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Healthcare utilization and costs after cranial epilepsy surgery and vagus nerve stimulation in pediatric drug-resistant epilepsy: a nationwide cohort study

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Pediatric drug-resistant epilepsy (DRE) affects 30–40% of children with epilepsy, resulting in medical costs significantly higher than those of controlled epilepsy. Cranial epilepsy surgery (CES) and vagus nerve stimulation (VNS) are key interventions; however, their long-term economic impact remains ambiguous. Using South Korea's National Health Insurance claims data (2007–2022), we examined healthcare utilization and costs among children with DRE treated with antiseizure medications (ASM) only, CES, or VNS. Of the cohort included 6020 patients, of whom 5407 (89.8%) received ASM-only treatment, 396 (6.6%) underwent CES, and 217 (3.6%) received VNS. Post-CES, emergency department (ED) visits declined by 65%, overall length of stay (LOS) by 45%, epilepsy-specific admissions by 49% and epilepsy-specific LOS by 83%. Interrupted time series analysis revealed a sustained monthly reduction in total costs, consistent with fewer high-risk encounters. Post-VNS, ED visits fell by 41%, admissions by 39%, and LOS by 44%, with reductions in epilepsy-related admissions; however, outpatient visits remained unchanged. Both CES and VNS significantly reduce acute-care needs in pediatric DRE. CES yields the greatest and most durable benefits, while VNS shifts care from emergency and inpatient settings to scheduled outpatient follow-up, offering a valuable alternative when surgery is not feasible.

Keywords Drug-resistant epilepsy, Epilepsy surgery, Vagus nerve stimulation, Health care costs, Pediatric neurology

Epidemiology and socioeconomic burden of pediatric drug-resistant epilepsy

Pediatric epilepsy is a common neurological disorder that affects approximately 0.5–1% of children worldwide[1]. Approximately 30–40% of patients develop drug-resistant epilepsy (DRE), characterized by failure to achieve seizure control despite trials of at least two well-tolerated and appropriately chosen antiseizure medications (ASMs)[2,3]. Pediatric patients with DRE continue to experience unpredictable and recurrent seizures. These episodes often require substantial healthcare utilization to manage both acute symptoms and complications. Previous studies have consistently shown that pediatric DRE is associated with increased healthcare utilization and considerable economic burden[4–12]. Children with DRE frequently require complex care, including recurrent emergency department (ED) visits for acute seizures, hospitalizations for prolonged or refractory seizures, and specialist consultations for medication adjustment and adverse effect management[4,5]. Clinical studies have revealed that children with refractory epilepsy have 2.5 times greater hospitalization rates[6,7].

Consequently, direct medical costs for DRE are estimated to be four to nine times higher than those for well-controlled epilepsy[8]. A U.S. study showed annual costs reaching $30,343 for uncontrolled epilepsy compared with $18,206 for stable epilepsy[9]. Beyond direct expenses, the economic impact includes substantial indirect expenses such as caregiving, lost productivity, and special education needs[10].

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Comorbidities such as developmental delays, learning disabilities, and behavioral problems are also common in children with DRE, further compounding both direct and indirect costs[11]. In South Korea, the total socioeconomic burden of epilepsy was estimated at approximately Korean Won (KRW) 536 billion in 2010, with direct medical costs accounting for KRW 196.2 billion (36.6%) and indirect costs totaling KRW 304.2 billion, with adolescents under 20 years representing 24.5% of the total burden[12].

Cranial epilepsy surgery and vagus nerve stimulation as treatments for pediatric DRE

Cranial epilepsy surgery (CES) and vagus nerve stimulation (VNS) are considered key therapeutic options for children with DRE who do not respond adequately to ASMs. CES is generally indicated for patients with lesional epilepsy whose seizures remain uncontrolled despite adequate medical therapy. Conversely, VNS is considered for patients with drug-resistant epilepsy whose seizures are not well controlled with appropriate medications but who have generalized epilepsy, lack a clearly identifiable lesion, or are not suitable candidates for surgery[13]. These clinical indications are consistent with internationally accepted treatment guidelines and are similarly applied in South Korea. CES can help achieve seizure freedom in up to 80% of carefully selected patients with focal epilepsies[14], while VNS serves as an effective alternative for pediatric patients who are not eligible for surgery[15]. CES has been associated with reduced healthcare utilization following successful surgical outcomes, specifically reduced epilepsy-related hospitalizations, ED visits, and overall medical expenditures[16,17]. VNS has also been associated with these benefits[18–20]. These findings suggest that both interventions not only improve seizure control but also reduce medical costs by decreasing ED visits, hospitalizations, and overall medical expenditures[21,22].

Purpose

Although the clinical effectiveness of both CES and VNS is well established, their economic impact and differences in healthcare-utilization patterns have not been systematically compared in pediatric patients with DRE. Previous studies have often been focused on a single treatment modality or included mixed populations, limiting the applicability of their findings to children[23,24]. Therefore, this study aimed not only to quantify the individual economic impact of CES and VNS but also to directly compare changes in healthcare utilization and costs between the two interventions, using nationwide claims data.

Materials and methods

Data source

This retrospective cohort study was conducted using the Korean Health Insurance Review and Assessment Service (HIRA) database (January 1, 2002–December 31, 2022)[25].

