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The preoperative incidence of raised intracranial pressure in nonsyndromic sagittal craniosynostosis is underestimated in the literature

Clinical article

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Object. The presence of raised intracranial pressure (ICP) in untreated nonsyndromic, isolated sagittal craniosynostosis (SC) is an important functional indication for surgery.

Methods. A retrospective review was performed of all 284 patients presenting with SC to the Oxford Craniofacial Unit between 1995 and 2010.

Results. Intraparenchymal ICP monitoring was performed in 39 children following a standard unit protocol. Monitoring of ICP was offered for all patients in whom nonoperative management was considered on the basis of minimal deformity or in cases in which parents were reluctant to agree to corrective surgery. These patients presented at an older age than the rest of the cohort (mean age 56 months), with marked scaphocephaly (16/39, 41%), mild scaphocephaly (11, 28%), or no scaphocephalic deformity (12, 31%). Raised ICP was found in 17 (44%) patients, with no significant difference in its incidence among the 3 different deformity types. Raised ICP was not predicted by the presence of symptoms of ICP or developmental delay or by ophthalmological or radiological findings.

Conclusions. The incidence of raised ICP in SC reported here is greater than that previously published in the literature. The lack of a reliable noninvasive method to identify individuals with elevated ICP in SC mandates consideration of intraparenchymal ICP monitoring in all patients for whom nonoperative management is contemplated. *(http://thejns.org/doi/abs/10.3171/2014.8.PEDS1425)*

Key Words • **intracranial pressure** • **intracranial hypertension** • **sagittal craniosynostosis** • **craniofacial**

Single-suture nonsyndromic sagittal craniosynostosis (SC) is the most common form of craniosynostosis, affecting between 1 in 2000 and 1 in 5000 children, with a 4:1 male-to-female ratio.[30,32,56] Most patients present in infancy or early childhood with a scaphocephalic head shape and associated calvarial abnormalities.[10] Historically this morphological deformity alone has been a sufficient indication for corrective transcranial surgery. Furthermore, it is now recognized that raised intracranial pressure (ICP) occurs in this group of patients, with an estimated preoperative incidence between 4.5% and 24%.[6,22,40,41,49,50] Therefore, the treatment of possible preexisting raised ICP, or the prevention of future ICP, provides a clear functional indication for surgery, in addition to the need to correct the morphological deformity present in these children.

However, a number of patients have only mild scaphocephalic deformity or no scaphocephaly at all, despite having SC. The aesthetic indications for corrective surgery in this group are much weaker, or absent, and parents are likely to be understandably more reluctant to agree to a transcranial procedure with its attendant risks for a minor aesthetic benefit. The incidence of raised ICP in these patients has not been previously reported in the literature, although a recent study conducted by our unit in 6 nonscaphocephalic SC patients who underwent ICP monitoring showed that 4 (67%) had elevated ICP.[36] This high rate may reflect an underlying increased risk of raised ICP in mild or nonscaphocephalic patients compared with the SC population as a whole. Alternately, it may be a function of the patients' age (mean 46 months), given that Renier et al.[41] previously found a correlated increase in ICP

Abbreviations used in this paper: ICP = intracranial pressure; SC = sagittal craniosynostosis.

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with age, up to 6 years of age, in craniosynostosis. Whatever the etiology, a high rate of raised ICP in SC patients with mild deformity who are less likely to undergo a corrective procedure is potentially significant for those affected individuals. We therefore reviewed a single cohort of patients with nonsyndromic isolated SC to investigate the incidence and associations of elevated ICP in children who did not undergo corrective surgery.

Methods

A retrospective review was performed of the medical records of all patients presenting with isolated SC to the Oxford Craniofacial Unit between January 1995 and December 2010. All patients included in the study had a diagnosis of isolated SC confirmed on radiological imaging and were managed by the unit. The following were excluded: 1) individuals who transferred their care to another unit after their initial visit or who failed to attend all subsequent investigations and clinic appointments; 2) patients identified on screening to have either genetic mutations or syndromic conditions known to be associated with craniosynostosis; and 3) patients with SC considered secondary to perinatal intraventricular hemorrhage, hydrocephalus, or CSF shunting procedures. The study was conducted in accordance with local ethics committee regulations.

