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ARTICLE

Healthcare-associated infection after spinal cord injury in a tertiary rehabilitation center in South Korea: a retrospective chart audit

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Abstract

Study design A retrospective observational study.

Objective To identify the difference between patients with and without healthcare-associated infection (HAI) after spinal cord injury (SCI), changes in the quantity of rehabilitation after HAI, and resistance to and application of empirical antibiotics.

Setting University hospital-affiliated rehabilitation center.

Methods Altogether, 338 patients with SCI receiving inpatient rehabilitation from January 2015 to March 2018 were categorized into two groups based on the presence or absence of HAI. Demographic and clinical characteristics, amount of rehabilitation performance between before and after HAI, resistance to antibiotics, and empirical antibiotic change rates were investigated.

Results In 79 patients, 117 HAI cases occurred, with an overall incidence of 34.6%. Male sex, complete SCI, and trauma history were more frequent in the HAI group than in the non-HAI group. Length of stay (LOS) was longer at 28.9 days in the HAI group. The incidence of lower respiratory tract infections (LRIs) and urinary tract infections (UTIs) was 5.0 and 16.9%, respectively. The rehabilitation loss rates due to LRIs and UTIs were 40.0 and 20.2%, respectively, which were not statistically significant. The rates of resistance to recommended empirical antibiotics for LRIs and UTIs were 26.9–57.7% and 54.2–67.8%, respectively. The rates of empirical antibiotic changes for LRIs and UTIs were 35.3 and 43.9%, respectively.

Conclusions HAI after SCI was more common in men, complete SCI and trauma history. LOS was prolonged in the HAI group. A quantitative reduction of rehabilitation treatment after HAI was observed, but further research is needed for validation.

Introduction

Spinal cord injury (SCI) can lead to complications and failure in the internal organs below the neurological level of injury (NLI). The atelectasis and restricted sputum expectoration due to respiratory failure after SCI are known risk factors for respiratory infections [1]. Subsequently, increased intravesical pressure and/or bladder overdistension after SCI results in ischemia and mucosal breaks in the bladder walls, which can lower the resistance against urinary tract infections (UTIs) [2]. Additionally, the pressure sore risk increases because of paralysis-induced compression and secondary factors (e.g., urinary and fecal incontinence); consequently, the soft tissue infection risk increases [3].

Infection is associated with mortality in patients with SCI; hence, infection control for these patients is important. According to data from the National Spinal Cord Injury Statistical Center (USA), respiratory system diseases (21.9%) were the leading cause of death among patients with SCI (65.4% of which were pneumonia cases), followed by other infectious diseases (12.0%) [4]. While various epidemiological studies have indicated the infection incidence among patients with SCI [5–8], they mostly reported infection incidence rates, Thus, an in-depth analysis of healthcare-associated infection (HAI) in patients with SCI during inpatient rehabilitation is lacking.

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The present study aimed to identify the difference between patients with and without HAI after SCI at a rehabilitation center affiliated with a tertiary university hospital, changes in quantity of rehabilitation after HAI, and resistance to and application of empirical antibiotics.

Materials and methods

In this study, we performed a retrospective review of medical records. Patients with cervical and thoracic spinal cord injuries were included. Altogether, 338 patients with SCI receiving inpatient rehabilitation at a tertiary center from January 2015 to March 2018 were initially enrolled. They included patients who were transferred to a rehabilitation center after acute/subacute care of SCI in other departments of either our or another hospital, and patients who required re-hospitalization for evaluation and rehabilitation due to worsening neurologic/medical symptoms or functions. Demographic and clinical characteristics, including sex, age, height, body mass index, etiology of injury, NLI, American Spinal Injury Association impairment scale (AIS), diabetes mellitus (DM) history, hemoglobin A1C (HbA1c) level in DM patients, injury duration, and LOS in the department of rehabilitation medicine were analyzed.

Patient groups

The US Centers for Disease Control and Prevention/ National Healthcare Safety Network (CDC/NHSN) defines HAI as an infection in which all elements of a site-specific infection criterion are first present together on or after the third hospital day (admission day is day 1) [9]. The present study used C-reactive protein (CRP) for objective and efficient screening of patients. After the computerized classification of patients with a history of CRP elevation to ≥5.0 mg/dL or CRP < 5.0 mg/dL during hospitalization, entire medical record of each patient with a history of CRP elevation to ≥5.0 mg/dL was reviewed (Fig. 1). Then, if they met the CDC/NHSN definition of HAI [9], they were classified as HAI group; otherwise, they were classified as non-HAI group. Patients with CRP < 5.0 mg/dL, CRP elevation to ≥5.0 mg/dL but without an infection, and community-acquired infection were assigned to non-HAI group (Fig. 1). These two groups were further categorized into subacute SCI and chronic SCI subgroups according to whether the time interval from injury event to rehabilitation center admission or transfer was ≥1 or <1 year. Moreover, the HAI group was further categorized into single HAI and recurrent HAI subgroups. The recurrent HAI group included patients without abnormalities in the routine laboratory test results for >7 days after the laboratory results, including CRP levels, imaging findings, and infection symptoms, and were normalized from a previous infection, but another infection occurred after that period.

