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RESEARCH

Management of cerebrospinal-fluid-related intracranial abnormalities in frontoethmoidal encephalocele using "Shunt algorithm for frontoethmoidal encephalocele" (SAFE)

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Abstract

A cerebrospinal-fluid-related (CSF-related) problem occurred in 25-30% of frontoethmoidal encephalocele (FEE) cases. Since there was no algorithm or guideline, the judgment to treat the CSF-related problem often relies upon the surgeon's experience. In our institution, the early shunt was preferable to treat the problem, but it added risks to the children. We developed an algorithm, "Shunt Algorithm for Frontoethmoidal Encephalocele" (SAFE), to guide the surgeon in making the most reasonable decision. To evaluate the SAFE's efficacy in reducing unnecessary early shunting for FEE with CSF-related intracranial abnormality. Medical records of FEE patients with CSF-related abnormalities treated from January 2007 to December 2019 were reviewed. The patients were divided into two groups: before the SAFE group as group 1 (2007 – 2011) and after the SAFE group as group 2 (2012 – 2019). We excluded FEE patients without CSF-related abnormalities. We compared the number of shunts and the complications between the two groups. One hundred and twenty-nine patient's medical records were reviewed. The males were predominating (79 versus 50 patients) with an average age of 58.2±7.1 months old (6 to 276 months old). Ventriculomegaly was found in 18 cases, arachnoid cysts in 46 cases, porencephalic cysts in 19 cases, and ventricular malformation in 46 cases. Group 1, with a score of 4 to 7 (19 cases), received an early shunt along with the FEE repair. Complications occurred in 7 patients of this group. Group 2, with a score of 4-7, received shunts only after the complication occurred in 3 cases (pseudomeningocele unresponsive with conservative treatment and re-operation in 2 cases; a sign of intracranial hypertension in 1 case). No complication occurred in this group. Groups 1 and 2, with scores of 8 or higher (6 and 8 cases, respectively), underwent direct shunt, with one complication (exposed shunt) in each group. The SAFE decision algorithm for FEE with CSF-related intracranial abnormalities has proven effective in reducing unnecessary shunting and the rate of shunt complications.

Keywords Neural tube defect · Frontoethmoidal encephalocele · Disease · Child Health

Introduction

Frontoethmoidal encephalocele (FEE) is a specific form of neural tube defect characterized by herniation of intracranial contents (dura, brain, CSF) through a congenital defect in the anterior cranial bone beyond the normal confines of the skull. It is rarely seen in Western countries but continues to be seen frequently in Southeast Asian countries, especially in Thailand, Malaysia, Burma, Cambodia, Pakistan, India, and Indonesia [1–4].

Surgical intervention for children with FEE should be done to correct facial dysmorphia and impairment of binocular vision and to avoid increasing size of the FEE caused by increasing brain prolapse and risk of infection of the central nervous system due to ulcerated or ruptured FEE [5–7].

Approximately 20-25% of FEE harbor one or more intracranial abnormalities [1, 8–11]. For the purpose of this study, the authors categorized the abnormalities into two groups: CSF-related and non-CSF-related. The most common abnormalities were ventriculomegaly, hydrocephalus, ventricular malformation, and cysts in the form of arachnoid cysts or porencephalic cysts. Agenesis of the corpus callosum, temporal lobe, or vermis was included in the latter category.

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Before 2012, almost all CSF-related abnormalities were shunted in our institution, leaving only cases of small cysts with no shunt. The surgeons' justifications for putting an early shunt in our institution were reducing the risk of CSF leakage, preventing further progression of the cyst or ventriculomegaly, providing a better intracranial environment, and reducing the burden of multi-step surgeries. However, it led to a higher number of shunt complications.

To reduce the rate of early shunting, we developed an algorithm, "Shunt Algorithm for Frontoethmoidal Encephalocele" (SAFE) in 2010. The SAFE was based on clinical signs, morphological, and radiological features, including the neurological signs, the skin, the volume and content of the FEE sac, the size of the external bone defect, the exit pathway's length, the nature of the CSF-related intracranial abnormalities, and the connection between intra- and extracranial CSF. Starting in January 2012, SAFE has been used by all surgeons at our institution treating children with FEE harboring CSF-related intracranial abnormality. This study evaluated the effectiveness of the SAFE in reducing the shunt rate and its complications.