In those patients in whom it was performed, ICP monitoring was conducted over a 24- to 48-hour period using an intraparenchymal Codman MicroSensor (Johnson & Johnson Professionals, Inc.) placed in the right or left frontal lobe. An ICP with a baseline consistently above 15 mm Hg or more than 3 B-type waves in a 24-hour period during sleep was classified as raised.[55]

Statistical analysis was performed using the Minitab statistical software package (version 16; Minitab Inc.). The outcome of interest was whether a patient had raised ICP. Predictors of interest included age at surgery (months), scaphocephalic deformity (marked, mild, or none), symptoms of raised ICP, developmental delay, ophthalmological findings, and radiographic findings. Univariate logistic regression modeling was used to describe the association of each predictor with the outcome.

Results

Between 1995 and 2010, 284 new SC patients (217 male, 67 female) were seen. Generally, infants presenting before 6 months of age underwent a modified sagittal strip procedure, whereas those presenting after 6 months of age underwent calvarial remodeling. Ninety-four patients (33%) underwent modified strip craniectomy (mean age at presentation 4.2 months), and 139 patients (49%) underwent calvarial remodeling (mean age at presentation 10.8 months).

The remaining 51 patients (18%) comprised 6 adults and 45 children. The adults presented at a mean age of 24.4 years (range 18.6–37.2 years), all having failed to have been diagnosed with scaphocephaly in childhood. One adult had experienced a long history of recurrent headaches with episodes of vomiting and was found to have marked beaten-copper appearance of the calvaria on radiological imaging. He underwent ICP monitoring, and the results were normal. All 6 adults were discharged without further surgical intervention.

The 45 children presented at a later mean age (56 months, range 9–163 months) than the rest of the cohort (Fig. 1). Twenty-six patients had either nonscaphocephalic SC (cephalic index > 75; n = 13) or clinically mild scaphocephaly (cephalic index 70–75; n = 13); in none of these cases was surgical correction thought to be warranted on aesthetic grounds alone. Nineteen patients had a significant scaphocephalic deformity (cephalic index < 70), but either the parents were unwilling to agree to transcranial surgery for aesthetic reasons only (n = 15) or there was a relative contraindication to surgery either from a preexisting comorbidity (n = 1) or from the religious beliefs of the family preventing the use of blood transfusion should the need arise (n = 3).

Nonscaphocephalic patients had SC diagnosed based on radiological imaging performed for an abnormal head shape, including posterior plagiocephaly, brachycephaly, turricephaly with frontal bossing, a metopic ridge, a saddle deformity of the vertex with an occipital bullet, microcephaly, and macrocephaly. One patient had SC diagnosed coincidentally when imaged for an unrelated scalp

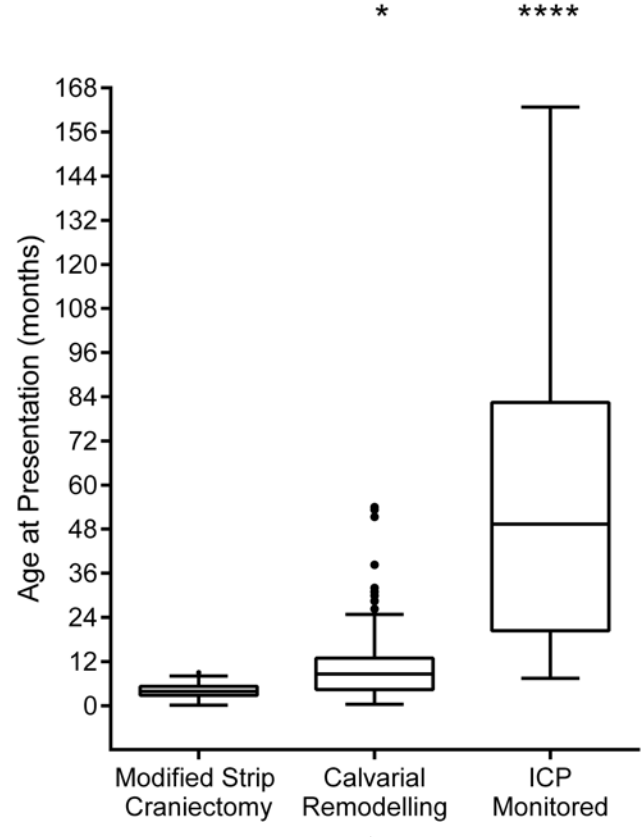

Fig. 1. Tukey box-and-whisker plot of age at presentation in children with SC. The ICP-monitored group also includes 6 patients who were offered ICP monitoring but declined. Mean age of the ICP-monitored group was significantly greater than means of the other 2 groups (****p < 0.0001), and mean age of the calvarial remodeling group was greater than that of the strip craniectomy group (*p < 0.05, Tukey's multiple comparison test).