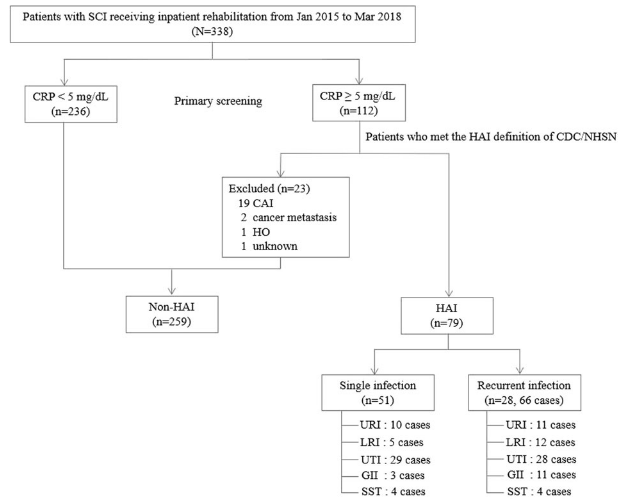

Fig. 1 Flow diagram of patient group classification. SCI spinal cord injury, CRP C-reactive protein, CDC/NHSH The US Centers for Disease Control and Prevention/National Healthcare Safety Network, CAI community-acquired infection, HO heterotopic ossification, HAI healthcare-associated infection, URI upper respiratory infection, LRI lower respiratory infection, UTI urinary tract infection, GII gastrointestinal infection, SST skin and soft tissue infection.

Measurement of rehabilitation treatment loss

Inpatient rehabilitation in South Korea is generally available from Monday to Friday, excluding Sunday and national holidays, with a shortened schedule on Saturday. To compare the amount of rehabilitation treatment between, before, and after CRP elevation, patients in whom the first day (D-day) of CRP elevation to ≥5.0 mg/dL was Monday, Tuesday, or Wednesday were selected. Subsequently, the amount of rehabilitation treatment at 2 days before and 2 days after D-day ($D-2$ and $D+2$, respectively) were compared to that at 3 days before D-day (D-3). However, if D-day was Monday or Tuesday, rehabilitation amount before and after D-day were compared based on the rehabilitation amount of the last Friday. The number of rehabilitation performance units per day (1 unit was equivalent to 30 minutes of treatment) was referred to as the amount of treatment.

Infection investigation: pathogens and antibiotic resistance

Regarding lower respiratory tract infections (LRIs) and UTIs, microorganisms cultured in body fluids and blood were considered as pathogens, and frequency of these pathogens and their resistance to antibiotics were analyzed. Empirical antibiotics were initially used for LRIs and UTIs, and antibiotics used after culture test were investigated to analyze the rate of antibiotic change.

Statistical analysis

Collected data were statistically analyzed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). To compare the differences between two groups, χ^2 test or Fisher's exact test was used for categorical data. Depending on data normality, *t*-test or Mann–Whitney U test was used to analyze continuous data. Multiple linear regression analysis was conducted once to analyze the relationship between LOS (dependent variable), AIS grade (A, B, C, and D; independent variable), and HAI status (independent variable). Friedman test, a non-parametric test, was used to analyze the significance of rehabilitation treatment loss after HAI. Statistical significance was defined as $p < 0.05$.

Results

Of 338 patients with SCI, 259 were assigned to the non-HAI group, including patients with community-acquired infection ($n = 19$), cancer metastasis ($n = 2$), heterotopic ossification ($n = 1$), and unknown cause ($n = 1$). Seventy-nine out of 102 patients with a history of CRP elevation to ≥5 mg/dL were assigned to the HAI group (Fig. 1). The analysis of demographic characteristics revealed significantly higher proportion of men in the HAI group than in the non-HAI group (odds ratio [OR] 2.85, 95% confidence interval [CI], 1.55–5.29, $p = 0.001$). No significant differences in age (mean difference [MD] 2.35, 95% CI, −1.375.77, $p = 0.195$), height (MD 0.01, 95% CI, −1.323.93, $p = 0.364$), body mass index (MD −0.41, 95% CI, −1.30 to 0.48, $p = 0.404$), DM history (OR 1.48, 95% CI, 0.71–3.06, $p = 0.292$), and NLI (OR 0.82, 95% CI, 0.49–1.37, $p = 0.443$) were noted between the two groups. The HAI group had a higher proportion of patients with complete SCI (OR 4.11, 95% CI, 2.28–7.41, $p < 0.001$), trauma history (OR 2.44, 95% CI, 1.38–4.33, $p = 0.002$), and longer LOS (MD 2.89, 95% CI, 20.4–38.8, $p < 0.001$) than the non-HAI group (Table 1). For the subacute and chronic SCI subgroups, tendency similar to that observed in the analysis of all patients was noted, except for age, which was higher in the chronic HAI subgroup than in the chronic non-HAI group (MD 7.10, 95% CI 1.78–12.26, $p = 0.008$) (Table 1). Multiple linear regression analysis of the relationship between LOS, AIS grade, and infection status revealed that when AIS D was used as the reference category, partial regression coefficients (βi) for the presence of infection, AIS A, AIS B, and AIS C, were 24.41 ($p < 0.01$), 18.37 ($p < 0.01$), 8.03 ($p = 0.304$), and 6.82 ($p = 0.603$), respectively.