Patient selection

Data of patients with DRE were extracted from the HIRA database using an operational definition through the following steps. First, patients younger than 18 years were selected based on epilepsy-related diagnoses according to the Korean Standard Classification of Diseases (KCD) codes, which were modified from the International Statistical Classification of Diseases (ICD) and Related Health Problems, 10th Revision: G40.x (epilepsy), G41.x (status epilepticus), and R56.8 (seizure).

Second, patients who met at least one of the following criteria[26–28] were included: (1) a minimum of two healthcare visits with G40.x on different days including any combination of outpatient visits, ED visits, or hospital admissions; (2) at least one visit with G40.x and another visit with R56.8 on separate days; (3) a primary diagnosis code G40.x with a prescription for ASMs; or (4) a primary diagnosis code G40.x during an inpatient admission or ED visit.

Third, from our epilepsy cohort, patients with DRE were identified using specific KCD 8th codes indicating intractable epilepsy (G40.x1), which shares the same hierarchical structure as the ICD-10-CM code used in the United States[29], or procedure codes for CES or VNS (S4733–S4737 and S0433–S0434). CES included resective and disconnective procedures performed via craniotomy, identified by the following procedure codes: temporal lobectomy (S4733 and S4734), extratemporal lobectomy (S0433), cortical resection (S0434), corpus callosotomy (S4735), hemispherectomy or hemispherotomy (S4736), and multiple cortical resection (S4737). VNS implantation was identified using the procedure code S4730, which corresponds to surgical implantation of a vagus nerve stimulator device. Patients who had previously used ASMs, had DRE-related diagnostic codes, or had received VNS or CES before 2009 were then excluded.

Fourth, DRE was operationally defined as treatment with at least three combined or sequential ASMs after the initial epilepsy diagnosis[2]. Individuals aged 18 years or older at the index date (date of initial prescription for the third ASMs) were excluded. To isolate the impact of each treatment modality, patients who underwent both VNS and CES or underwent the same procedure more than once were excluded.

Fifth, the identified patients with DRE were categorized into three groups based on their treatment. The ASM-only group comprised patients who met the operational definition of DRE but were managed exclusively with ASMs and had no history of VNS or CES, regardless of the degree of seizure control. This group served as a non-surgical comparator representing pharmacologically managed DRE. The VNS group included patients who received VNS in addition to ASMs, and the CES group included those who underwent CES in addition to ASMs.

Outcomes

The primary outcomes were total and epilepsy-related medical costs and healthcare utilization, assessed separately for each treatment group. Medical costs were defined as reimbursed payments recorded in the HIRA database, serving as a proxy for direct medical expenditures. Healthcare utilization was evaluated based on the number of outpatient visits, ED visits, inpatient admissions, and hospitalization days. All outcomes were assessed annually

and compared between the pre- and post-intervention periods. Epilepsy-related outcomes were identified using claims with the primary epilepsy diagnosis codes. Direct costs related to the implementation of CES and VNS (i.e., costs incurred on the day of CES or VNS) were excluded from the analysis of both total and epilepsy-related costs and examined separately. Secondary outcomes included temporal trends in monthly average medical costs over the 36-month period before and after each intervention.

Statistical analysis

Demographic characteristics were compared across the three treatment groups (ASM only, CES, and VNS) using the chi-square test for categorical variables. Comorbidities were classified according to ICD-10 diagnostic codes and defined by the presence of at least one relevant diagnosis during the study period.

Healthcare utilization and costs were summarized as medians with interquartile ranges (IQRs). To compare these outcomes across the three groups, the Kruskal–Wallis test was performed. For within-group comparisons, the Wilcoxon signed-rank test was applied. This test was used to specifically compare the median value of the entire period before the intervention, starting from the index date, with the median value of the entire period after the intervention until the end of observation.

To evaluate within-group changes from the pre- to post-intervention period, generalized linear models (GLMs) with a negative binomial distribution were applied to address overdispersion. For outcomes with a high proportion of zero values, zero-inflated negative binomial (ZINB) models were initially attempted. In cases where model convergence failed, simplified negative binomial GLMs without random effects were used as fallback models. The results are reported as rate ratios (RRs) with corresponding 95% confidence intervals (CIs) and p-values.

To evaluate medical cost changes following interventions, an interrupted time-series (ITS) analysis was performed using segmented regression on a fixed 36-month period before and after the interventions. Monthly average cost was used for this analysis because it better reflect the actual cost patterns when patients receive multiple months' worth of medication or treatment in a single visit. The number of patients per month served as the denominator. The segmented regression model was used to examine three parameters: pre-intervention slope, immediate-level change, and slope change. Post-intervention slope significance was assessed via linear hypothesis testing. All statistical analyses were performed using R software (version 4.4.0), with statistical significance set at $p < 0.05$.

Ethics approval

This study was approved by the Institutional Review Board of Eunpyeong St. Mary's Hospital, The Catholic University of Korea (approval number: PC25ZISI0114). The requirement for informed consent was waived by the ethics committee, as this study used anonymized administrative data provided by the Health Insurance Review and Assessment Service of South Korea. All methods were carried out in accordance with relevant guidelines and regulations, and in compliance with the Declaration of Helsinki.

