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SYSTEMATIC REVIEW AND META-ANALYSIS

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Five-Year Long-Term Prognosis of Epileptic Children After Hemispheric Surgery

A Systematic Review and Meta-analysis

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Abstract: To estimate children's long-term seizure outcomes after hemispheric surgery and the associated predictors.

A systematic review of 4 databases and a meta-analysis were performed from January 1, 1995 to August 31, 2015. The databases included PubMed, Embase, Science Direct, and Web of Science; patients were classified into the Engel Class I group and the Engel Class II to IV group, according to their seizure outcomes. Nine potential predictors were then stratified across the groups and estimated using the Wilcoxon rank-sum test for continuous variables and the Chi-squared test for categorical variables.

The search yielded 15 retrospective studies, with a total sample size of 380. Five years after surgery, 268 (0.71, 95% confidence interval [CI]: 0.64–0.78) children were seizure free; the seizure onset age in the Engel Class I group was significantly higher than that of the Engel Class II to IV group (standardized mean difference [SMD] = 0.26, 95% CI: 0.03–0.49, $P = 0.028$); specifically, when predicting the positive long-term outcomes, the odds ratio for late onset age (≥3.6 months, median value of the Engel Class II–IV group) versus early onset age was 2.65 (95% CI: 1.454–4.836, $z = 3.18$, $P = 0.001$). The abnormal magnetic resonance imaging (MRI) findings were more predictive for positive seizure outcomes than the normal findings (odds ratio [OR] = 4.60, 95% CI: 1.27–16.62, $P = 0.02$).

Following hemispheric surgery, the long-term prognosis of children with epilepsy was good. Late seizure onset (age ≥ 3.6 months) and abnormal MRI findings were positive predictors for long-term seizure control in children.

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Abbreviations: CI = confidence interval, OR = odds ratio, SMD = standardized mean difference.

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INTRODUCTION

Hemispheric surgery, including anatomic hemispherectomy, traditional functional hemispherectomy, peri-insular hemispherotomy, and so on, has been proven to be an effective treatment for patients with epilepsy arising from varies etiologies, such as Rasmussen encephalitis, Sturge–Weber syndrome, stroke, diffuse hemispheric cortical dysplasia, and tumor.[1–5] In the short term, many single or pooled analyses have reported good seizure outcomes in children with epilepsy following hemispheric surgery; the seizure-free rate (Engel Class I) ranges from 43% to 78%.[6–12] Some researchers have conducted long-term follow-ups (more than 5 years); however, most evidence is based on a single study.[13–28] Hu et al[29] have pooled a seizure-free rate of 73% from 1528 patients (56 studies) who underwent hemispheric surgery. However, the subjects in their study covered all age ranges; therefore, their conclusion was not specifically for children. Englot et al[30] have conducted a meta-analysis of the predictive indicators for children with epilepsy; however, the participants were restricted to pediatric patients with extra-temporal lobe epilepsy, and the follow-up period was not long term (i.e., >1 year). Téllez-Zenteno et al[31] have observed long-term (follow-up time >5 years) seizure outcomes following epilepsy surgery; however, he also included patients of all ages. Considering that surgery results differ substantially between children and adults, no strong long-term evidence concerning seizure outcomes in children, or the factors associated with these outcomes have been reported.

We performed a systematic review and meta-analysis to explore the long-term (a mean/median follow-up time ≥5 years) seizure control outcomes in epileptic children, and we also attempted to identify the predictors of the long-term prognosis of these children.

METHODS

Study Selection

Two reviewers independently identified English-language articles from the PubMed, Embase, Science Direct, and Web of Science databases from January 1, 1995 to August 31, 2015 (a period of at least 20 years). The query was performed using the following search terms alone and in combination: hemispherectomy, hemispherotomy, hemidecortication, hemicortectomy, frontal lobe, parietal lobe, occipital lobe, extra-temporal, surgery, disconnection, resection, seizure, epilepsy, pediatric, children, and adolescent. Ethical approval is not required for a meta-analysis.

Inclusion and Exclusion Criteria

The following inclusion criteria were applied: original articles with a sample size of at least 10 patients; the study subjects were children with epilepsy (younger than 19 years of

age) undergoing hemispheric surgery; the studies had a minimum mean/median follow-up time of 5 years; the seizure outcome of every included patient was reported; and for each child, the study reported the patient sex, age at onset, age at surgery, seizure type, etiology, seizure duration time, status epilepticus, surgical side, and MRI findings. We excluded duplicate publications (i.e., studies with any overlapping patient populations from the same center); commentaries, reviews, and other types of articles were also excluded.