Among the 117 HAI cases, there were 21 (17.9%) upper respiratory infections (URIs), 17 (14.5%) LRIs, 57 (48.7%) UTIs, 14 (12.0%) gastrointestinal infections (GIIs), and 8 (6.8%) skin and soft tissue infections (SSTs). In 338 patients, 117 HAIs occurred, resulting in an overall incidence of 34.6%. The infection incidence in 338 patients was 5.0% ($n = 17$) for LRIs and 16.9% ($n = 57$) for UTIs.

When the HAI group was subcategorized into single HAI and recurrent HAI subgroups, no significant differences in age (MD −1.26, 95% CI, −8.275.28, $p = 0.720$) and proportion of complete SCI (OR 1.19, 95% CI, 0.46–3.07, $p = 0.725$) and DM history (OR 0.56, 95% CI, 0.14–2.27, $p = 0.412$) were observed between the two subgroups. Although the recurrent HAI subgroup had a higher proportion of men (OR 2.56, 95% CI, 0.66–10.10, $p = 0.162$) and shorter injury duration (MD −9.00, 95% CI, −26.84.90, $p = 0.366$) than the single HAI group, the differences were not significant. The recurrent HAI group had a significantly longer LOS (MD 31.5, 95% CI, 15.248.2, $p < 0.001$) and higher HbA1c level (MD 0.91, 95% CI, 0.391.47, $p = 0.013$) than the single HAI group (Table 2).

Within the HAI group, 41 patients showed elevated CRP levels on Monday, Tuesday, or Wednesday. When comparing the amount of rehabilitation before and after HAI in these patients, an overall decrease was up to 23% (minimum 19%, $p = 0.239$) was noted after HAI. In each infected group, the decrease was up to 28% (minimum 19%, $p = 0.950$), 40% (minimum 20%, $p = 0.734$), 20% (minimum 6%, $p = 0.324$), 50% (minimum 21%, $p = 0.758$), and 17% (minimum 6%, $p = 0.340$) for URI, LRI, UTI, GII, and SST, respectively, but the difference was not significant (Fig. 2).

Pathogens were cultured 26 times in 17 LRI cases, with *Staphylococcus aureus* (23.1%), *Klebsiella pneumoniae* (19.2%), *Pseudomonas aeruginosa* (15.4%), and *Acinetobacter baumannii* (15.4%) accounting for 73.1% of all pathogens. Pathogens were cultured 49 times in 57 UTI cases, with *Escherichia coli* (50.8%) and *K. pneumoniae* (20.3%), accounting for 71.1% of all pathogens.

Regarding resistance against empirical antibiotics recommended for LRIs as an HAI (Infectious Diseases Society of America [IDSA]/American Thoracic Society standard) [10], resistance rates of 57.7, 34.6, 30.8, and 26.9% were found against quinolones, antipseudomonal penicillin (AP), fourth-generation cephalosporins, and carbapenem, respectively (Table 3). Regarding resistance against empirical antibiotics recommended for UTIs as a HAI (IDSA standard) [11], resistance rates of 67.8 and 54.2% were shown against quinolones and trimethoprim-sulfamethoxazole (TMP/SMX), respectively, whereas a resistance rate of 59.3% was shown against third-generation

Table 1 Comparison of the characteristics between the non-HAI and HAI groups with SCI.

All SCI (subacute SCI/ chronic SCI)	Non-HAI ($n = 259$) (178/81)	HAI ($n = 79$) (57/22)	OR or MD (95% CI)	p-value
Sex (n)				
Men	155	64	**2.85 (1.55–5.29)**	**0.001**
Women	104	15	1 (ref)	
Subacute				
Men	114	47	**2.63 (1.25–5.75)**	**0.009**
Women	64	10	1 (ref)	
Chronic				
Men	41	15	**3.31 (1.12–9.85)**	**0.025**
Women	40	5	1 (ref)	
Age (years)	58.6 (57.9–60.3)	61.0 (57.6–64.1)	2.35 (−1.37–5.77)	0.195
Subacute	59.9 (57.7–62.0)	60.2 (56.0–64.5)	0.32 (−4.49–4.98)	0.882
Chronic	55.8 (52.8–58.6)	62.9 (58.7–66.9)	**7.10 (1.78–12.26)**	**0.008**
Height (m)	1.65 (1.63–1.66)	1.66 (1.64–1.68)	0.01 (−1.32–3.93)	0.364
Subacute	1.64 (1.63–1.66)	1.66 (1.64–1.69)	0.02 (−0.69–4.81)	0.209
Chronic	1.65 (1.63–1.68)	1.64 (1.60–1.68)	−0.01 (−5.60–4.44)	0.831
BMI (kg/m^2)	24.3 (23.8–24.8)	23.9 (23.1–24.8)	−0.41 (−1.30–0.48)	0.404
Subacute	24.5 (23.8–25.0)	23.8 (22.9–24.7)	−0.64 (−1.68–0.44)	0.282
Chronic	24.0 (23.2–24.9)	24.2 (22.7–25.7)	0.12 (−1.79–1.84)	0.892
Diabetes mellitus (n)	28	2	1.48 (0.71–3.06)	0.292
Subacute	17	8	1.55 (0.63–3.80)	0.339
Chronic	11	4	1.41 (0.40–4.97)	0.587
HbA1c (%)	7.13 (7.00–7.32)	7.38 (6.97–7.85)	0.25 (−0.21–0.76)	0.241
Subacute	7.17 (6.91–7.41)	7.40 (6.80–8.10)	0.23 (−0.41–0.93)	0.447
Chronic	7.07 (6.82–7.33)	7.35 (6.70–8.00)	0.27 (−0.30–0.90)	0.348
NLI (n)				
Cervical myelopathy	160	45	0.82 (0.49–1.37)	0.443
Thoracic myelopathy	99	34	1 (ref)	
Subacute				
Cervical myelopathy	108	34	0.96 (0.52–1.76)	0.890
Thoracic myelopathy	70	23	1 (ref)	
Chronic				
Cervical myelopathy	52	11	0.56 (0.22–1.45)	0.226
Thoracic myelopathy	29	11	1 (ref)	
AIS (n)				
Complete injury	32	29	**4.11 (2.28–7.41)**	**<0.001**
Incomplete injury	227	50	1 (ref)	
Subacute				
Complete injury	18	16	**3.47 (1.63–7.39)**	**0.001**
Incomplete injury	160	41	1 (ref)	
Chronic				
Complete injury	14	13	**6.93 (2.47–19.30)**	**<0.001**
Incomplete injury	67	9	1 (ref)	
Etiology (n)				
Traumatic injury	146	60	**2.44 (1.38–4.33)**	**0.002**
Non-traumatic injury	113	19	1 (ref)	
Subacute				

