tests for the logistic regression model. Stat Med 1997; 16:965–80
31. Manchikanti L, Pampati V, Hirsch JA: Retrospective cohort study of usage patterns of epidural injections for spinal pain in the US fee-for-service Medicare population from 2000 to 2014. BMJ Open 2016; 6:e013042
32. Manchikanti L, Singh V, Datta S, Cohen SP, Hirsch JA; American Society of Interventional Pain Physicians: Comprehensive review of epidemiology, scope, and impact of spinal pain. Pain Physician 2009; 12:E35–70
33. Baek SR, Lim JY, Lim JY, Park JH, Lee JJ, Lee SB, Kim KW, Paik NJ: Prevalence of musculoskeletal pain in an elderly Korean population: Results from the Korean Longitudinal Study on Health and Aging (KLoSHA). Arch Gerontol Geriatr 2010; 51:e46–51
34. Cho KH, Chung Y, Roh YK, Cho B, Kim CH, Lee HS: Health care for older persons: A country profile-Korea. J Am Geriatr Soc 2004; 52:1199–204
35. Lamé IE, Peters ML, Vlaeyen JW, Kleef Mv, Patijn J: Quality of life in chronic pain is more associated with beliefs about pain, than with pain intensity. Eur J Pain 2005; 9:15–24
36. National Health Insurance Service, Health Insurance Review & Assessment Service: 2014 National Health Insurance Statistical Yearbook. Seoul, National Health Insurance Service, Health Insurance Review and Assessment Service, 2014
37. Kwon S: Thirty years of national health insurance in South Korea: Lessons for achieving universal health care coverage. Health Policy Plan 2009; 24:63–71
38. Health Insurance Review and Assessment Service: Statistics on Medical Resources. Available at: http://opendata.hira.or.kr. Accessed November 6, 2019.
39. Ruppen W, Derry S, McQuay H, Moore RA: Incidence of epidural hematoma, infection, and neurologic injury in obstetric patients with epidural analgesia/anesthesia. Anesthesiology 2006; 105:394–9
40. Reihsaus E, Waldbaur H, Seeling W: Spinal epidural abscess: A meta-analysis of 915 patients. Neurosurg Rev 2000; 23:175–205
41. Niebauer J, Volk HD, Kemp M, Dominguez M, Schumann RR, Rauchhaus M, Poole-Wilson PA, Coats AJ, Anker SD: Endotoxin and immune activation in chronic heart failure: A prospective cohort study. Lancet 1999; 353:1838–42
42. Albillos A, Lario M, Álvarez-Mon M: Cirrhosis-associated immune dysfunction: Distinctive features and clinical relevance. J Hepatol 2014; 61:1385–96
43. Sabroe I, Postma D, Heijink I, Dockrell DH: The yin and the yang of immunosuppression with inhaled corticosteroids. Thorax 2013; 68:1085–7
44. Kidd DP: Neurological complications of Behçet’s syndrome. J Neurol 2017; 264:2178–83
45. Ahn YH, Kim MJ: Health care needs of elderly in a rural community in Korea. Public Health Nurs 2004; 21:153–61
46. Change of drug label: Triamcinolone acetonide (2013-79). 2013. Available at: https://www.fda.gov/media/88483/download. Accessed November 7, 2019.
47. U.S. Food and Drug Administration. Shoulder. Kenalog-10 (triamcinolone acetonide) injection and Kenalog-40 (triamcinolone acetonide) injection. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/012041s045lbl.pdf. Accessed November 7, 2019.
48. Van Boxem K, Rijsdijk M, Hans G, de Jong J, Kallewaard JW, Vissers K, van Kleef M, Rathmell JP, Van Zundert J: Safe use of epidural corticosteroid injections: Recommendations of the WIP Benelux Work Group. Pain Pract 2019; 19:61–92
49. Seavey JG, Balazs GC, Steelman T, Helgeson M, Gwinn DE, Wagner SC: The effect of preoperative lumbar epidural corticosteroid injection on postoperative infection rate in patients undergoing single-level lumbar decompression. Spine J 2017; 17:1209–14

50. Yang S, Werner BC, Cancienne JM, Hassanzadeh H, Shimer AL, Shen FH, Singla A: Preoperative epidural injections are associated with increased risk of infection after single-level lumbar decompression. Spine J 2016; 16:191–6

51. Abrecht CR, Saba R, Greenberg P, Rathmell JP, Urman RD: A contemporary medicolegal analysis of outpatient interventional pain procedures: 2009–2016. Anesth Analg 2019; 129:255–62