Data Extraction

The following variables were extracted: first author name, publication year, number of patients, patient sex, seizure onset age, seizure duration, seizure type, age at surgery, surgery side, MRI findings, epilepsia continua, etiology, and seizure outcome. Variables 4 to 13 were potential predictors of interest; however, other variables of interest (e.g., seizure frequency, ECG findings, and so on) were not extracted or analyzed because of insufficient data.

Statistical Analysis

The Wilcoxon rank-sum test and Chi-squared test were used to perform initial between-group comparisons, according to variable type, and these comparisons were completed in SAS 9.4. The potential predictors of seizure control were then analyzed in a separate meta-analysis. The meta-analysis procedure was conducted in STATA 13.1. The ratio,

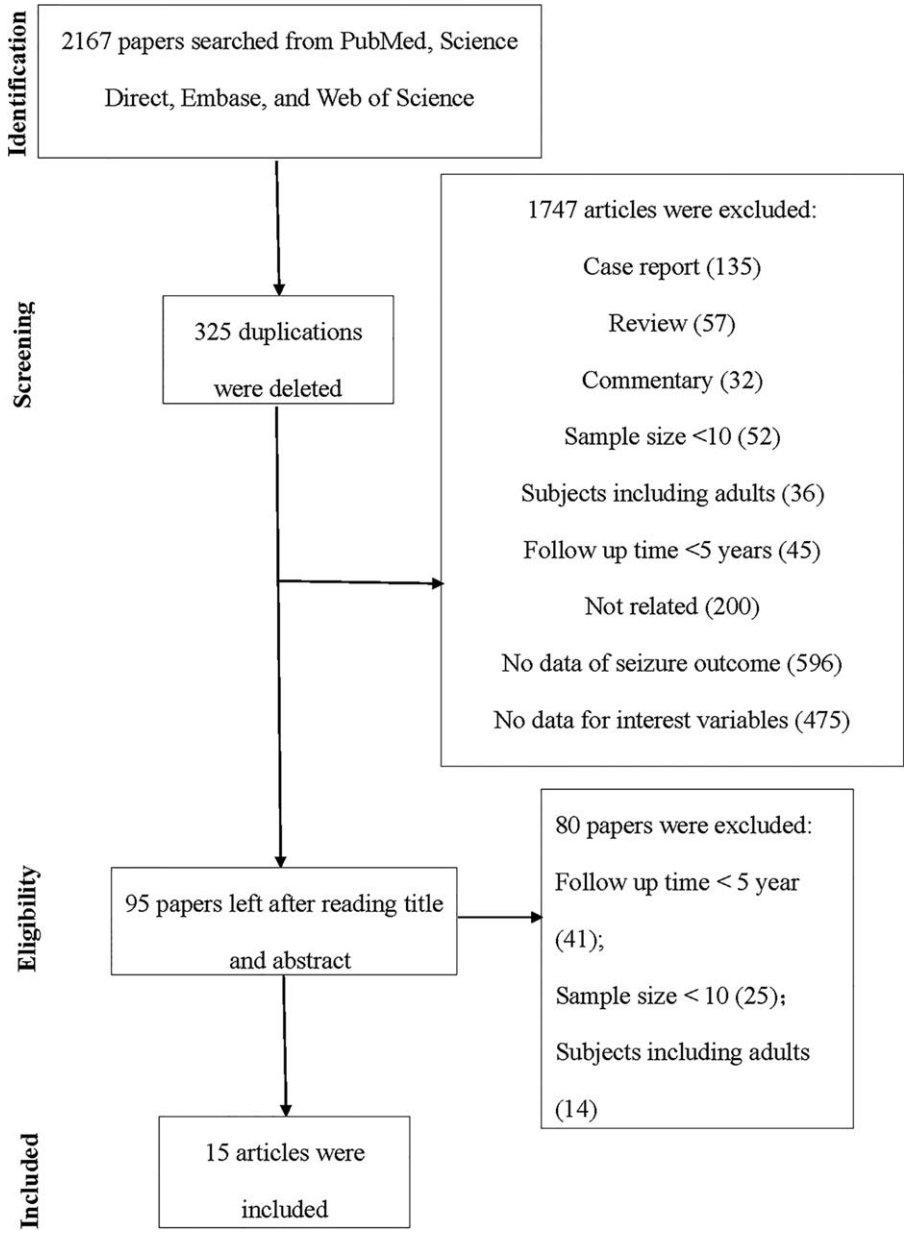

FIGURE 1. A flow chart of the article selection.