Method

The study has been approved by The Ethical Committee in Health Research of Dr. Soetomo General Hospital Surabaya and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Medical records of FEE patients with cerebrospinal fluid (CSF)-related intracranial abnormalities treated from January 2007 to December 2019 were reviewed. Two surgeons (the authors) were involved in the patient's care. Clinical and radiological results were documented. The type of the FEE was based on Suwanwela's classification. All patients were followed up for at least six months after. The patients were divided into two groups: 1) Group 1 consists of patients treated before the institution of SAFE (year 2007 – 2011), and 2) Group 2 of patients treated after SAFE (2012 – 2019). We excluded FEE patients without CSF-related abnormalities. They were assessed and treated according to the "Shunt Algorithm for Frontoethmoidal Encephalocele" (SAFE) scoring system. The primary outcomes were 1) the incidence of internal leakage or CSF-related wound dehiscence; 2) the incidence of new or progressive neurological deficit; 3) the rate of shunted and non-shunted cases; and (4) shunt-related complication (Figure 1).

Shunt algorithm for frontoethmoidal encephalocele (SAFE)

The SAFE consists of a scoring table and a decision tree. The scoring system was based on the clinical, morphological, and radiological findings. The clinical findings include any neurological deficit related to intracranial abnormalities and mass pulsatility. The morphological findings include the skin covering the mass and the size of the FEE. The type and size of intracranial abnormalities, the size of the internal bony defect, the size of the mass, the content of the mass (mostly CSF, gliotic mass, parenchyma, or mix of CSF and parenchyma), the length of exit pathway, and the existence of CSF connection between the intracranial and extracranial mass through the exit pathway can be examined by radiological study. The exit pathway is the distance between internal and external bony defects where the herniated intracranial content makes its way out (Fig 2). In a patient with FEE characterized by multiple exit pathways, this variable is scored based on the shortest measured pathway. The frontonasal encephalocele's exit pathway is near zero as the internal and external bony defect is at the same bone. The mass volume is determined using a sphere or elliptical form volume formula. According to their volume, FEE is qualitatively considered as a small-sized mass when the volume is less than five cc, medium-sized for lesions between 5-15 cc, and large-sized for a lesion of 15 cc or more. The CSF canal in the exit pathway is a cyst that extends beyond the usual confines of the intracranial cavity.

The radiological features comprise the length of the exit pathway, size of the external bone defect, large cyst or bilateral cyst, and the occurrence of CSF canal in the exit pathway that connects the intra- and extracranial cavity. A shorter exit pathway tends to have a larger bony defect. Significant bony defects will allow CSF to creep through the thin dura easily. Each of the determining features is scored and summed. The summary of the features and their scores is presented in Fig. 1.

The score obtained from the table is plotted in the decision tree (Figure 3). The no-shunt policy is advisable for a SAFE score of less than 3. For SAFE scores 3 to 8, the shunt may be considered when the patient experiences persistent CSF leakage or progressive enlargement of the cyst/ ventricle indicated by clinical and radiological findings. For a SAFE score of more than 8, the shunt is warranted.

Result

One hundred and twenty-nine patients (79 male and 50 female patients) with a mean age of 58.2+7.1 months old (range from 6 to 276 months old) were diagnosed with FEE with CSF-related intracranial abnormalities. Group 1 consisted of 57 patients, and Group 2 included 72 eligible patients. Ninety-nine patients were diagnosed with nasoethmoidal, 9 with nasoorbital, 4 with nasofrontal, and 17 with nasoethmoid/nasoorbital type of frontoethmoidal encephalocele.

Fig. 1 SAFE scoring system.