Results

Demographics of study population

A total of 6,020 pediatric patients with DRE were included in this study, comprising 5407 patients (89.8%) in the ASM–only group, 217 patients (3.6%) in the VNS group, and 396 patients (6.6%) in the CES group (Table 1). Sex distribution was similar across the groups ($p = 0.903$), but age at DRE diagnosis and at intervention varied (both $p < 0.001$). The ASM–only and CES groups had the highest proportion of patients aged under 4 years at the index date (41.1% and 48.7%, respectively), while the VNS group had the highest proportion of patients aged 4–11 years (43.3%). The proportion of Medical Aid patients was higher in the ASM-only group (9.8%) than in the CES (5.3%) or VNS (5.1%) group ($p = 0.007$). The VNS group had higher prevalence rates of comorbidities, such as mental and behavioral disorders (71.9%), endocrine and metabolic diseases (76.5%), diseases of the nervous system without epilepsy (74.2%), and diseases of the musculoskeletal system and connective tissue (88.0%), as well as injury, poisoning, and certain other consequences of external causes (91.7%). The ASM-only group had higher rates of certain conditions originating in the perinatal period (14.7%), while the CES group had higher rates of congenital malformations, deformations, chromosomal abnormalities (45.7%), and neoplasms (27.0%).

Healthcare utilization

Annual healthcare utilization varied among the three treatment groups (Table 2). Regarding overall healthcare utilization, the VNS group had more ED visits, inpatient admissions, and length of stay (LOS) than others ($p < 0.05$ for all). However, the number of outpatient visits was similar across groups ($p = 0.45$). Regarding epilepsy-specific healthcare utilization, the VNS group consistently showed higher utilization across all categories (all $p < 0.001$). This group had the highest healthcare utilization rates across all components of both overall and epilepsy-specific healthcare utilization.

Several changes in healthcare utilization before and after the intervention were observed in both the CES and VNS groups (Table 3). In the CES group, overall ED visits (RR 0.35, $p < 0.001$) and LOS (RR 0.55, $p < 0.001$) decreased, with no changes in outpatient visits and inpatient admissions. Epilepsy-specific inpatient admissions (RR 0.51, $p < 0.001$) and LOS (RR 0.17, $p < 0.001$) decreased. In the VNS group, overall healthcare utilization decreased. Epilepsy-specific rates of ED visits (RR 0.64, $p = 0.01$), inpatient admissions (RR 0.54, $p = 0.002$), and LOS (RR 0.46, $p < 0.001$) decreased, with no changes in outpatient visits.

Medical costs

The CES group demonstrated a decrease in overall median annual medical costs (from 9036 to 2970 thousand KRW, $p < 0.001$), whereas the VNS group showed an increase (from 6496 to 7981 thousand KRW, $p < 0.001$).

	Total (*N* = 6,020)	ASM–only (*N* = 5,407)	CES (*N* = 496)	VNS (*N* = 217)	*P**
Sex					0.903
Male	3356 (55.8)	3009 (55.7)	224 (56.6)	123 (56.7)	
Age at index date					< 0.001
< 4 year	2484 (41.3)	2223 (41.1)	193 (48.7)	68 (31.3)	
4–11 year	1858 (30.9)	1640 (30.3)	124 (31.3)	94 (43.3)	
12–18 year	1678 (27.9)	1544 (28.6)	79 (20.0)	55 (25.4)	
Age at intervention					< 0.001
< 4 year	125 (20.6)	–	120 (30.7)	5 (2.3)	
4–11 year	259 (42.6)	–	162 (41.4)	97 (44.7)	
12–18 year	156 (25.7)	–	75 (19.2)	81 (37.3)	
≥ 18 year	68 (11.2)	–	34 (8.7)	34 (15.7)	
Insurance					0.007
National Health Insurance	5453 (90.6)	4877 (90.2)	375 (94.7)	201 (94.9)	
Medical aid	567 (9.4)	530 (9.8)	21 (5.3)	23 (5.1)	
Comorbidity and underlying disease†					
I. Certain infectious and parasitic disease	5331	4765 (88.1)	366 (92.4)	200 (92.2)	0.008
II. Neoplasms	833	691 (12.8)	107 (27.0)	35 (16.1)	< 0.00
III. Disease of the blood and blood-forming organs and certain disorders involving the immune mechanism	2367	2124 (39.3)	155 (39.1)	88 (40.6)	0.93
IV. Endocrine, nutritional, and metabolic diseases	4435	3991 (73.8)	278 (70.2)	166 (76.5)	0.18
V. Mental and behavioral disorders	3786	3383 (62.6)	247 (62.4)	156 (71.9)	0.02
VI. Diseases of the nervous system	3788	3381 (62.5)	246 (62.1)	161 (74.2)	0.002
VII. Diseases of the eye and adnexa	4994	4446 (82.2)	357 (90.2)	191 (88.0)	< 0.001
VIII. Diseases of the ear and mastoid process	3934	3505 (64.8)	279 (70.5)	150 (69.1)	0.04
IX. Diseases of circulatory system	2057	1842 (34.1)	135 (34.1)	80 (36.9)	0.7
X. Diseases of the respiratory system	5942	5331 (98.6)	394 (99.5)	217 (100.0)	0.07
XI. Diseases of the digestive system	5759	5156 (95.4)	386 (97.5)	217 (100.0)	< 0.001
XII. Diseases of the skin and subcutaneous tissue	5386	4809 (88.9)	366 (92.4)	211 (97.2)	< 0.001
XIII. Diseases of the musculoskeletal system and connective tissue	4685	4180 (77.3)	314 (79.3)	191 (88.0)	< 0.001
XIV. Diseases of the genitourinary system	3042	2703 (50.0)	205 (51.8)	134 (61.8)	0.003
XV. Pregnancy, childbirth, and the puerperium	41	38 (0.7)	3 (0.8)	0 (0.0)	0.55
XVI. Certain conditions originating in the perinatal period	839	796 (14.7)	26 (6.6)	17 (7.8)	< 0.001
XVII. Congenital malformations, deformations, and chromosomal abnormalities	1676	1441 (26.7)	181 (45.7)	54 (24.9)	< 0.001
XVIII. Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	5781	5187 (95.9)	380 (96.0)	214 (98.6)	0.14
XIX. Injury, poisoning, and certain other consequences of external causes	4920	4375 (80.9)	346 (87.4)	199 (91.7)	< 0.001
XX. External causes of morbidity and mortality	149	128 (2.4)	13 (3.3)	8 (3.7)	0.27
XXI. Factors influencing health status and contact with health services	4554	4034 (74.6)	331 (83.6)	189 (87.1)	< 0.001
XXII. Codes for special purposes	130	119 (2.2)	5 (1.3)	6 (2.8)	0.35