lesion. Another child was imaged because his mother was known to carry a fibroblast growth factor receptor mutation, although this was excluded in the patient by genetic analysis.

Five patients, 3 with a mild scaphocephaly and 2 with a significant scaphocephaly, presented with sufficiently marked developmental delay for parents and the craniofacial team to question whether the child would gain any psychosocial benefit from a more normal head shape after surgery. Moderate developmental delay was identified in an additional 9 patients. All patients presenting with a developmental delay were encouraged to have ICP monitoring because of the concern that their developmental delay might be associated with raised ICP.

Eight patients manifested possible symptoms of raised ICP at presentation: persistent headaches (n = 1), nocturnal wakening in distress with head holding or banging (sleep disturbance; n = 2), or deteriorating attention span with a decline in academic attainment (irritability; n = 5). Two of these children also had a developmental delay. All patients underwent an ophthalmological assessment. None were found to have papilledema.

Cranial CT scans demonstrated signs suggestive of raised ICP, including diffuse beaten-copper appearance of the calvaria, a reduction in the volume of the extra-axial subarachnoid spaces, or effacement of the sulci, in 30 patients who went on to have ICP monitoring. Fourteen patients with positive radiological findings proved to have raised ICP on monitoring; the remaining 16 patients had a normal ICP. Overall, radiological investigations had a sensitivity of 82% and a specificity of 27%. When all signs other than beaten-copper appearance were considered together, sensitivity declined to 65% but specificity rose to 64%. Monitoring of ICP was considered for all patients as a routine part of the preoperative decision-making protocol. Upon review, 4 patients with no history of developmental delay or symptoms of raised ICP and normal radiological findings were deemed not to require ICP monitoring. An additional patient who had only mild beaten-copper appearance of the calvaria on imaging but otherwise was developing well and had no signs or symptoms suggestive of raised ICP was viewed not to need monitoring. One child was offered ICP monitoring, which was declined by the family. Of these 6 patients, 4 continue to undergo follow-up and 2 were discharged at 16 years of age. All remained well and asymptomatic when last reviewed.

A total of 39 children underwent ICP monitoring at a mean age of 65 months (range 17–169 months) (Table 1). Of these, 17 (44%; 95% CI 28%–59%) were found to have elevated ICP (Tables 1 and 2); one had a normal initial ICP but after a progressive deterioration in behavior was found to have elevated ICP on monitoring 30 months later (Table 2, Case 13). Another patient had borderline raised ICP with an overnight baseline of 15 mm Hg and 2 B-waves (Table 2, Case 6). The incidence of raised ICP was higher in patients with mild or absent deformity (64% and 43%, respectively) than in those with marked scaphocephaly (31%), although this was not statistically significant (Tables 1 and 3). The incidence of raised ICP was not affected by the age of the patient ($F = 0.24$, $p = 0.63$, linear regression analysis). The presence of neither preoperative symptoms nor radiological signs suggested raised ICP, and developmental delay was not significantly more common in patients with elevated ICP (Table 3).

All patients with abnormal ICP underwent calvarial remodeling, including the child with nonscaphocephalic SC and borderline ICP. Five children with ICP in the normal range underwent calvarial remodeling. One child with mild scaphocephaly became clinically more scaphocephalic over time, and surgery was performed at the parents' request. Four children with marked scaphocephaly also underwent corrective surgery at their parents' request.

Among patients who underwent calvarial remodeling for raised ICP, 6 patients underwent a further episode of ICP monitoring for new symptoms or signs suggestive of raised ICP at a mean of 49 months after their primary remodeling procedure (Table 2). None proved to have raised ICP. One further patient who had normal initial ICP but underwent calvarial remodeling for marked scaphocephaly later developed morning headaches, irritability, and a decline in academic performance. She had repeat ICP monitoring at 39 months after her primary surgery, and her ICP was found to be normal.