Variabel	Score		
	0	1	2
1. Sign of neurological deficit	None	-	exist and correlated
2. Pulsatile mass	None	Yes	-
3. The covering skin	Intact skin	Membranous or very thin	-
4. The size of the mass	< 5 cc	medium size (5-15 cc)	large (>15 cc)
5. The size of the bony defect	< 0.5 cm	0.5 - 1.5 cm	> 1.5 cm
6. The content of the FEE sac	Gliotic tissue or solid mass only	Mixed content, more solid than CSF	Mostly CSF or few solid part
7. The length of the exit pathway	> 1.5 cm	0.5 - 1.5 cm	< 0.5 cm
8. The overall size of intracranial CSF sac (cyst and/or ventricle) in both hemispheres*	 Normal, mild enlargement or very small cyst	 Focal ventricular enlargement** or medium size cyst	 More than one hemisphere
9. A connection between intra- and extracranial CSF sac via the exit pathway*	 No connection	 Exist but very small (Ø <0.5 cm)	 Exist and obvious (Ø >0.5 cm)

*The condition and radiological appearance may vary.
** Focal enlargement involves only one part of the ventricle (anterior or posterior horn or single ventricle) with the total sum of less than hemisphere.

CSF-related congenital brain anomalies consisted of arachnoid cysts in 46 cases (36%), porencephalic cysts in 19 cases (15%), ventricular malformation in 46 cases (36%), and ventriculomegaly in 18 cases (14%). Ventriculomegaly occupied 90 percent of the left hemisphere without motoric and sensory function deficit in one patient. Other non-CSF intracranial abnormalities were also found as agenesis of the corpus callosum in 4 cases of cavum verge in 5 cases.

FEE was medium in 49 patients, large in 56 patients, and very large in 24 patients. Thirteen out of 50 patients with large- and very large-sized masses (four nasoorbital, three nasoethmoid, and six nasoethmoid/nasoorbital type cases) had an intra-lesion cyst or CSF tunnel from intra- to extracranial mass via the exit pathway.

The nasofrontal type appeared with burst lesions/ very short exit pathways. Eighty percent of nasoethmoidal cases had a medium and long exit pathway. A summary of patient demographic data and FEE presentation is listed in Table 1. The final score obtained using a SAFE scoring table, the