Table 1. Characteristics of pediatric patients with drug-resistant epilepsy. Values are presented as numbers (%). †Its percentages represent the proportions of the total patient cohort. Disease categories followed the International Classification of Diseases (ICD-10) coding system. *P-values were calculated using the chi-square test. ASM, antiseizure medication; VNS, vagus nerve stimulation.

The CES group demonstrated a decrease in epilepsy-specific median annual medical costs (from 5726 to 1941 thousand KRW, $p < 0.001$), whereas the VNS group showed an increase (from 3808 to 4587 thousand KRW, $p < 0.001$) (Table 4).

Interrupted time series analysis for medical costs

In the CES group, total medical costs showed a pre-intervention increase of 24.2 thousand KRW per month ($p < 0.001$). In the month of CES, an immediate decrease of 218.6 thousand KRW ($p = 0.04$) was observed, followed by a continued decrease of 19.1 thousand KRW per month ($p < 0.001$) (Fig. 1A). A similar pattern was observed for epilepsy-specific costs. An increase of 24.5 thousand KRW per month was observed before surgery ($p < 0.001$), followed by an immediate decrease of 371.8 thousand KRW in the month of surgical intervention ($p < 0.001$) and a subsequent monthly decrease of 11.2 thousand KRW ($p < 0.001$) (Fig. 1B).

The VNS group showed different patterns. For total medical costs, no trend was observed before intervention ($p = 0.18$), but a decrease of 243.5 thousand KRW in the month of VNS was observed ($p = 0.03$). The post-intervention trend showed no change ($p = 0.06$) (Fig. 2A). The pre-intervention trend for epilepsy-specific costs

	Total (*N* = 6,020)	ASM–only (*N* = 5,407)	CES (*N* = 496)	VNS (*N* = 217)	*P*[*]
Overall healthcare utilization					
Outpatient visits	25.1 [15.0–47.3]	25.1 [14.9–47.4]	25.0 [15.2–47.2]	25.5 [18.0–44.2]	0.45
ED visits	0.5 [0.1–1.3]	0.5 [0.1–1.3]	0.4 [0.2–1.0]	0.7 [0.3–1.3]	0.004
Inpatient admissions	0.4 [0.1–1.3]	0.4 [0.1–1.3]	0.5 [0.3–1.2]	0.6 [0.3–1.1]	< 0.001
Annualized length of stay (days)	2.0 [0.3–11.4]	1.8 [0.2–12.0]	2.8 [1.14–9.9]	3.2 [1.5–8.2]	< 0.001
Epilepsy-specific healthcare utilization					
Outpatient visits	6.5 [3.6–11.2]	6.3 [3.5–10.8]	7.1 [4.0–14.9]	10.3 [7.6–14.4]	< 0.001
ED visits	0.1 [0.0–0.5]	0.1 [0.0–0.5]	0.1 [0.0–0.3]	0.2 [0.0–0.8]	< 0.001
Inpatient admissions	0.2 [0.0–0.8]	0.1 [0.0–0.8]	0.5 [0.2–1.0]	0.5 [0.2–1.0]	< 0.001
Annualized length of stay (days)	0.6 [0.0–5.9]	0.3 [0.0–5.5]	2.4 [0.9–8.4]	2.9 [0.9–7.4]	< 0.001

Table 2. Comparison of overall and epilepsy-specific healthcare utilization across treatment groups. Values are presented as median [interquartile range]. Annual encounters were calculated by dividing the total utilization by individual follow-up years. Overall utilization included all medical encounters, whereas epilepsy-specific utilization was limited to encounters with ICD-10 codes G40–G41. Healthcare services related to the VNS or CES procedures were excluded. [*]P-values for between-group comparisons, calculated using Kruskal–Wallis test. ASM, antiseizure medication; VNS, vagus nerve stimulation; CES, cranial electrical stimulation; ED, emergency department.