All 39 children who underwent ICP monitoring continue to undergo follow-up. Patients who manifested symptoms suggestive of raised ICP but who were found to have normal ICP on monitoring experienced an improvement or resolution of their symptoms over time. Computed tomography was not routinely performed during follow-up to minimize radiation exposure. No patient has required a repeat calvarial remodeling procedure.

Discussion

The overall incidence of raised ICP in patients who underwent ICP monitoring in this study was 44%. If the 6 patients in whom ICP monitoring was considered but not performed are taken into account, assuming a negative ICP reading in those cases, the rate falls to 38%. This incidence is still greater than that observed in other series of nonoperated scaphocephalic patients.[4,6,22,40,41,49,50] This difference may be explained by either the greater age of our patients or the high proportion of mild and nonscaphocephalic patients in the group.

Of the published series, only Arnaud et al.[6] reported the mean age of their scaphocephalic patients at the time of ICP monitoring; their mean age was 1 year and the incidence of elevated ICP was 13.4%. The mean age of patients in our study was 4 years 8 months. Renier et al.[41] noted a rise in ICP with age to 6 years, and Arnaud et al.[6] found a significantly increased incidence of raised ICP in patients older than 1 year compared with younger patients. Seruya et al.[43] reported intracranial hypertension in 9 (82%) of 11 patients who underwent calvarial remodeling at a mean age of 40.5 months for delayed-presentation SC. Conversely, Thompson et al.[50] found an inverse relationship between age and ICP in scaphocephaly. In our patient group, age was not associated with raised ICP. However, given the older age of the group as a whole and the 31% incidence of raised ICP among patients with

TABLE 1: Children who underwent ICP monitoring

Deformity*	No. of Patients	Mean Age at Presentation (mos)	Mean Cephalic Index	Characteristic†				
				Developmental Delay	Symptoms of Raised ICP	Radiological Signs of Raised ICP	Raised ICP (%)	Calvarial Remodeling
marked scaphocephaly	16	58	66.2	8	1	13	5 (31)	9
mild scaphocephaly	11	43	72.4	3‡	3	9	7 (64)	8
nonscaphocephalic	12	65	84.4	3‡	4	8	5 (42)§	6
total	39	56	73.5	14‡	8	30	17 (44)	23

* Marked scaphocephaly = cephalic index < 70; mild scaphocephaly = cephalic index 70–75; nonscaphocephalic = cephalic index > 75.
† Values are the number of patients with the characteristic.
‡ Two patients, 1 with a mild scaphocephaly and 1 nonscaphocephalic, had developmental delay related to cerebral palsy.
§ An additional patient in this group had borderline elevated ICP and subsequently underwent calvarial remodeling.

marked scaphocephaly, which is higher than other published rates, the incidence of abnormal ICP may well increase with age in this population. This view is supported by the 1 patient in this study who, after a normal ICP recording, suffered behavioral deterioration and was found to have raised ICP more than 2 years later.

Although some questions remain as to what constitutes normal ICP in infants, it is broadly accepted that adult thresholds are appropriate in children older than 1 year, who have more rigid calvaria, when assessing ICP in craniosynostosis.[6,20,35,41,49,50,54,55] There were no infants in this study; the youngest child was 17 months of age at ICP monitoring.

Previous studies that have performed overnight ICP monitoring in craniosynostosis have all defined abnormally raised ICP, or intracranial hypertension, as a baseline ICP of 15 mm Hg or greater, irrespective of whether an extradural or subdural device was used.[6,20,22,36,41,49–52] The pathological significance of multiple B-type waves is also well recognized.[20,41,55] An upper normal threshold of 15 mm Hg is commonly used in other chronic conditions, including hydrocephalus,[12,55] although some authors rely on a higher threshold of 20 mm Hg, such as in the case of idiopathic ICP.[24] If the higher threshold of 20 mm Hg were used to define raised ICP in this study, 6 of 39 patients (15%) would have been deemed to have raised ICP.