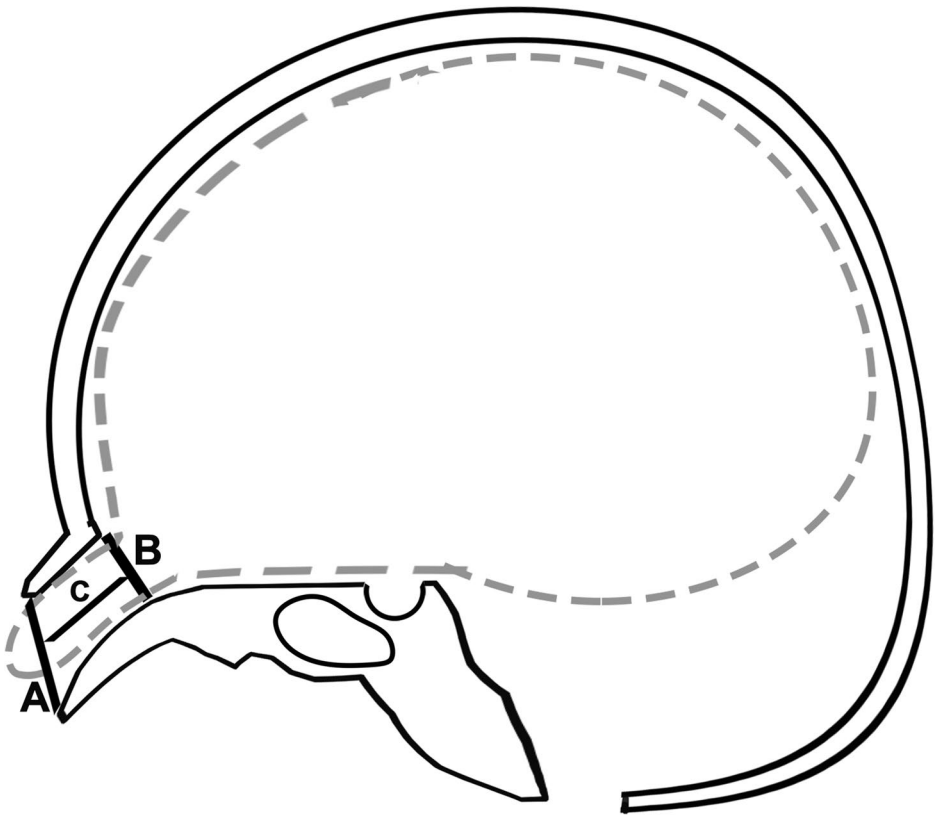

Fig. 2 Schematic picture of the FEE to delineate the external bony defect (**A**), internal bony defect (**B**), and the exit pathway (**C**).

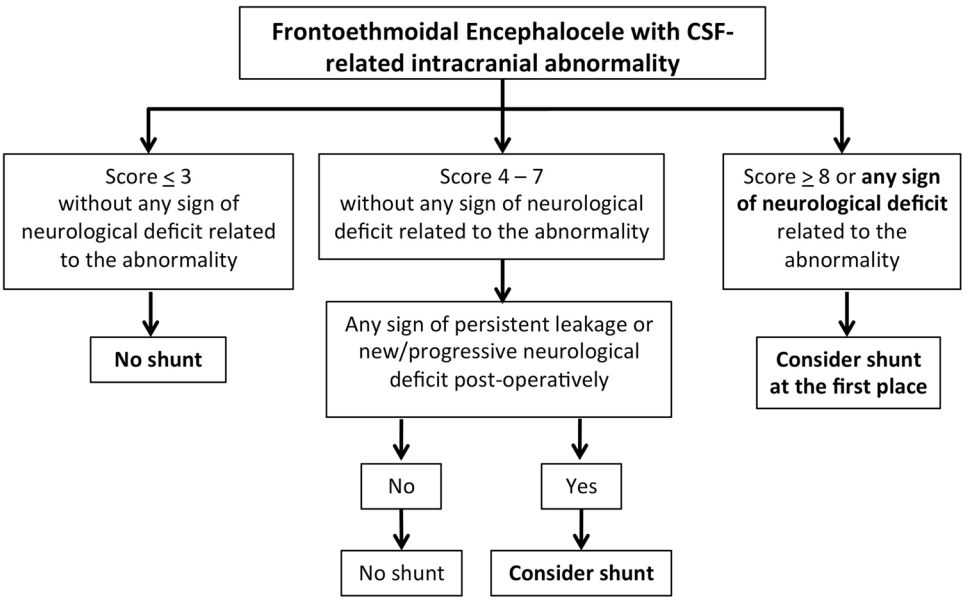

Fig. 3 Decision tree for score obtained from SAFE scoring system. The repair of FEE can be done without the shunt in the low risk (score 3 or less) and medium risk (score 4-7) groups. The high-risk group (score 8 or more) should undergo the repair of FEE simultaneously with shunt placement.

complications, and the final decision to shunt are summarized in Figure 4.

Either group 1 or 2 with a SAFE score of 3 or less received no shunt. Nineteen out of 42 group 1 patients with SAFE scores 4 - 7 underwent surgery for the encephalocele and VP in the first place. Meanwhile, only 3 group 2 patients proceeded to shunt surgery due to persistent leakage (2 patients) and a sign of high intracranial pressure. During the postoperative period of group 2, early CSF leakage was observed in 10 patients. Four patients had pseudomeningocele, and the rest had CSF leakage resulting in wound dehiscence. Pseudomeningocele patients underwent

Table 1 Summary of patient characteristic

Variabel	Group 1 (2007-2011)	Group 2 (2012 – 2019)	Total
Number of patients	57	72	129
Gender			
Male	37	42	79
Female	20	30	50
Type of FEE			
Nasoethmoidal	45	54	99
Nasofrontal	1	3	4
Nasoorbital	3	6	9
Nasoethmoid-nasoorbital	8	9	17
Size of the FEE			
Medium	21	28	49
Large	24	32	56
Very large	14	10	24
Content of the sac			
Mostly solid	34	43	77
Mostly cystic	15	13	28
Mixed	10	12	22
Type of CSF-related abnormality*			
Ventriculomegaly	7	11	18
Arachnoid cyst	14	18	32
Anterior Temporal cyst	10	14	24
Ventricular malformation	29	23	52
Porencephalic cyst	10	9	19
SAFE Score			
3 or less	9	12	21
4 to 7	42	52	94
8 or higher	6	8	14