	CES (*N* = 496)		VNS (*N* = 217)	
	RR (95% CI)	*P*	RR (95% CI)	*P*
Overall healthcare utilization				
Outpatient visits	0.96 (0.84–1.09)	0.49	0.81 (0.7–0.94)	0.01
ED visits	0.35 (0.28–0.43)	< 0.001	0.59 (0.46–0.76)	< 0.001
Inpatient admissions	0.95 (0.75–1.21)	0.67	0.61 (0.45–0.83)	0.002
Length of stay (days)	0.55 (0.42–0.72)	< 0.001	0.56 (0.39–0.8)	0.02
Epilepsy-specific healthcare utilization				
Outpatient visits	0.98 (0.83–1.15)	0.77	1.09 (0.92–1.29)	0.33
ED visits	0.92 (0.72–1.18)	0.53	0.64 (0.46–0.88)	0.01
Inpatient admissions	0.51 (0.38–0.67)	< 0.001	0.54 (0.37–0.8)	0.002
length of stay (days)	0.17 (0.12–0.24)	< 0.001	0.46 (0.33–0.63)	< 0.001

Table 3. Within-Group changes in annual healthcare utilization before and after Intervention. P-values for within-group comparisons were derived using Negative Binomial Generalized Linear Models. VNS, vagus nerve stimulation; CES, cranial electrical stimulation; ED, emergency department.

was not statistically significant ($p = 0.20$). However, a decrease in the month of VNS (223.8 thousand KRW, $p = 0.005$), followed by a monthly increase of 6.8 thousand KRW was observed ($p = 0.01$) (Fig. 2B).

The median direct costs were 16,528 thousand KRW for CES and 16,904 thousand KRW for VNS, with no difference between the groups ($p = 0.37$).

Discussion

Summary of main findings

We compared healthcare utilization among pediatric patients with DRE treated with ASM-only, ASM plus CES, or ASM plus VNS. CES led to the largest and most durable clinical gains in overall ED visits, inpatient admissions, and LOS, as well as in epilepsy-specific admissions, and hospitalization duration. VNS also resulted in reductions in acute care use, although outpatient follow-up remained unchanged. Cost analyses showed that CES reversed the increasing presurgical cost trend and achieved long-term reductions in both total and epilepsy-specific medical costs. VNS resulted in an initial cost reduction, but epilepsy-specific expenses gradually increased afterward.

Interpretation of healthcare utilization pattern

In the CES group, overall healthcare utilization decreased, with fewer ED visits and shorter LOS. Epilepsy-related inpatient admissions and duration of hospitalization also reduced. These findings suggest that CES may help reduce seizure severity and, thus, the serious condition that led to long-term hospitalization. This is a clinically meaningful outcome, considering that while the primary goal of epilepsy surgery is complete seizure elimination[30], reducing the frequency or intensity of severe seizures that impair quality of life represents an important secondary objective when seizure freedom is not achievable[31]. However, CES did not affect the number of epilepsy-related outpatient or ED visits. Intensive postoperative follow-up is essential to monitor for

	Total ($N=6,020$)	ASM–only ($N=5,407$)	CES ($N=496$)			VNS ($N=217$)			$P^{\dagger}$
			Before	After	P^{*}	Before	After	P^{*}	
Overall medical costs									
Total costs (1000 KRW)									
Median [IQR]	30,083 [13,701–68,012]	25,881 [12,572–62,150]	57,594 [42,211–90,123]			75,083 [52,258–111,762]			< 0.001
			15,567 [8142–29,526]	39,405 [26,687–63,841]	< 0.001	26,884 [17,972–50,100]	44,018 [27,557–67,198]	< 0.001	
Mean ± SD	60,180 ± 134,336	555,768 ± 114,772	82,905 ± 84,562			128,636 ± 392,387			0.71
			25,394 ± 35,252	57,511 ± 72,405	< 0.001	65,469 ± 27,0415	63,166 ± 126,344	0.83	
Annual costs (1000 KRW)									
Median [IQR]	4635 [2337–11,738]	4082 [2214–11,339]	8096 [4858–14,161]			9430 [6367–14,838]			< 0.001
			9036 [5055–18,113]	2970 [1000–10,418]	< 0.001	6496 [4224–10,967]	7981 [4464–20,486]	< 0.001	
Mean ± SD	14,069 ± 19,322	13,913 ± 125,536	14,963 ± 24,674			16,326 ± 34,793			< 0.001
			18,677 ± 37,010	17,545 ± 77,699	< 0.001	14,336 ± 37,701	37,166 ± 156,080	0.018	
Epilepsy-specific medical costs									
Total costs (1000 KRW)									
Median [IQR]	10,666 [4061–26,818]	9141 [3547–21,118]	40,372 [25,110–57,500]			50,501 [36,354–76,120]			< 0.001
			11,045 [5,081–19,503]	26,841 [14,492–41,528]	< 0.001	3808 [2380–6181]	4587 [2149–10,112]	< 0.001	
Mean ± SD	23,490 ± 44,606	19,659 ± 38,541	49,023 ± 53,988			72,356 ± 94,745			< 0.001
			15,018 ± 16,762	34,005 ± 47,860	< 0.001	31,571 ± 87,1050	40,785 ± 29,455	0.13	
Annual costs (1000 KRW)									
Median [IQR]	1731 [727–4274]	1524 [647–3387]	5123 [2901–9400]			6460 [4603–9532]			< 0.001
			5726 [2792–11,427]	1941 [625–6947]	< 0.001	3808 [2380–6181]	4587 [2149–10,112]	< 0.001	
Mean ± SD	4979 ± 1637	4415 ± 16,110	9352 ± 20,778			9384 ± 11,071			< 0.001
			13,526 ± 35,461	8978 ± 423,637	0.03	7282 ± 15,019	15,845 ± 48,478	0.004	