TABLE 1. Basic Information of Included Studies

Study Order	Study	Follow-Up, mo	Sample	Variables Reported
A	Babini M 2013	85.2	30	1, 2, 3, 4, 5, 6, 7, 8, 9
B	Bahi-Buisson N 2007	108	11	1, 2, 3, 5, 6, 8, 9
C	Battaglia D 2006	75	45	1, 2, 3, 5, 6, 7, 9
D	Bourgeois M 2007	88.2	27	2, 3, 7, 8
E	Caraballo R 2011	114	45	1, 2, 3, 5, 6, 7,
F	Curtiss S 2001	73.56	43	1, 2, 3, 4,
G	Di Rocco C 2006	125	20	3
H	Guzzetta F 2006	60.58	12	1, 2, 3, 4, 5, 7
I	Honda R 2013	78.8	12	1, 2, 3, 4, 6, 9
J	Kumar RM 2015	62.4	25	2, 3, 5, 9
K	Lee YJ 2014	152.4	12	2, 3, 5, 8, 9
L	Lettori D 2007	78	19	1, 2, 4, 5, 6, 8
M	Liava A 2012	75.48	53	2, 3, 4, 5, 6, 8
N	Sinclair DB 2003	82.8	42	1, 2, 3, 5, 6, 9
O	Viggedal G 2012	120	17	1, 4, 5, 8, 9

1 = sex, 2 = age at onset, 3 = age at surgery, 4 = surgery side, 5 = etiology, 6 = epilepsy type, 7 = seizure duration, 8 = epilepsia partialis continua, 9 = MRI findings.

All studies were ordered and coded from A to O for sensitivity analysis.

SMD and OR were calculated in accordance with the data type. Between-study heterogeneity was assessed using Cochran Q and I square (I^2) tests. A random-effects or fixed-effects model was then selected to estimate the overall effect size. A Z test was performed to continue hypothesis testing of the overall effect size. Finally, publication bias was assessed with a funnel plot and, if necessary, with Egger test.

RESULTS

For the 15 included studies (Figure 1), the patients ranged in age from 0.25 to 312 months (median, 50 months) at the time of surgery, and the minimum median postoperative follow-up time was 60.28 months.[13–24,26–28] Each study included 11 to 53 patients, and 5 years after surgery, 268 (71%) of the children were seizure free. Detailed information for each included study is summarized in Table 1.

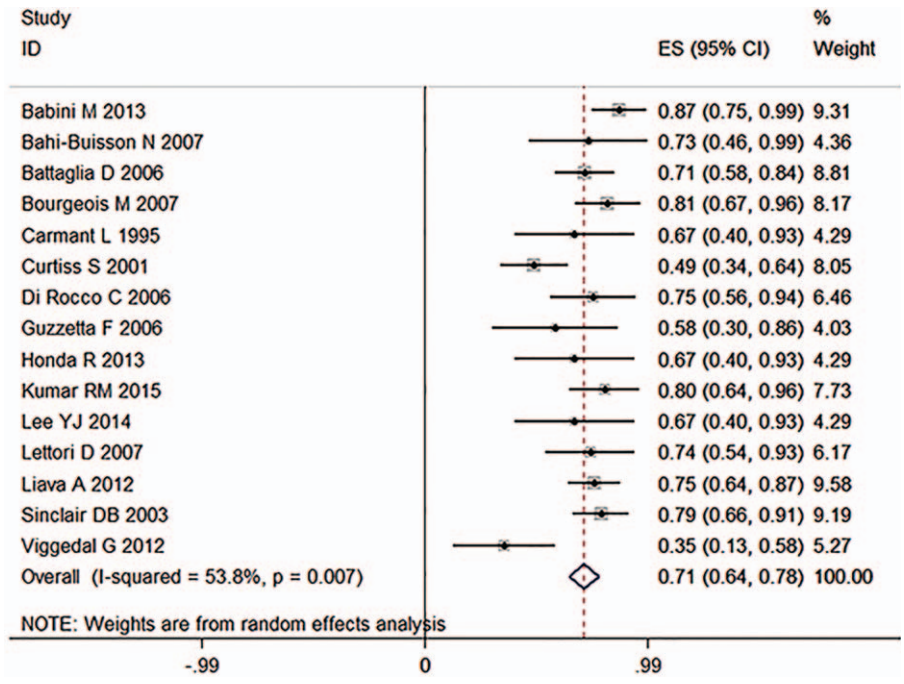

FIGURE 2. A forest plot of the children's long-term seizure outcomes following hemispheric surgery.