*Some patients harbor multiple types of CSF-related abnormalities.

periodic CSF aspiration until the leakage resolved on follow-up. Patients with skin breakdown had to go for skin and dural repair. Four out of 6 patients who underwent skin and dural repair had persistent CSF leakage. Persistent leakage of more than two weeks was managed with a VP shunt. One patient with ventriculomegaly complained of persistent headaches and vomiting two weeks after the FEE repair. CT scan obtained during re-admission showed a progressive hydrocephalus. Ventriculoperitoneal shunting was performed on these patients without any complications.

Shunt complications occurred in seven patients of Group 1 during follow-up. Exposed shunts due to wound dehiscence occurred in four patients, and two others presented to the hospital with anal extrusion of the distal shunt. The onset of complications varied from 2 to 7 months. All patients underwent further treatment to manage the infected shunts. The patients with an SAFE score of 8 or higher underwent shunt surgery (6 cases from group 1 and 8 cases from group 2). Shunt infections occurred in one patient from each group. A summary of the results is presented in Figure 4. The t-test statistical analysis showed a significant complication rate difference (p= 0.002) between the moderate risk subgroups (score 4-7).

Discussion

The FEE is more prevalent in Southeast Asian countries than in other parts of the world. This unique geographical distribution is not yet clearly elucidated. Flatz and Sukthomya studied the possible factors influencing the prevalence of FEE. They came to two factors: environmental and genetic factors. They proposed the hypothesis that both factors may play a role in the form of 1) inheritance by a gene with dominant manifestation but low penetrance and, possibly, low expressivity – known as "micro-manifestations," and 2) polygenic inheritance [12]. However, these hypotheses still need to be thoroughly studied.

Intracranial structural anomalies accompany sincipital encephalocele in 15 to 40% of cases [1, 8–11]. Sibayan *et al.* reported in their series that the intracranial abnormalities rate was as high as 55% of sincipital encephalocele cases [13]. The most frequent findings were CSF-related intracranial abnormalities such as ventriculomegaly, arachnoid cyst, porencephalic cyst, and ventricular malformation [1, 2, 14]. Suwanwela *et al.* postulated that vascular traction might alter the growth of some parts of the brain, causing agenesis, hypoplasia, porencephalic cysts, or irregular brain-ventricle configuration [3, 13].

Before SAFE implementation, these CSF-related abnormalities raised concern among surgeons in our institution that it might affect the outcome of the FEE patients. They argued that early shunt might help reduce the risk of CSF leakage, prevent further progression of the cyst or abnormal ventricles, provide a better intracranial environment, and reduce the burden of multi-step surgeries. Instead of gaining a better outcome, the complications of the early shunt complicated the patient's management. Shunt infection and shunt migration were among them.

In 2010, we developed an algorithm to predict the FEE patients that might benefit from early shunt. Clinical, radiological, and surgical findings were reviewed to find the factors influencing the surgical results. We categorized the clinical-radiological findings into four groups: clinical, content, connector, and connectivity – the 4C. The factors in our series that were unlikely to cause complications included gliotic mass, normal skin, small bony defect, long exit pathway, and no connection between intra- and extracranial CSF sac. In contrast, the factors likely to cause complications comprised FEE sacs containing mostly CSF, membranous