Table 4. Comparison of overall and epilepsy-specific medical costs across treatment groups. Values are presented as median [interquartile range] and mean ± standard deviation. *P-values for within-group comparisons (before versus after intervention) were calculated using the Wilcoxon signed-rank test. †P-values for between-group comparisons, calculated using Kruskal–Wallis test. The overall medical costs included all medical expenses regardless of the diagnosis. Epilepsy-specific medical costs only included expenses related to epilepsy-related diagnoses (ICD-10 codes G40–G41). Total costs represented the cumulative medical costs over the entire follow-up period. The annual costs were calculated by dividing the total costs by the individual follow-up years. For patients in the VNS and Surgery groups, "Before" refers to the period prior to the respective intervention, and "After" refers to the period following the intervention. All costs related to the VNS and CES operations were excluded from the analysis. All costs are expressed in Korean Won (KRW). ASM, antiseizure medication; VNS, vagus nerve stimulation; KRW: Korean Won.

potential complications, adjust medications, and assess neuropsychological outcomes. Long-term and systematic follow-up after epilepsy surgery is important for patient prognosis management, and outpatient visits may be maintained or temporarily increased during this process[32].

In the VNS group, reductions in the overall and epilepsy-related acute care use, including ED visits, hospitalizations, and LOS, was also observed. This suggests that VNS not only improved seizure control but also reduced the occurrence and treatment of comorbid conditions, which may indirectly reflect improvements in patient well-being. These findings are consistent with those of previous studies showing a 25–57% reduction in hospitalization rates and a 26–56% reduction in ED visits after VNS[18]. Such improvements have been linked to reduced seizure-related emergencies, including head trauma and status epilepticus, and overall quality of life improvement following VNS[18]. Furthermore, the number of epilepsy-related ED visits, hospitalization rate, and LOS decreased. The observed decrease in high-risk encounters likely reflects improved seizure control, as VNS is known to reduce both seizure frequency[20] and severity[15]. Outpatient visits remained unchanged or increased slightly, consistent with the clinical requirements for regular follow-ups for several months to two years of therapy. These include device management, medication adjustment, and stimulation parameter optimization[20]. The tendency for VNS implantation to occur at age 4 or older is likely influenced by the device's finite battery life. Delaying the initial procedure can reduce the total number of replacement surgeries a patient requires over their lifetime.

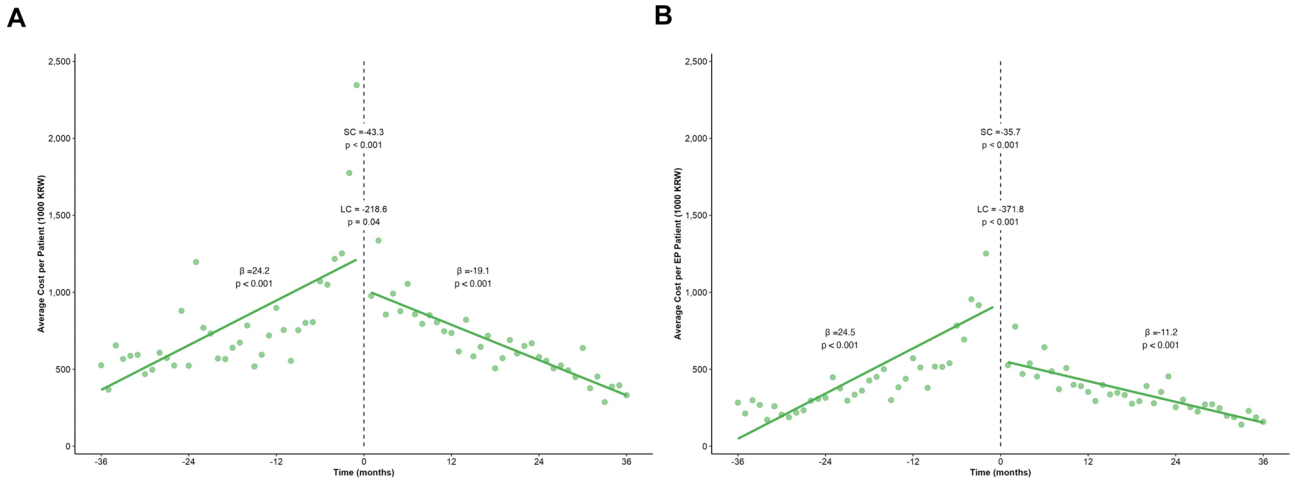

Fig. 1. Interrupted time series analysis of medical costs for the CES group. (**A**) Total medical costs and (**B**) epilepsy-specific medical costs over 36 months before and after surgery. The vertical dashed line indicates the time of surgical intervention (month 0). Green dots represent average monthly costs per patient. Direct CES costs at time 0 excluded. Solid green lines show fitted regression lines. β represents the slope coefficient (monthly change in costs), LC represents the level change at intervention, and SC represents the slope change after intervention. All costs are presented in 1000 KRW. CES, cranial epilepsy surgery; β, beta coefficient; LC, level change; SC, slope change; KRW, Korean Won.