Table 1 (continued)

All SCI (subacute SCI/ chronic SCI)	Non-HAI ($n=259$) (178/81)	HAI ($n=79$) (57/22)	OR or MD (95% CI)	p-value
Traumatic injury	97	43	**2.57 (1.31–5.01)**	**0.005**
Non-traumatic injury	81	14	1 (ref)	
Chronic				
Traumatic injury	49	17	2.22 (0.75–6.62)	0.146
Non-traumatic injury	32	5	1 (ref)	
Duration of injury (years)	1.81 (1.37–2.31)	1.73 (1.04–2.57)	−0.08 (−0.90–0.88)	0.871
Subacute	0.24 (0.22–0.27)	0.24 (0.20–0.029)	0.00 (−0.05–0.05)	0.941
Chronic	5.24 (4.08–6.48)	5.59 (3.67–7.62)	0.35 (−1.94–2.72)	0.786
LOS in RM (days)	47.8 (44.3–50.7)	76.8 (68.7–86.0)	**28.9 (20.4–38.8)**	**<0.001**
Subacute	54.1 (50.2–58.0)	83.4 (72.3–94.2)	**29.3 (17.4–40.1)**	**0.001**
Chronic	34.1 (29.8–38.9)	59.5 (48.1–71.4)	**25.4 (13.2–37.5)**	**<0.001**

Data are presented as mean (95% CI) or as *n*.

HAI healthcare-associated infection, *SCI* spinal cord injury, *OD* odds ratio for dichotomous data, *MD* mean difference for continuous data, *CI* confidence interval, *BMI* body mass index, *HbA1c* hemoglobin A1C, *NLI* neurological level of injury, *AIS* American Spinal Injury Association impairment scale, *LOS* length of stay, *RM* department of rehabilitation medicine.

Table 2 Comparison of the characteristics between the single HAI and recurrent HAI groups with SCI.

	Single HAI ($n=51$)	Recurrent HAI ($n=28$)	OR or MD (95% CI)	p-value
Infection events (n)	51	66		
Sex (n)				
Men	39	25	2.56 (0.66–10.10)	0.165
Women	12	3	1 (ref)	
Age (years)	61.4 (57.1–65.3)	60.14 (54.0–65.7)	−1.26 (−8.27–5.28)	0.720
NLI (n)				
Cervical myelopathy	26	19	2.03 (0.77–5.33)	0.147
Thoracic myelopathy	25	9	1 (ref)	
AIS (n)				
Complete injury	18	11	1.19 (0.46–3.07)	0.725
Incomplete injury	33	17	1 (ref)	
Diabetes mellitus (n)	9	3	0.56 (0.14–2.27)	0.412
HbA1c (%)	6.70 (6.50–6.90)	7.61 (7.14–8.12)	**0.91 (0.39–1.47)**	**0.013**
Duration of injury (months)	24.7 (12.2–40.0)	15.2 (9.3–22.8)	−9.00 (−26.8–4.90)	0.366
LOS in RM (days)	65.5 (55.2–76.1)	97.1 (84.6–111.0)	**31.5 (15.2–48.2)**	**<0.001**

Data are presented as mean (95% CI) or as *n*.