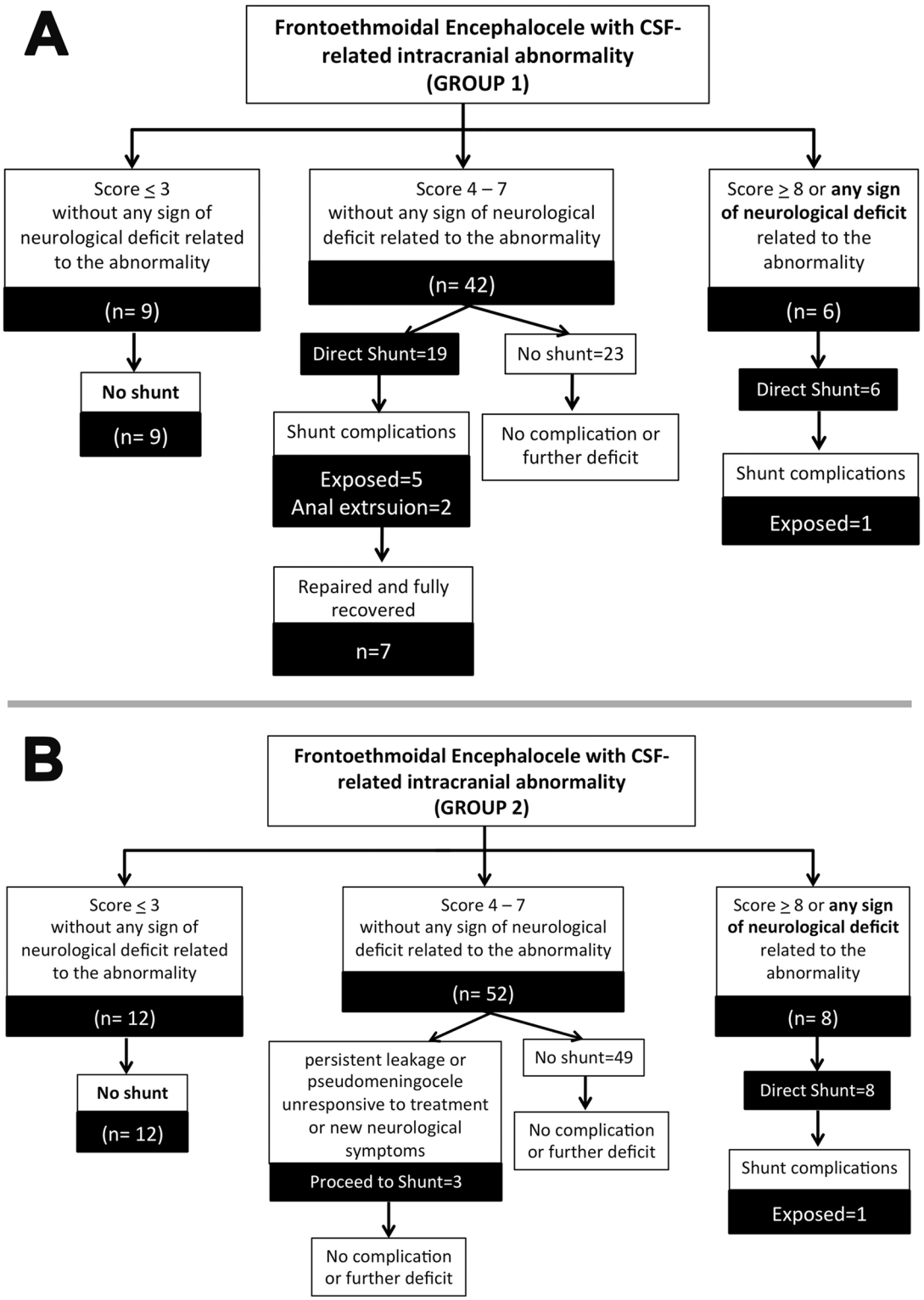

Fig. 4 The summary of the SAFE scoring results and the patient's fate between Group 1 (**A**) and Group 2 (**B**).

skin, significant bone defects, short exit pathways, and intra- and extracranial CSF connections. Any neurological signs related to the abnormalities must be addressed accordingly.

The comparison between groups in our study showed that the overall rate of shunt placement after the institution of SAFE dropped from 43% to 15%. The subset of group 2

patients with a score of 4-7 mainly benefited from the SAFE scoring, as it reduced the shunt placement from 45% to 5%. We followed the patient for at least six months. We found no declining function or neurological deficit due to its CSF-related intracranial abnormalities.