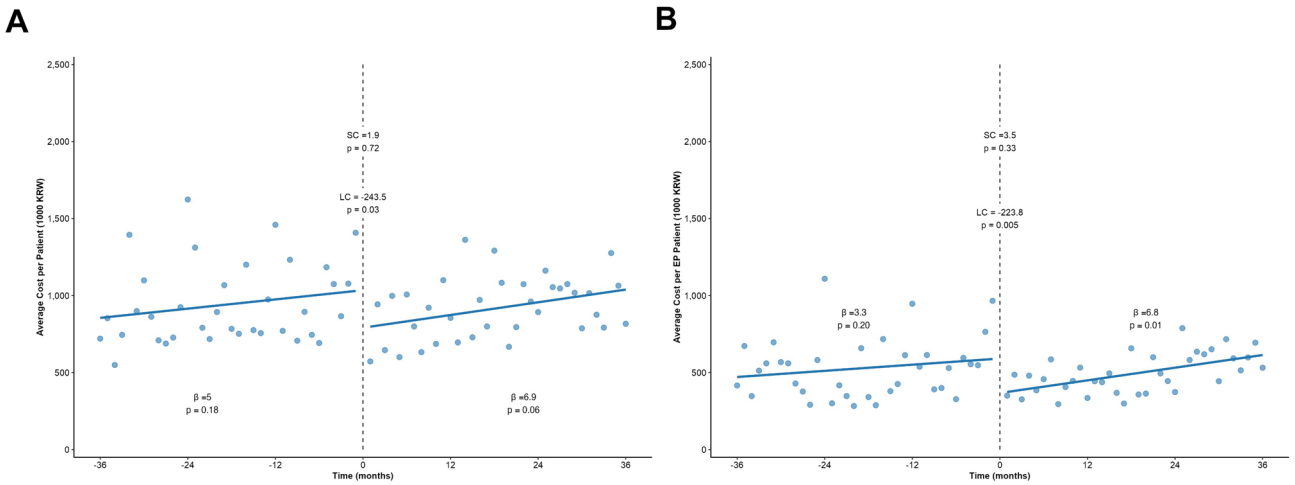

Fig. 2. Interrupted time series analysis of medical costs for the VNS group. (**A**) Total medical costs and (**B**) epilepsy-specific medical costs over 36 months before and after VNS. The vertical dashed line indicates the time of VNS intervention (month 0). Blue dots represent average monthly costs per patient. Direct VNS costs at time 0 excluded. Solid blue lines show fitted regression lines. β represents the slope coefficient (monthly change in costs), LC represents the level change at intervention, and SC represents the slope change after intervention. All costs are presented in 1000 KRW. VNS, vagus nerve stimulation; β, beta coefficient; LC, level change; SC, slope change; KRW, Korean Won.

Cost implications and economic significance

In the CES group, both total and epilepsy-specific medical costs significantly decreased following surgery. These long-term savings align with the findings of previous studies. One study conducted among pediatric Medicaid beneficiaries revealed an average reduction of $6806 in direct costs, with sustained savings maintained over a 5-year follow-up period[33]. Subsequent studies confirmed that cost reductions persisted beyond the immediate postoperative phase[34], reflecting decreased reliance on emergency and inpatient care, medication use, and other seizure-related health services[35].

In contrast, the VNS group showed a short-term reduction in epilepsy-related medical costs immediately after device implantation. However, these benefits were not sustained over time, as epilepsy-specific expenditures gradually increased (Fig. 2B). Although overall medical costs remained relatively stable during the post-intervention period, cost-effectiveness remained limited. This pattern reflects the palliative nature of VNS,

which focuses on reducing seizure frequency and severity rather than achieving seizure freedom[15]. Previous economic analyses have yielded mixed results. One pediatric study showed annual epilepsy-related cost savings of $3254 through reduced hospitalizations[20], while another indicated that VNS reduced costs by 50% compared with alternative neuromodulation therapies within one year[36]. However, these initial benefits were offset by the increasing long-term maintenance costs associated with device maintenance. Notably, 46% of the patients required battery replacement or revision surgery during follow-up[37].

These findings underscore the fundamental therapeutic differences between CES and VNS. CES functions as a curative intervention aimed at definitive seizure control through the resection of epileptogenic foci[23], whereas VNS provides a palliative intervention for patients not eligible for surgery, offering partial seizure control and reduced emergency care reliance[24].

Seizure severity and comorbidity as cost drivers

Epilepsy-related healthcare utilization and medical costs often reflect underlying seizure severity, especially when direct clinical data are unavailable. Greater seizure burden and associated comorbidities have been shown to be major drivers of economic costs in epilepsy[38]. In particular, uncontrolled seizures are strongly associated with psychiatric and systemic medical comorbidities, which substantially amplify healthcare utilization and cost[39].