HAI healthcare-associated infection, *SCI* spinal cord injury, *OR* odds rario for dichotomous data, *MD* mean difference for continuous data, *CI* confidencw interval, *NLI* neurological level of injury, *AIS* American Spinal Injury Association impairment scale, *HbA1c* hemoglobin A1C, *LOS* length of stay, *RM* department of rehabilitation medicine.

cephalosporins, which is additionally recommended in the Korean clinical guidelines (Table 3). As for the empirical antibiotics for LRIs, APs (58.9%) were the most commonly used, and the overall rate of antibiotic change after the culture test was 35.3%. Quinolones (100%) were changed most often (Table 3). Regarding empirical antibiotics for UTIs, quinolones (54.3%) were the most commonly used, and the overall rate of antibiotic change after the culture test was 43.9%. Cephalosporins (54.5%) showed the highest rate of empirical antibiotic change (Table 3).

Discussion

In the present study, we conducted an in-depth analysis of HAI in patients with SCI at a rehabilitation center affiliated to a tertiary university hospital. It can be seen that the proportion of male sex, complete SCI, and trauma history is higher in the HAI group than in the non-HAI group. Moreover, LOS was longer in the HAI group. Additionally, in patients with chronic SCI, the HAI group was older than the non-HAI group. In the HAI group with a DM history, the recurrent HAI subgroup had higher HbA1c levels and a longer LOS than the single HAI subgroup. The overall rate of quantity in rehabilitation treatment after HAI was reduced by 23% (40, 20, and 50% for LRIs, UTIs, and GIIs, respectively). The rates of resistance against recommended empirical antibiotics for LRIs and UTIs were 26.9–57.7% and 54.2–67.8%, respectively. Furthermore, the average rates of empirical antibiotic change used for LRIs and UTIs at our rehabilitation center were 35.3 and 43.9%, respectively.

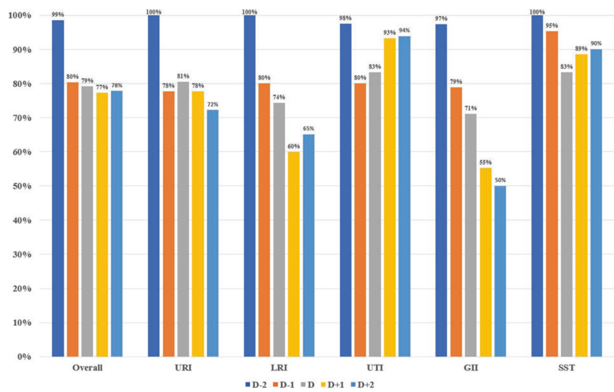

Fig. 2 Changes in the rehabilitation performance rate after healthcare-associated infection. Overall overall infection, URI upper respiratory infection, LRI lower respiratory infection, UTI urinary tract infection, GII gastrointestinal infection, SST skin and soft tissue infection.

Based on previous reports that CRP is the most useful among other parameters for indicating infection [12, 13], the present study used CRP for objective and efficient screening, not for diagnosis. A prior study suggested that a CRP cut-off value of 6.0 mg/dL was the most appropriate for diagnosing bacterial infection (sensitivity, 80.7%; specificity, 96.0%) [12]. Accordingly, before the present study, a preliminary study was conducted in 88 patients with SCI who received inpatient rehabilitation at our center between January and December 2015. The entire medical chart of each participant was reviewed, and 40 infection cases were confirmed. When the CRP cut-off value was set to 3.5, 4.0, 4.5, 5.0, and 6.0 mg/dL, the sensitivity was 87.1, 86.5, 85.0, 85.0, and 75.0%, respectively, whereas the specificity was 90.7, 90.7, 94.9, 100.0, and 100.0%, respectively. Based on these results, the cut-off value in the present study was set to 5.0 mg/dL.

Our results indicated that infection was more prevalent in men and patients with complete SCI. Such findings were consistent with those of previous studies that analyzed factors associated with the prevalence of LRIs in patients with acute SCI [14]. A similar tendency for infection prevalence in men was also reported by a study on 30,288

Table 3 Pathogen resistance to antibiotics and rate of empirical antibiotic change.

Antibiotics	LRI			UTI		
	Resistance (%)	Case (*n*, %)	Change rate (%)	Resistance (%)	Case (*n*, %)	Change rate (%)
Overall	34.3	17 (100)	35.3	34.5	57 (100)	43.9
Quinolone[a,b,c]	57.7	2 (11.8)	100	67.8	31 (54.3)	51.6
Penicillin derivative	73.1	–	–	72.4	–	–
Antipseudomonal penicillin[a]	34.6	10 (58.9)	30.0	27.1	11 (19.3)	18.2
4th generation cephalosporin[a]	30.8	4 (23.4)	25.0	47.5	–	–
3rd generation cephalosporin[c]	30.1	–	–	59.3	11 (19.3)	54.5
Carbapenem[a]	26.9	1 (5.9)	0	10.2	4 (7.1)	25.0
TMP/SMX[b]	24.4	–	–	54.2	–	–
Aminoglycoside	23.1	–	–	15.3	–	–
Tetracycline	30.8	–	–	32.9	–	–
Macrolide	15.4	–	–	8.5	–	–
Glycopeptide	0	–	–	1.7	–	–

Data are presented as *n* or as percentages.

LRI lower respiratory tract infection, *UTI* urinary tract infection, *TMP/SMX* trimethoprim-sulfamethoxazole.