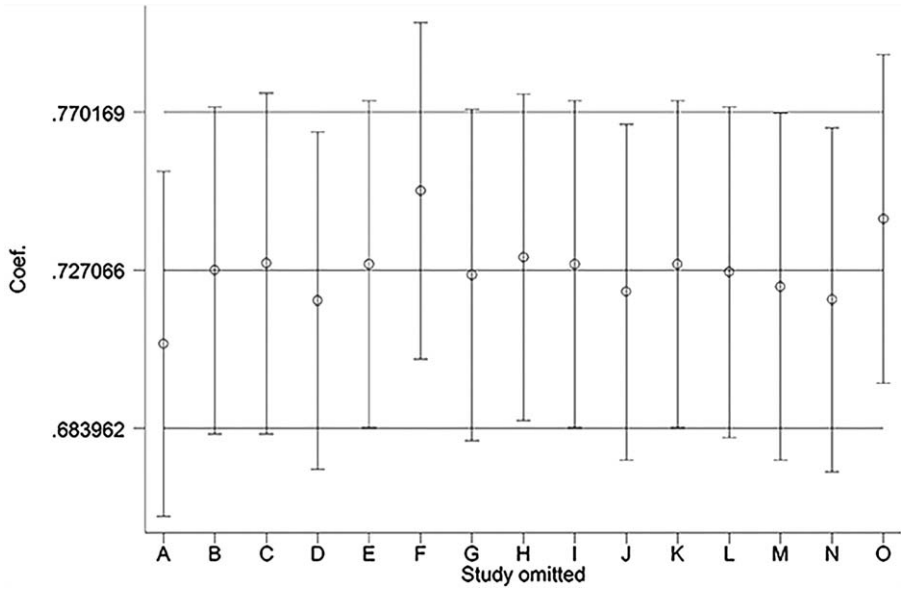

FIGURE 3. Sensitivity analysis of the children's long-term seizure outcomes after hemispheric surgery.

Long-term Seizure Outcomes

The heterogeneity test results showed an I^2 of 53.8% ($\chi^2 = 30.30$, d.f. = 14, $P = 0.007$), indicating that the between-study heterogeneity was large; thus, the random effects model was used to perform the meta-analysis.

The forest plot (Figure 2) showed that the pooled rate of seizure freedom was 0.71 (95% CI: 0.642–0.776, $z = 20.77$, $P < 0.05$), and it was statistically significant.

The sensitivity analysis (Figure 3) showed that after removing study A (Table 1) or study F (Table 1), the overall effect size and its confidence interval changed substantially, indicating that these two studies might be the origin of heterogeneity. Therefore, the forest plot was repeated three additional times after removing study A, study F, and studies A and F; the I square results were 47%, 33.7%, and 22.2%, respectively. Therefore, study F contributed most to the heterogeneity.

The funnel plot (Figure 4) showed that the studies were not all symmetrically distributed, and two studies were outside the 95% confidence interval. Therefore, Egger test was performed again to verify the presence of publication bias.

The Egger plot (Figure 4) showed that the 95% confidence interval of the bias included 0 (95% CI: −4.664, 0.409), and the Egger test showed that the coefficient of bias was −2.128 (95% CI: −4.664, 0.409, $P = 0.093$); therefore, publication bias was not found.

Potential Predictors

To explore the potential predictors of long-term seizure control, seizure outcomes were stratified across 10 variables (Table 2), and the Engel Class I patients were compared with the Engel Class II to IV patients. For the categorical variables of gender, seizure type, epilepsy continua, surgery side, and etiology, the Chi-squared test P values were all above 0.05, indicating that distribution of these factors was similar between the two outcome groups. For the MRI findings, the P value was 0.026, which was statistically significant. The seizure free rate in the abnormal MRI group (67/82) was higher than that in the normal MRI group (11/20), and further meta-analysis was performed to calculate the odds ratio. For continuous variables, the age at surgery ($P = 0.426$) and epilepsy duration time ($P = 0.853$) did not differ between the two outcome groups; however, the seizure onset age tended to be younger in the Engel Class II to IV group (median = 3.6 months) compared with the Engel Class I group (median = 8.35 months), with a P value of 0.006. A meta-analysis was performed to calculate the standardized mean difference.

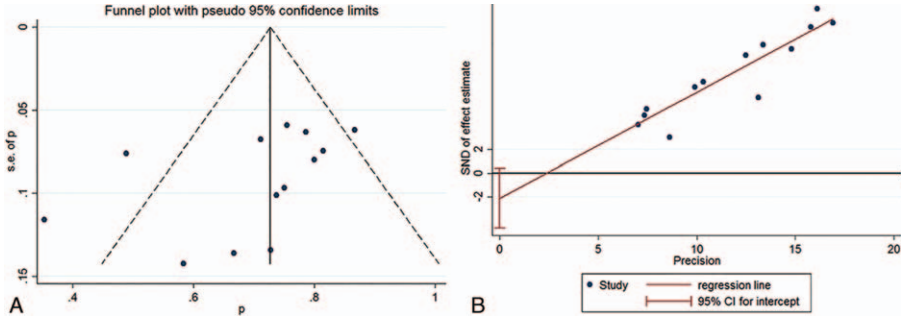

FIGURE 4. Published reports of the children's long-term seizure outcomes after hemispheric surgery.