In our study, both the CES and VNS groups had higher epilepsy-related medical costs than the ASM-only group (Table 1), suggesting that these cohorts included patients with more severe diseases. Comorbidity patterns further support this: the VNS group had the highest overall prevalence of comorbid conditions across most disease categories, while the CES group showed elevated rates in specific domains. Consequently, total medical costs were highest in the VNS group, followed by the CES group. Among congenital malformations, brain-related congenital abnormalities were present in 26.6% of CES patients, compared with 9.22% in the VNS group and 7.59% in the ASM-only group. This finding is consistent with clinical practice, in which children with epilepsy due to congenital brain anomalies are more often considered for CES[40]. In addition, patients with higher seizure severity have increased rates of psychiatric comorbidities[41]. Consistent with this, the VNS group in our study had the highest psychiatric comorbidity rates and the greatest healthcare utilization and cost burden, suggesting that these patients likely represent the most severely ill clinical subgroup.

By contrast, the ASM-only group represents pharmacologically managed DRE, likely including patients with less severe seizure semiology or those who were not yet surgical candidates during the observation period. It can be reasonably inferred that seizure severity in this group was milder than in the CES or VNS groups, as patients with more severe or refractory seizures are generally more likely to undergo those interventions. Although the overall healthcare utilization and medical costs of the ASM-only group were lower, CES or VNS may still provide meaningful clinical and economic benefits for appropriately selected individuals.

Clinical implications

Our findings have important clinical implications for optimizing treatment selection in pediatric patients with DRE. The distinct healthcare utilization profiles of CES and VNS reflect their fundamentally different therapeutic roles. As a curative intervention, CES was associated with sustained seizure control, marked reductions in ED visits and hospitalizations, and long-term medical cost savings. It may be especially suitable for patients with structurally identifiable seizure foci and those burdened by frequent hospital admissions[42]. However, the need for a 5–7-day postoperative hospital stay and months of intensive outpatient follow-up should be considered[43]. In contrast, VNS offers a palliative option that can lower the need for acute care in patients with diffuse or non-resectable epilepsy. This is valuable for patients with unpredictable seizure patterns or comorbidities requiring frequent unplanned care[44]. Although its effects on seizure control and cost reduction are less robust than those of CES, VNS resulted in stabilization of total healthcare expenditures following an initial decline, likely owing to reduced indirect, non-epilepsy-related healthcare use. Notably, previous studies have shown limited success in achieving seizure freedom with VNS[45] and gradual increases in epilepsy-related costs related to device maintenance over time[46]. Therefore, while VNS contributes to cost containment and care stabilization in the short term, its long-term economic impact remains uncertain. A longer follow-up period is needed to assess sustained cost trajectories and potential benefits more accurately.

Finally, our analysis revealed socioeconomic disparities in access to neurosurgical treatment. The lower proportions of Medical Aid recipients receiving CES (5.3%) and VNS (5.1%) compared with the ASM-only group (9.8%) suggest potential barriers to equitable access. This underscores the importance of expanding insurance coverage and support for vulnerable pediatric populations requiring advanced epilepsy care.

Strengths and limitations

This study has significant methodological strengths, primarily the use of comprehensive nationwide data over an extended period, which enhanced the statistical power and generalizability of the findings. Furthermore, independent analysis of CES and VNS interventions enabled precise pre- and post-treatment comparisons, clearly establishing the therapeutic effects attributable to each modality. However, an inherent limitation of the retrospective cohort design was the inability to directly quantify key parameters, such as seizure frequency and severity. Instead, indirect comparisons were made using data on medical costs and comorbidities. Moreover, although the KCD classification system theoretically distinguishes focal (G40.0–G40.2) and generalized (G40.3–G40.4) epilepsy, the frequent use of unspecified codes such as G40.9 (epilepsy, unspecified) in administrative claims data prevented reliable differentiation between these types. As a result, subgroup analyses by epilepsy type could not be conducted. Therefore, future research should be conducted using a prospective design to analyze the cost-effectiveness of VNS and CES using direct clinical outcomes, such as seizure frequency and severity, and should also incorporate patient-reported outcomes together with healthcare utilization and medical cost data to

provide a more comprehensive assessment of their patient-centered and economic impact. Broader economic evaluations are warranted to encompass indirect societal costs, such as caregiver burden and productivity losses.

Conclusions

Both CES and VNS substantially reduce acute-care utilization in children with DRE, but their economic and clinical profiles diverge. CES achieves the largest and most durable reductions in ED visits, hospital admissions, and LOS, reflecting its curative potential and translating into sustained cost savings VNS also decreases acute-care burden and converts unplanned encounters to scheduled outpatient follow-up, providing a clinically meaningful option for children who are not surgical candidates, though with less durable economic benefits. By directly comparing the two interventions, our study fills a critical evidence gap regarding their relative economic impact and supports a tiered treatment strategy: early consideration of CES when resection is feasible and strategic use of VNS when it is not. Future prospective studies are needed to evaluate long-term outcomes, including seizure frequency, quality of life, and healthcare costs, to further refine evidence-based treatment selection.

Data availability

The data that support the findings of this study were obtained from the Health Insurance Review and Assessment Service (HIRA) of South Korea (approval number: M20230914001). These data are not publicly available due to institutional restrictions but are available upon reasonable request with permission from HIRA (http://opendata.hira.or.kr). All data provided by HIRA are fully anonymized and de-identified prior to release.

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Author contributions

A.C. designed the data collection instruments, collected the data, and performed the initial analyses and drafted the initial manuscript. S.K. coordinated and supervised the data collection and critically reviewed the analysis. J.L. conceived the study, provided critical revisions for important intellectual content, and oversaw the project. All authors approved the final manuscript and agreed to be accountable for every aspect of this study.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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