[a]Recommended empirical antibiotics of Infectious Diseases Society of America and American Thoracic Society for healthcare-associated lower respiratory infection.

[b]Recommended empirical antibiotics of Infectious Diseases Society of America for catheter-associated urinary tract infection.

[c]Recommended empirical antibiotics of Korean clinical practice guideline for catheter-associated urinary tract infection.

trauma patients, and this tendency was more prominent in patients with severe trauma than in those with mild trauma [15]. A previous study that examined the characteristics of SCI according to sex reported a higher percentage of AIS A and B in men with SCI [16]. They mentioned that the difference in injury mechanism could partially explain these results. Although motor vehicle accidents are the most common cause of SCI in both men and women, approximately 70% of deaths occur in men. There may be differences in the severity of motor vehicle accidents. The higher ratio of sports-related and bicycle accidents in men than in women is related to SCI severity [16]. DM is a known risk factor for infection [17]. We found no significant difference in DM prevalence and HbA1c level between the HAI and non-HAI groups. However, in the HAI group, the HbA1c level was significantly higher in recurrent HAI subgroup than in the single HAI subgroup. In a previous study conducted in the UK, 85312 patients' primary care data, the relative risk of infection was evaluated according to the degree of DM control [18]. In this study, the optimal control group (HbA1c 6–7%) had an incidence rate ratio of 1.41, whereas that of the poor control group (HbA1c > 11%) increased to 4.70. Although HbA1c level of the recurrent HAI subgroup was 7.61 (95% CI, 7.14–8.12), the level of blood sugar control was not very poor because the HbA1c level was 7–8%, indicating that there was no significant increase in the risk compared to that of the previous study, but it was significantly higher than that of the single HAI subgroup at 6.70 (95% CI, 6.50–6–90).

The incidence of LRIs and UTIs in the present study was relatively lower than that reported in previous epidemiological studies for patients with SCI (LRIs: 5.6–18.2%; UTIs: 11.8–23.1%) [5–8]. Nonetheless, this incidence was much higher than the HAI incidence of 4.0% (LRIs: 0.98%; UTIs: 0.58%) reported by a 2015 CDC study on 12,299 general patients [19] and the HAI incidence of 3.7% (LRIs: 0.6%; UTIs: 1.12%) reported by a 1996 study on 15 acute hospitals in Korea [20]. Studies on HAI incidence in people with stroke showed a similar tendency for SCI, with an incidence of 4.0–17.2 and 8.3–30.5% for LRIs and UTIs, respectively [21, 22].

The results suggest that HAI causes an increase in LOS, but without adequate control for confounding; thus, further prospective studies are needed to confirm this. However, this is consistent with the findings of previous studies [14, 23]. Multiple linear regression analysis of infection status, AIS, and LOS revealed that infection status had a significant impact on prolonged LOS. The mean LOS was prolonged by 29.3 days in the HAI group (vs. the non-HAI group) and by 31.3 days in the recurrent infection subgroup (vs. the single infection subgroup). Even considering the mean antibiotic use of 13.1 days, it can be seen that a rehabilitation period extension occurred. In a previous study conducted in the UK, the average LOS for SCI patients undergoing specialist rehabilitation was 72.8 days, and the average medical cost was 32813 pounds [24]. Referring to previous study, the prolonged LOS of HAI group most likely accounts for the additional medical cost of 13,206 pounds.

A quantitative reduction of rehabilitation treatment after HAI was observed, but it was not statistically significant. The low statistical power is suspected to be a result of the insufficient number of patients in our study. Improving the statistical power in this study was limited because all applicable patients were analyzed, thus our results warrant further investigation in a larger patient cohort. The rate of rehabilitation treatment loss due to infection was the highest in GIIs, but SSTs did not show a significant difference. Because most GII cases are accompanied by diarrhea, it is common in clinical practice for patients or caregivers to be reluctant to undergo rehabilitation treatment because of the aftercare for diarrhea or to discontinue rehabilitation treatment to avoid dealing with diarrhea that occurs during treatment. *Clostridioides difficile* infection is propagated by contact and consequently requires isolation during rehabilitation treatment, which might have led to such results. In the present study, pressure ulcer was the cause of all SSTs. Before infection, the numbers of rehabilitation units for participants with URIs, LRIs, UTIs, and GIIs were 6.0, 5.8, 6.0, and 6.3, respectively, whereas that for participants with SSTs was 2.67. This is speculated to be because the change in the treatment loss rate after infections is small, as the patients were already receiving reduced rehabilitation treatment before infection because of postural limitations due to pressure ulcers.