TABLE 2. Seizure Outcomes Stratified by Factors of Interest

	Engel Class		
Factor	**I**	**II–IV**	***P***
Demographic characteristics			
Gender			
Male	93	43	0.564
Female	62	33	
Age at onset	8.35 (2.93–50.25)	3.6 (0.23–34.8)	0.006
Age at surgery	50.5 (12–132)	48 (12.25–113.1)	0.426
Epilepsy characteristics			
Epilepsy duration	23 (6–51.40)	16.5 (6–51.55)	0.853
Seizure type			
Partial	142	44	0.430
Generalized	18	8	
Epilepsy continua			
Yes	53	20	0.091
No	46	8	
Surgery characteristics			
Surgery side			
Left	59	30	0.924
Right	63	33	
Etiology			
Dysplasia	80	33	0.729
Vascular	33	10	
Tuberous sclerosis complex	7	2	
Tumor	74	22	
MRI findings			
Normal	11	9	0.026
Abnormal	67	15	

Patients were classified into two groups: seizure free (Engel Class I) or continued to have seizures (Engel Class II–IV).

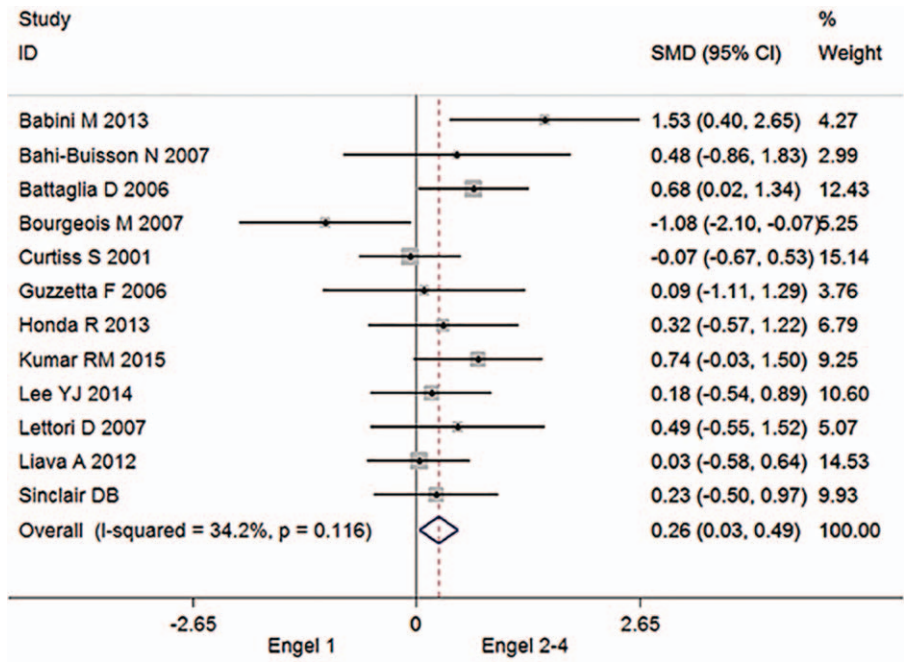

FIGURE 5. A forest plot of the age of onset among children with epilepsy.

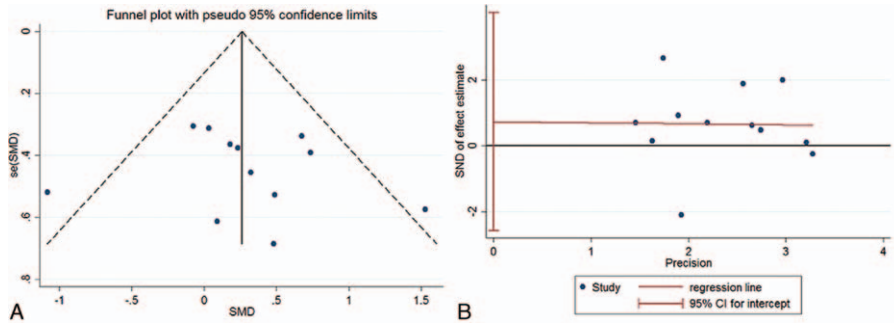

FIGURE 6. Published reports of age of onset among children with epilepsy.