Intraparenchymal ICP monitoring remains the most reliable and reproducible method at our disposal to assess ICP and is associated with an infrequent and minor complication rate.[20,31,39,55] The lower rate of raised ICP observed by Renier et al.[41] may be due to their use of a less sensitive extradural method of monitoring.[11]

Milder deformities in single-suture craniosynostosis have been associated with high rates of elevated ICP.[21,27] Consistent with those reports, the highest rate in this study was observed in mildly scaphocephalic patients (64%). Whether age at presentation or the type of deformity is more significant in the development of raised ICP is debatable, because children with milder deformities are more likely to present at an older age.

Twelve of 45 children (27%) in our study presented with some degree of neurodevelopmental delay or learning difficulties not attributable to other factors. This rate is consistent with findings of several studies that examined developmental attainment, learning disability, and speech and language abnormalities in isolated SC.[7,8,13,14,33,44,46] Although, in 1982, Renier et al.[41] found that raised ICP was correlated with lower IQ, more recent studies[6,23,34] have failed to confirm the relationship between elevated ICP and neurocognitive outcomes in SC or other single-suture craniosynostosis. The lack of a correlation between developmental delay and raised ICP found in the present study supports the hypothesis that there is no simple causal relationship between ICP and neurocognitive anomalies found in SC.[25] Three-dimensional imaging studies performed by Aldridge et al.[2,3] indicate that primary structural CNS abnormalities are present in some patients with SC, suggesting an alternative explanation for some of the neurocognitive abnormalities observed.[29]

Whatever the ultimate cause of neurocognitive abnormalities proves to be in SC, elevated ICP should not be dismissed as a benign finding without possible functional consequences for the individual. The sequelae of chronically raised ICP include visual loss and psychomotor impairment.[38,53] In other pediatric neurological conditions, elevated ICP has been correlated with impaired myelination and later poor neurodevelopmental scores.[26] Further, several PET studies in children with isolated single-suture craniosynostosis have found areas of cerebral hypoperfusion associated with the stenosed suture, which resolve after corrective surgery.[16,17,42]

In the literature, only Arnaud et al.[6] measured ICP in a population that had not undergone corrective surgery and then followed their neurocognitive development over time. They found a significant correlation between developmental quotient and final IQ of patients who had avoided surgery. All patients with proven raised ICP (n = 4) had an IQ exceeding 90 on final assessment. Interestingly, however, the correlation between developmental quotient and final IQ was much poorer in patients who did not undergo surgery (r = 0.3) than in those who did undergo surgery (r = 0.64). Perhaps the reduced correlation observed in the nonsurgical group could be accounted for by either the patients with raised ICP declining in IQ, though not to the threshold of 90, or some patients with initially normal ICP subsequently developing raised ICP and experiencing a relative drop in IQ.

Several studies have found no significant improvement in neurodevelopmental outcomes after corrective surgery.[13,28,45,47] However, it is difficult to infer anything

TABLE 2: Patients with abnormal ICP on monitoring*

Case No.	Age (yrs), Sex	Cephalic Index	DD	Symptoms of Raised ICP	Radiological Signs	Nocturnal ICP Baseline (mm Hg)	Repeat ICP Monitoring	Interval From CR (mos)	Indication for Repeat Monitoring	Repeat ICP
1	1.6, F	88	no	irritability, sleep disturbance	no	16–19	yes	19	headaches, irritability	normal
2	1.9, M	75	no	sleep disturbance	yes	>20	no			
3	1.9, F	70	no	no	yes	>20	no			
4	2.1, M	74	no	no	no	15 >3 B-waves	no			
5	4.8, M	76	no	no	yes	>20	no			
6	3.3, M	87	no	no	yes	10–14	no			
7	3.4, M	63	no	no	yes	15 >3 B-waves	no			
8	3.7, M	75	no	no	yes	16–19	yes	33	irritability	normal
9	3.9, M	67	yes	no	yes	16–19	no			
10	5.6, M	66	no	no	yes	15 >3 B-waves	no			
11	4.3, F	71	yes	no	yes	16–19	yes	111	irritability, radiological signs	normal
12	4.8, M	76	yes (CP)	no	yes	10–14 >3 B-waves	no			
13	8.2, M	81	yes	irritability	yes	10–14 >3 B-waves	yes	39	irritability, plateau HC	normal
14	5.4, M	74	yes	no	no	20	no			
15	6.2, F	83	no	no	yes	20	yes	28	nocturnal headaches	normal
16	5.4, M	71	yes	no	yes	16–19	no			
17	8.5, M	78	yes	no	yes	>20	yes	66	headaches, irritability	normal
18	11.4, M	72	yes	irritability	yes	10–14 >3 B-waves	no			