In the US, the use of APs, fourth-generation cephalosporins, or quinolones + carbapenem are recommended for LRIs, which is HAI with a low expected mortality rate [11]. However, in Europe, carbapenem, third-generation cephalosporins, or quinolones are recommended for such cases [25]. However, quinolones, which showed the highest resistance among the recommended empirical antibiotics, were replaced in all cases when it was used at our rehabilitation center; thus, it would be impossible to use this antibiotic as an empirical treatment for LRI at our center. The United States guidelines recommend TMP/SMX and quinolone as empirical antibiotics for UTIs [12], whereas the Korean clinical guidelines recommend quinolone and third-generation cephalosporin because resistance to TMP/SMX was found to be very high in Korea through local surveillance [26]. Thus, it would be necessary to develop clinical guidelines that sufficiently account for the state of local resistance to antibiotics through local surveillance for effective empirical antibiotic administration. Nonetheless, according to a study conducted by the World Health Organization, only five out of 63 clinical guidelines for

UTIs worldwide fully satisfy such criteria [27]. Accordingly, the Bayesian weighted incidence syndromic antibiogram approach was recommended for deciding empirical antibiotics with consideration of the pathogen emergence and antibiotic resistance rates [28]. Therefore, if empirical antibiotic therapy tailored to a country or institution based on local surveillance could be applied, then rehabilitation treatment loss and prolonged LOS could be minimized through an effective infection treatment.

Study limitations

Owing to its retrospective nature, the present study has the following limitations. First, the respiratory and urinary status at infection onset could not be accurately identified; consequently, there were limitations in the additional analysis of risk factors for infection. Moreover, because the overall functions of all patients were not re-assessed at the time of discharge, there were limitations in the comparison of functional recovery at the time of discharge between the infected and non-infected groups. However, it can be indirectly surmised from the prolonged LOS in the infected group that HAI is one of the factors that limited functional recovery through rehabilitation.

This study used CRP as a tool for screening individuals suspected of having an infection. Although CRP is not an absolute diagnostic criterion for infection, it is a known inflammatory factor that is typically elevated in the presence of infection and has been reported to be highly associated with infection severity [29, 30]. According to our preliminary study of the present study, when the CRP cut-off value was 5.0 mg/dL, the sensitivity was 85.0%. Therefore, our HAI incidence might have been slightly underestimated, but patients with mild infection could be excluded.

Currently, only infections in intensive care units and surgical site infections are investigated in Korea for HAI control; thus, there were limitations in causatively verifying the infection control level at our center. However, our center is affiliated to a tertiary national university hospital and is among the largest rehabilitation centers in Korea. Chungnam National University Hospital has been accredited as a tertiary hospital by the Korea Institute for Healthcare Accreditation operated by the Ministry of Health and Welfare (2015.02.07–2023.02.06), and our center has received a 3-year accreditation (2017.10–2020.09) from the Commission on Accreditation of Rehabilitation Facilities. Therefore, our center operates an infection control system that meets national and international standards.

The results of this study are only preliminary but could be used to guide further studies in this area. Importantly, to determine whether HAI causes prolonged LOS and reduced rehabilitation, a prospective cohort study is required in which all assumptions about the relationship among possible confounders, mediators, and moderators are schematically determined prior to the study and declared in a Directional Acyclic Graph. This graph can then be used as a priori to identify the minimum set of variables that need to be measured and adjusted for the analysis.

Conclusion

HAI was more common in men and patients with complete SCI and trauma history. The HAI group had longer LOS than the non-HAI group. Moreover, we observed a quantitative reduction of rehabilitation treatment after HAI, but further large-scale prospective research is needed to confirm our results. Additionally, it is necessary to consider local surveillance of HAI pathogen resistance and the change rate of empirical antibiotics. Further research is required to evaluate the effect of tailored empirical antibiotics on rehabilitation.

Data availability

The dataset generated or analyzed in the current study is available from the corresponding author upon reasonable request.

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Author contributions C.W.M. had full access to all data in the present study and takes responsibility for the integrity of the data and the accuracy of data analysis. I.Y.J. and Y.Z.X. revised the manuscript for important intellectual content. The concept and design of the study were handled by KHC.

Compliance with ethical standards

Ethical approval The study was approved by the Institutional Review Board of Chungnam National University Hospital, Korea (IRB No. 2018-11-054-002). The requirement for the acquisition of informed consent from the patients was waived owing to the retrospective nature of this study.

Conflict of interest The authors declare that they have no conflict of interest.

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References

1. Schilero GJ, Spungen AM, Bauman WA, Radulovic M, Lesser M. Pulmonary function and spinal cord injury. Respir Physiol Neurobiol. 2009;166:129–41.
2. Linsenmeyer TA. Catheter-associated urinary tract infections in persons with neurogenic bladders. J Spinal Cord Med. 2018;41:132–41.