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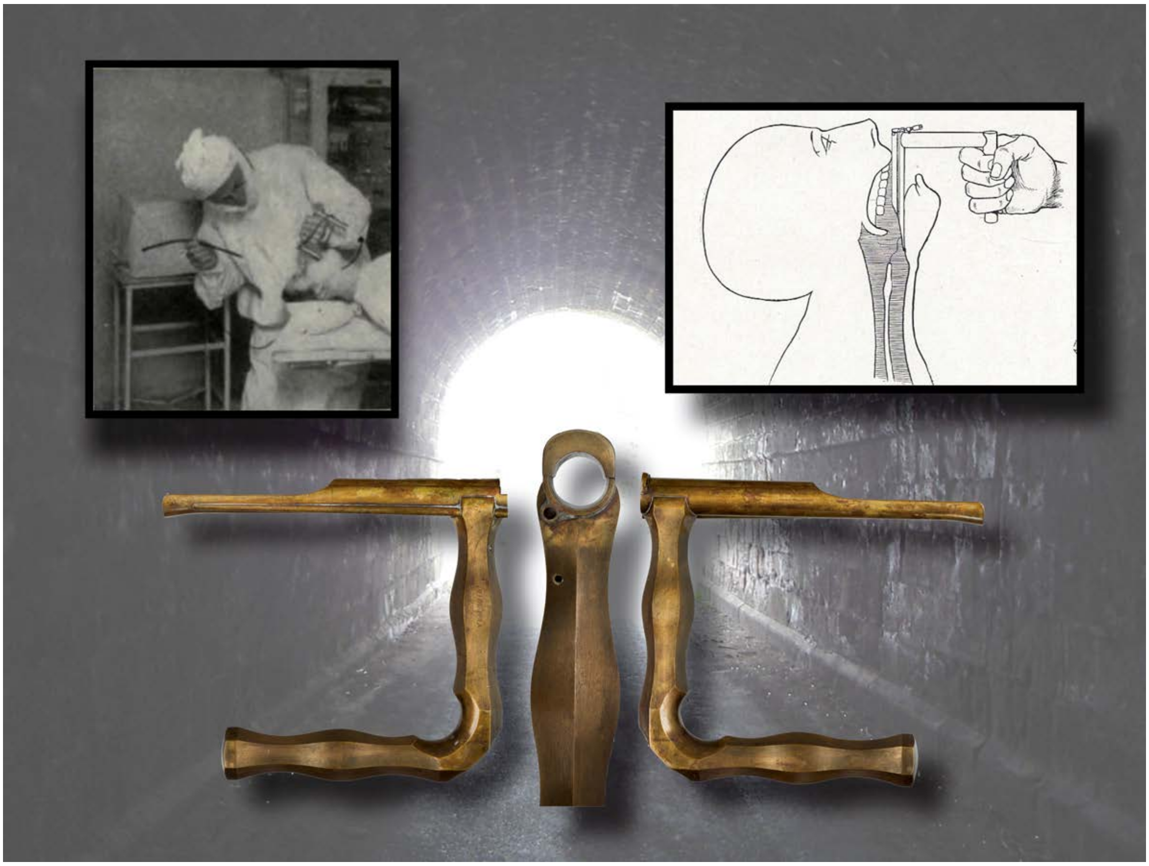
Chevalier Jackson's Laryngoscope: Seeing Light at the End of the Tunnel



Later in life, Chevalier Jackson, M.D. (1865 to 1958) would liken Pittsburgh, his birthplace, to a "dark, cold, damp cellar" where "soot, grime and black dirt covered everything." One day, schoolmates left him bound and blindfolded in an abandoned coal mine, only to be rescued by a man chasing his runaway dog. The tables turned in his adolescence when Jackson himself salvaged a dropped drill bit from a deep oil well using an instrument of his own design. By 1890, he had invented his first endoscope for foreign body retrieval from the dim, collapsible channel of the esophagus. While bronchoscopy originated in Germany, Jackson pioneered the procedure in the United States, maneuvering through winding airways to recover lost items. When he invented his namesake laryngoscope (*center*), which featured a distal light source, Jackson became the first to combine direct laryngeal visualization with endotracheal intubation. Ambidextrous with brush as well as scope, Jackson painted many scenes of sunlit water under cloudy skies during the decade that he struggled with tuberculosis. Through the dark tunnels of his life, Jackson always seemed to see the light. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology, Schaumburg, Illinois.)

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