Age at Seizure Onset

According to the forest plot (Figure 5), the I square result was 40.2%, and the *P* value of the heterogeneity test was 0.116. Thus, the between-study heterogeneity was relatively small, and a fixed effects model was applied to the meta-analysis. The patients were placed in two groups according to their seizure outcomes, and the age of onset of the patients in the Engel Class I group was significantly older than that of the patients in the Engel Class II to IV group. The SMD was 0.26 (95 CI: 0.03–0.49, $z = 2.2$, $P = 0.028$).

The funnel plot (Figure 6) showed a symmetrical distribution of the included articles; however, two studies were outside the 95% confidence interval. Therefore, Egger test was performed again. The Egger plot (Figure 6) showed that all included studies were within the 95% confidence interval, and Egger test showed that the coefficient of bias was 0.741 (95% CI: −2.570–4.053, $P = 0.629$); thus, publication bias is unlikely.

MRI Findings

Heterogeneity testing of predictor MRI showed an I square result of 12.7%, with a *P* value of 0.318 ($\chi^2 = 2.29$, d.f. = 2). Between-study heterogeneity was low, and a fixed effect model was applied to the analysis.

The forest plot (Figure 7) showed that the odds ratio of the different MRI results was 4.6 ($z = 2.33$, $P = 0.02$). Egger test indicated that the *P* value of bias was 0.923; therefore, there was no publication bias.

DISCUSSION

Results from 15 retrospective studies showed that 5 years after hemispheric surgery, 71% of all children were seizure free, indicating that the long-term prognosis for seizure control was good, even better than the short-term outcomes (69.3%).[32] This result was similar to the findings of Hamiwka et al[33] in a 10-year follow-up study: children who were seizure free shortly after surgery tended to remain seizure free in the long term. In a prospective population based observational study performed by Reinholdson et al,[34] the long-term follow-up also verified this finding (no difference in seizure control was observed between the 2-year, 5-year, and 10-year follow-ups). However, there was heterogeneity among the 15 included studies. The sensitivity analysis revealed that study A (Table 1) and study F (Table 1) originated the heterogeneity. Considering that the age of onset could significantly affect seizure outcomes, the median age of onset was calculated for each study. The median value of study A was larger (93 months) than that of study F (6 months) as well as the median value of all patients (7.1 months). MRI inspection

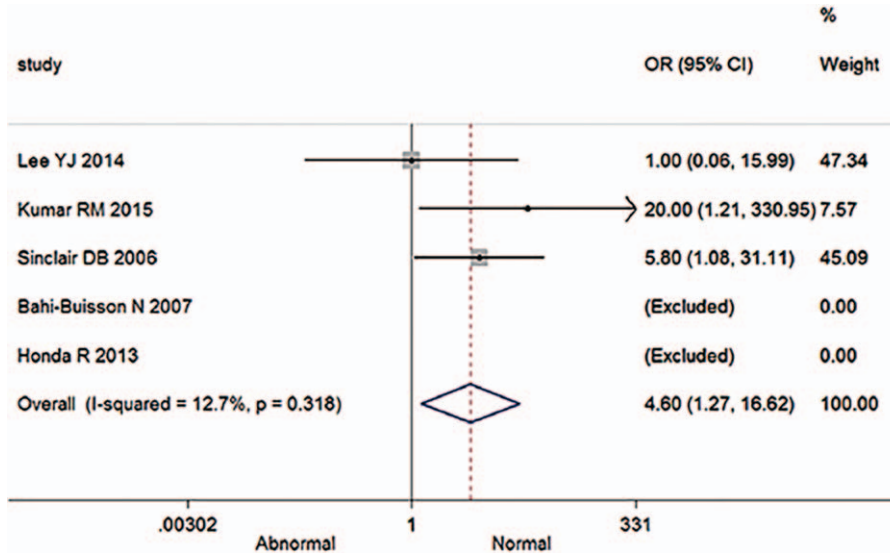

FIGURE 7. A forest plot of the MRI findings of the children with epilepsy.

was not compared because of the lack of data. This finding aligned with the following age of onset results.

As mentioned above, an early age of onset was a negative predictor of long-term seizure outcomes in children. This result was similar to that of Babini et al,[21] in a long-term study: a young age at seizure onset (in particular, younger than 4 years) was associated with poor seizure outcomes. Marras et al[35] have also reported a semblable result in cognitive function estimation after hemispheric surgery. In a myoclonic-astatic epilepsy study, Inoue et al[36] have described a similar finding: the age of onset in patients with refractory seizures was earlier than that patients with favorable prognoses (7–24 months versus 23–38 months). As Inoue et al[36] have mentioned, early onset exacerbates damage to the central nervous system and, possibly, intellectual disability. In addition, symptoms associated with an early age of onset, such as loss of consciousness or apnoea, can greatly harm brain development and, thus, affect patient prognosis.[37] An early age of onset may also play an important role in widely distributed dysplasia,[38] which is already known to cause poor mental outcomes. The odds ratio (early onset age versus late onset age in predicting negative seizure outcome) was up to 2.65, and early age onset should be treated as a strong predictor for poor seizure control. A more comprehensive evaluation is recommended for children with early onset epilepsy, and surgery should be performed at an early stage.