3. Brienza D, Krishnan S, Karg P, Sowa G, Allegretti AL. Predictors of pressure ulcer incidence following traumatic spinal cord injury: a secondary analysis of a prospective longitudinal study. Spinal Cord. 2018;56:28–34.
4. National Spinal Cord Injury Statistical Center. The 2017 annual statistical report for the spinal cord injury model systems. https://www.nscisc.uab.edu/Public/2017%20Annual%20Report%20-%20Complete%20Public%20Version.pdf. Accessed 9 Apr 2018.
5. Nwankwo OE, Uche EO. Epidemiological and treatment profiles of spinal cord injury in southeast Nigeria. Spinal Cord. 2013;51:448–52.
6. Lehre MA, Eriksen LM, Tirsit A, Bekele S, Petros S, Park KB, et al. Outcome in patients undergoing surgery for spinal injury in an Ethiopian hospital. J Neurosurg Spine. 2015;23:772–9.
7. Ning GZ, Mu ZP, Shangguan L, Tang Y, Li CQ, Zhang ZF, et al. Epidemiological features of traumatic spinal cord injury in Chongqing, China. J Spinal Cord Med. 2016;39:455–60.
8. Li HL, Xu H, Li YL, Sun SW, Song WY, Wu Q, et al. Epidemiology of traumatic spinal cord injury in Tianjin, China: an 18-year retrospective study of 735 cases. J Spinal Cord Med. 2019;42:778–85.
9. Centers for Disease Control and Prevention. CDC/NHSN surveillance definition of healthcare-associated infection and criteria for specific types of infections in the acute care setting. http://www.socinorte.com/wp-content/uploads/2013/03/Criterios-de-IN-2013.pdf. Accessed 10 Apr 2018.
10. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63:e61–111.
11. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis. 2010;50:625–63.
12. Liu A, Bui T, Van Nguyen H, Ong B, Shen Q, Kamalasena D. Serum C-reactive protein as a biomarker for early detection of bacterial infection in the older patient. Age Ageing. 2010;39:559–65.
13. Ticinesi A, Lauretani F, Nouvenne A, Porro E, Fanelli G, Maggio M, et al. C-reactive protein (CRP) measurement in geriatric patients hospitalized for acute infection. Eur J Intern Med. 2017;37:7–12.
14. Agostinello J, Battistuzzo CR, Batchelor PE. Early clinical predictors of pneumonia in critically ill spinal cord injured individuals: a retrospective cohort study. Spinal Cord. 2019;57:41–8.
15. Gannon CJ, Pasquale M, Tracy JK, McCarter RJ, Napolitano LM. Male gender is associated with increased risk for postinjury pneumonia. Shock. 2004;21:410–4.
16. Furlan JC, Craven BC, Fehlings MG. Sex-related discrepancies in the epidemiology, injury characteristics and outcomes after acute spine trauma: a retrospective cohort study. J Spinal Cord Med. 2019;42:10–20.
17. Vardakas KZ, Siempos II, Falagas ME. Diabetes mellitus as a risk factor for nosocomial pneumonia and associated mortality. Diabet Med. 2007;24:1168–71.
18. Critchley JA, Carey IM, Harris T, DeWilde S, Hosking FJ, Cook DG. Glycemic control and risk of infections among people with type 1 or type 2 diabetes in a large primary care cohort study. Diabetes Care. 2018;41:2127–35.
19. Magill SS, O'Leary E, Janelle SJ, Thompson DL, Dumyati G, Nadle J, et al. Changes in prevalence of health care-associated infections in U.S. hospitals. N. Engl J Med. 2018;379:1732–44.
20. Kim JM, Park ES, Jeong JS, Kim KM, Kim JM, Oh HS, et al. Multicenter surveillance study for nosocomial infections in major hospitals in Korea. Nosocomial Infection Surveillance Committee of the Korean Society for Nosocomial Infection Control. Am J Infect Control. 2000;28:454–8.
21. Indredavik B, Rohweder G, Naalsund E, Lydersen S. Medical complications in a comprehensive stroke unit and an early supported discharge service. Stroke. 2008;39:414–20.
22. Bae HJ, Yoon DS, Lee J, Kim BK, Koo JS, Kwon O, et al. In-hospital medical complications and long-term mortality after ischemic stroke. Stroke. 2005;36:2441–5.
23. Jaja BNR, Jiang F, Badhiwala JH, Schär R, Kurpad S, Grossman RG, et al. Association of pneumonia, wound infection, and sepsis with clinical outcomes after acute traumatic spinal cord injury. J Neurotrauma. 2019;36:3044–50.
24. Turner-Stokes L, Williams H, Bill A, Bassett P, Sephton K. Cost-efficiency of specialist inpatient rehabilitation for working-aged adults with complex neurological disabilities: a multi centre cohort analysis of a national clinical data set. BMJ Open. 2016;6:e010238.
25. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H, et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT). Eur Respir J. 2017;50:1700582.
26. Kim WB, Cho KH, Lee SW, Yang HJ, Yun JH, Lee KW, et al. Recent antimicrobial susceptibilities for uropathogenic *Escherichia coli* in patients with community acquired urinary tract infections: a multicenter study. Urogenit Trac Infect. 2017;12:28–34.
27. Elias C, Moja L, Mertz D, Loeb M, Forte G, Magrini N. Guideline recommendations and antimicrobial resistance: the need for a change. BMJ Open. 2017;7:e016264.
28. Tandogdu Z, Kakariadis ETA, Naber K, Wagenlehner F, Bjerklund Johansen TE. Appropriate empiric antibiotic choices in health care associated urinary tract infections in urology departments in Europe from 2006 to 2015: a Bayesian analytical approach applied in a surveillance study. PLoS ONE. 2019;14:e0214710.
29. Haran JP, Suner S, Gardiner F. Correlation of C-reactive protein to severity of symptoms in acute influenza A infection. J Emerg Trauma Shock. 2012;5:149–52.
30. Porfyridis I, Georgiadis G, Vogazianos P, Mitis G, Georgiou A. C-reactive protein, procalcitonin, clinical pulmonary infection score, and pneumonia severity scores in nursing home acquired pneumonia. Respir Care. 2014;59:574–81.