After SAFE implementation, the arguments of persistent CSF leakage, progressive cysts or ventriculomegaly, or progressive developmental problems were not proven in most patients who did not receive an early shunt [1, 34]. The CSF leakage was successfully managed by conservative treatment within two weeks after the onset in almost all of our patients. Two patients (one exposed shunt and one anal extruded shunt) had normal CSF. They underwent shunt removal and were observed for any deterioration. During the follow-up, there was no deterioration or neurological deficit. The patients received no new shunt. When applying the SAFE algorithm to the cohort prior to 2012, the 19 patients could have possibly avoided getting a shunt. This is quite a significant impact as 7 of those 19 patients had pretty severe shunt-related complications.

The SAFE score also emphasizes the proper definition of hydrocephalus. The term hydrocephalus should be used in a condition of active progressive distension of the ventricular system of the brain as the result of inadequate cerebrospinal fluid flow from its production site within the cerebral ventricles to the absorption site into the systemic circulation [15–18]. The term ventriculomegaly for non-progressive enlargement of a ventricular system that shows no sign of high intracranial pressure may be more appropriate. The altered shape and size of the ventricle due to the traction effect resembles the appearance of ventriculomegaly with irregular shape in imaging studies that most radiologists concluded as hydrocephalus.

Intracranial arachnoid cysts of various sizes and locations were the second most common CSF-related abnormalities. The most common location was the middle fossa and Sylvian fissure, the most typical site of the intracranial arachnoid cyst [19, 20]. Despite the surgical indication debate, we are unsure if the pathogenesis of arachnoid cysts in encephaloceles is similar to one without encephaloceles [21, 22]. There is no apparent agreement between the results of the surgery (morphological changes) and the alleviation of symptoms [23, 24]. We found a favorable developmental outcome in our FEE patients with untreated middle fossa arachnoid cysts during the SAFE follow-up period.

In some cases, the intracranial arachnoid cyst was connected with the extracranial CSF cyst through the exit pathway. A pulsatile mass was present in a patient with a large CSF sac directly connected to an intracranial arachnoid cyst via a large bore of the CSF canal in the exit pathway [13, 25].

Pseudomeningocele could be managed with minimal intervention using periodic needle aspiration and acetazolamide administration. It resolved within 7 to 14 days under conservative therapy [26]. Persistent leakage (2 weeks or more), despite the conservative therapy (aspiration, bandaging, or lumbar puncture), and the sign of fistula or inflammation around the leakage site were the indications for reoperation [27, 28].

The shunt complication rate dropped significantly from 30% to 9%—the complications presented as exposed shunts in 7 cases and anal extrusion in 2 cases. Five exposed-shunt and one anal extruded shunt patients had shunt infections. Antibiotics were administered until the CSF profile was normalized. The patients had subsequent shunt surgery, and no complications occurred during the two-year follow-up.

Patients with FEE treated at our institution generally come from low-income families, and a high rate of malnutrition is seen in our pediatric patient population. Thus, we hypothesize that these local risk factors contributed to the shunt infections observed in this series.

The SAFE algorithm resulted in a lower early shunting and shunt complications rate. It helps prevent unnecessary shunt surgery, lowering the cost of surgery and reducing the burden of the patients due to complications.

Conclusion

The SAFE decision algorithm for FEE with CSF-related intracranial abnormalities has proven effective in reducing unnecessary early shunting and the rate of shunt complications.

Author contributions MAP and WS wrote the main manuscript text and prepared all the figures. All authors reviewed the manuscript.

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Data availability The authors confirm that the data supporting the findings of this study are available.

Declarations

Competing interests The authors declare no competing interests.

Ethical approval The Ethical Committee In Health Research Dr. Soetomo General Hospital Surabaya reviewed and approved the study (Ethical Clearance No. 457/Panke.KKE/VII/2017; date: August 9, 2017). The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

No formal consent is required for this study.

Conflict of interest The authors declare no competing interests.

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