For the MRI findings, it was quite interesting that a normal MRI finding was associated with relatively poor long-term seizure outcomes (OR = 4.6). This finding was similar to that of Englot et al,[30] who found that among patients with abnormal MRI findings, 216 were Engel Class I versus 146 patients who were Engel Class II to IV, while in the normal MRI group, the numbers were 73 versus 71, respectively. Lazow et al[39] have also observed that seizure outcomes were favorable in MRI-negative patients. Fong et al[40] have recommended pre-surgical evaluation of patients with temporal lobe epilepsy, even those with normal MRI findings. In this study, the MRI findings were stratified across onset ages (classified by the median value), and no significant relationship was found. Given that MRI findings are only a type of inspection, there may be no cause-and-effect relationship between MRI findings and seizure outcomes; however, a comprehensive pre-surgical evaluation is still recommended for epileptic children with normal MRI findings.

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REFERENCES

1. Liubinas SV, Cassidy D, Roten A, et al. Tailored cortical resection following image guided subdural grid implantation for medically refractory epilepsy. *J Clin Neurosci.* 2009;16:1398–1408.
2. Pinto AL, Lohani S, Bergin AM, et al. Surgery for intractable epilepsy due to unilateral brain disease: a retrospective study comparing hemispherectomy techniques. *Pediatr Neurol.* 2014;51:336–343.
3. Nelles M, Urbach H, Sassen R, et al. Functional hemispherectomy: postoperative motor state and correlation to preoperative DTI. *Neuroradiology.* 2015;57:1093–1102.
4. Otsuki T, Honda R, Takahashi A, et al. Surgical management of cortical dysplasia in infancy and early childhood. *Brain Dev.* 2013;35:802–809.
5. van Schooneveld MM, Jennekens-Schinkel A, van Rijen PC, et al. Hemispherectomy: a basis for mental development in children with epilepsy. *Epileptic Disord.* 2011;13:47–55.
6. Dorfer C, Czech T, Muhlebner-Fahrngruber A, et al. Disconnective surgery in posterior quadrantic epilepsy: experience in a consecutive series of 10 patients. *Neurosurg Focus.* 2013;34:E10.
7. Fohlen M, Lellouch A, Delalande O. Hypothalamic hamartoma with refractory epilepsy: surgical procedures and results in 18 patients. *Epileptic Disord.* 2003;5:267–273.
8. Villarejo-Ortega F, Garcia-Fernandez M, Fournier-Del CC, et al. Seizure and developmental outcomes after hemispherectomy in children and adolescents with intractable epilepsy. *Childs Nerv Syst.* 2013;29:475–488.
9. Ilyas M, Sivaswamy L, Asano E, et al. Seizure control following palliative resective surgery for intractable epilepsy-a pilot study. *Pediatr Neurol.* 2014;51:330–335.
10. Bittar RG, Rosenfeld JV, Klug GL, et al. Resective surgery in infants and young children with intractable epilepsy. *J Clin Neurosci.* 2002;9:142–146.
11. Liang S, Zhang G, Li Y, et al. Hemispherectomy in adults patients with severe unilateral epilepsy and hemiplegia. *Epilepsy Res.* 2013;106:257–263.
12. Yu T, Zhang G, Wang Y, et al. Surgical treatment for patients with symptomatic generalised seizures due to brain lesions. *Epilepsy Res.* 2015;112:92–99.
13. Battaglia D, Chieffo D, Lettori D, et al. Cognitive assessment in epilepsy surgery of children. *Childs Nerv Syst.* 2006;22:744–759.
14. Di Rocco C, Battaglia D, Pietrini D, et al. Hemimegalencephaly: clinical implications and surgical treatment. *Childs Nerv Syst.* 2006;22:852–866.
15. Bahi-Buisson N, Villanueva V, Bulteau C, et al. Long term response to steroid therapy in *Rasmussen encephalitis*. *Seizure.* 2007;16:485–492.
16. Honda R, Kaido T, Sugai K, et al. Long-term developmental outcome after early hemispherotomy for hemimegalencephaly in infants with epileptic encephalopathy. *Epilepsy Behav.* 2013;29:30–35.
17. Lee YJ, Kim EH, Yum MS, et al. Long-term outcomes of hemispheric disconnection in pediatric patients with intractable epilepsy. *J Clin Neurol.* 2014;10:101–107.
18. Bourgeois M, Crimmins DW, de Oliveira RS, et al. Surgical treatment of epilepsy in Sturge-Weber syndrome in children. *J Neurosurg.* 2007;106:20–28.
19. Lettori D, Battaglia D, Sacco A, et al. Early hemispherectomy in catastrophic epilepsy: a neuro-cognitive and epileptic long-term follow-up. *Seizure.* 2008;17:49–63.
20. Liava A, Francione S, Tassi L, et al. Individually tailored extratemporal epilepsy surgery in children: anatomo-electro-clinical features and outcome predictors in a population of 53 cases. *Epilepsy Behav.* 2012;25:68–80.
21. Babini M, Giulioni M, Galassi E, et al. Seizure outcome of surgical treatment of focal epilepsy associated with low-grade tumors in children. *J Neurosurg Pediatr.* 2013;11:214–223.
22. Kumar RM, Koh S, Knupp K, et al. Surgery for infants with catastrophic epilepsy: an analysis of complications and efficacy. *Childs Nerv Syst.* 2015;31:1479–1491.
23. Guzzetta F, Battaglia D, Di Rocco C, et al. Symptomatic epilepsy in children with poroencephalic cysts secondary to perinatal middle cerebral artery occlusion. *Childs Nerv Syst.* 2006;22:922–930.