* All ICP results were considered raised except Case 6, which was classified as borderline. Case 13 had a normal ICP on initial monitoring (not tabulated), but after new-onset irritability his ICP was found to be raised when monitoring was repeated 30 months later (listed in table). CP = cerebral palsy; CR = calvarial remodeling; DD = developmental delay; HC = head circumference.

TABLE 3: Symptoms and clinical signs associated with raised ICP in 39 patients

Symptoms/Signs	No. of Patients: Raised ICP (n = 17)	No. of Patients: Normal ICP (n = 22)	OR	p Value†
scaphocephaly				
marked	5	11		
mild	7	4	3.85	
absent	5	7	1.57	0.24
developmental delay*				
present	7	5		
absent	10	16	2.38	0.22
symptoms of raised ICP				
present	4	4		
absent	14	18	1.38	0.68
radiological signs of raised ICP				
present	14	16		
absent	3	6	2.18	0.31

* Two patients with cerebral palsy were excluded from this group.
† Logistic regression analysis.

directly from these observations without corresponding ICP data, because in the authors' and others' experience, raised ICP can occur after surgical corrective procedures.[9] Any resultant decline in neurocognitive function in affected individuals could mask an improvement in the overall group. Furthermore, there is contrary evidence that, after surgery, single-suture craniosynostosis patients are of normal intelligence during school-age years and patients with a proven raised preoperative ICP experience improved neurocognitive functioning.[15,27] With the evidence currently available in the literature, it remains reasonable to assume that continued chronically raised ICP in SC is liable to curtail an individual's neurocognitive development, even if it does not reliably cause a marked developmental delay and is not responsible for many of the developmental abnormalities seen in SC.

Symptoms suggestive of ICP, the presence of papilledema, and radiological studies did not usefully predict elevated ICP in this study. Eide et al.,[19,20] in 2 large series of pediatric patients with craniosynostosis, hydrocephalus, shunt failure, or idiopathic ICP, found that symptoms classically associated with raised ICP (headache, irritability, sleep disturbance, nausea, psychomotor delay, and seizures) did not correlate with or predict raised ICP in children, and our findings reflect this. Irritability and sleep disturbance, the most frequently encountered symptoms in our study, have a wide range of possible causes. Papilledema is unusual in children younger than 8 years with raised ICP in the context of craniosynostosis and thus is a sign of low sensitivity but very high specificity.[19,51] Tuite et al.[51] hypothesized that this may be due to either the difficulties inherent in examining the optic discs of poorly compliant infants or anatomical or physiological differences between young children and older children and adults. Conversely, radiological signs suggestive of raised ICP, particularly a diffuse beaten-copper appearance of the cranium, are common in children with craniosynostosis and increase in incidence with age.[1,52] They are thus poorly predictive of raised ICP.[52]

Visual evoked potential monitoring holds promise as a noninvasive technique for assessing ICP in craniosynostosis, but a high incidence of abnormal responses in craniosynostosis patients and variability in normal subjects suggest that currently this approach requires significant neurophysiological expertise.[5,18,37,48,55] Thus, given the high incidence of raised ICP in this study (44% overall), we believe that intraparenchymal ICP monitoring remains the only reliable method to identify elevated ICP in SC patients. It should be considered and used routinely in all patients for whom a nonoperative course of management is proposed, no matter the nature or severity of the calvarial deformity.

Conclusions

Raised ICP is common in late-presenting patients with SC, irrespective of their calvarial deformity. Previous studies that report the rate of raised ICP in SC likely underestimate its incidence in children who do not undergo corrective surgery. Because clinical and radiological findings are unreliable indicators of raised ICP in SC, intraparenchymal monitoring remains the principal method to accurately determine whether patients can appropriately be managed conservatively.

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Disclosure

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