24. Viggedal G, Kristjansdottir R, Olsson I, et al. Cognitive development from two to ten years after pediatric epilepsy surgery. *Epilepsy Behav.* 2012;25:2–08.

25. Caraballo R, Bartuluchi M, Cersosimo R, et al. Hemispherectomy in pediatric patients with epilepsy: a study of 45 cases with special emphasis on epileptic syndromes. *Childs Nerv Syst.* 2011;27:2131–2136.

26. Curtiss S, de Bode S, Mathern GW. Spoken language outcomes after hemispherectomy: factoring in etiology. *Brain Lang.* 2001;79:379–396.

27. Sinclair DB, Aronyk KE, Snyder TJ, et al. Pediatric epilepsy surgery at the University of Alberta: 1988–2000. *Pediatr Neurol.* 2003;29:302–311.

28. Carmant L, Kramer U, Riviello JJ, et al. EEG prior to hemispherectomy: correlation with outcome and pathology. *Electroencephalogr Clin Neurophysiol.* 1995;94:265–270.

29. Hu WH, Zhang C, Zhang K, et al. Hemispheric surgery for refractory epilepsy: a systematic review and meta-analysis with emphasis on seizure predictors and outcomes. *J Neurosurg.* 2016;124:952–961.

30. Englot DJ, Breshears JD, Sun PP, et al. Seizure outcomes after resective surgery for extra-temporal lobe epilepsy in pediatric patients. *J Neurosurg Pediatr.* 2013;12:126–133.

31. Tellez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. *Brain.* 2005;128:1188–1198.

32. Englot DJ, Magill ST, Han SJ, et al. Seizures in supratentorial meningioma: a systematic review and meta-analysis. *J Neurosurg.* 2015:1–10. DOI: 10.3171/2015.5.JNS15935.

33. Hamiwka L, Jayakar P, Resnick T, et al. Surgery for epilepsy due to cortical malformations: ten-year follow-up. *Epilepsia.* 2005;46:556–560.

34. Reinholdson J, Olsson I, Edelvik A, et al. Long-term follow-up after epilepsy surgery in infancy and early childhood—a prospective population based observational study. *Seizure.* 2015;30:83–89.

35. Marras CE, Granata T, Franzini A, et al. Hemispherotomy and functional hemispherectomy: indications and outcome. *Epilepsy Res.* 2010;89:104–112.

36. Inoue T, Ihara Y, Tomonoh Y, et al. Early onset and focal spike discharges as indicators of poor prognosis for myoclonic-astatic epilepsy. *Brain Dev.* 2014;36:613–619.

37. McGee J, Alekseeva N, Chernyshev O, et al. Traumatic brain injury and behavior: a practical approach. *Neurol Clin.* 2016;34:55–68.

38. Kobayashi K, Ohtsuka Y, Ohno S, et al. Age-related clinical and neurophysiologic characteristics of intractable epilepsy associated with cortical malformation. *Epilepsia.* 2001;42(Suppl 6):24–28.

39. Lazow SP, Thadani VM, Gilbert KL, et al. Outcome of frontal lobe epilepsy surgery. *Epilepsia.* 2012;53:1746–1755.

40. Fong JS, Jehi L, Najm I, et al. Seizure outcome and its predictors after temporal lobe epilepsy surgery in patients with normal MRI. *Epilepsia.* 2011;52:1393–1401.