Endoscopic 3rd ventriculocisternostomy: Procedural complications and long-term dysfunctions?

Ventriculocisternostomie endoscopique du troisième ventricule : complications procédurales et dysfonction à long terme ?

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\textbf{Abstract}

Background and purpose. – The endoscopic third ventriculostomy (ETV) has become the treatment of choice for managing non-communicating hydrocephalus. The aim of this study was to evaluate the efficacy and the morbi-mortality of this procedure and its long-term outcome.

Patients and methods. – This retrospective study involved 82 consecutive patients treated for non-communicating hydrocephalus by ETV, in a single centre, between June 1999 and November 2008. The main criterion of efficacy was clinical improvement with shunt independence. The secondary criteria were the ventricular size (third and lateral ventricles) outcome and the procedural morbidity and mortality. In order to determine the predictive factors of dysfunction, a uni- and multivariate analysis was conducted.

Results. – Divided in two groups, the overall success rate was 65.4\% in the paediatric group (\(n=26\)) and 83.9\% in the adult group (\(n=56\)), after respectively a mean follow-up of 59.1 ± 36.7 and 49.3 ± 27.7 months. A procedural complication occurred in 5 patients (6.1\%), with no procedure-related death. The predictive factors of ETV failure were an infectious aetiology and an age less than 16. Changes in ventricular size and success rate were independent.

Conclusions. – ETV is an effective procedure at long-term for the management of non-communicating hydrocephalus with low morbidity. Therefore, it should be considered as first-line treatment. Cerebrospinal meningitis infection and young age both expose patients to possible dysfunction.

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\textbf{Résumé}

Objectifs. – La ventriculocisternostomie endoscopique du plancher troisième ventricule est devenu le traitement de choix des hydrocéphalies non communicantes. Le but de cette étude était d'évaluer l'efficacité de cette procédure, la morbi-mortalité qui lui était associée et son suivi à long terme.

Patients et méthodes. – Cette étude rétrospective comprenait 82 patients consécutifs traités pour une hydrocéphalie non communicante par ventriculocisternostomie endoscopique, dans un centre unique, entre juin 1999 et novembre 2008. Le principal critère d'efficacité était l'amélioration clinique sans nécessité d'implantation d'une dérivation interne de LCS. Les critères secondaires étaient la taille des ventricules (ventricules latéraux et troisième ventricule), l'évolution à long terme et la morbi-mortalité procédurale. De plus, afin de déterminer des facteurs prédictifs de dysfonction, une analyse univariée et multivariée a été menée.

Résultats. – La population a été scindée en deux groupes : adultes et enfants. Le taux de succès dans le groupe pédiatrique (\(n=26\)) était 65.4\% et dans le groupe adulte (\(n=56\)) 83.9\% après un suivi moyen de respectivement 59,1 ± 36,7 et 49,3 ± 27,7 mois. Une complication procédurale est survenue chez cinq patients (6,1\%), sans mortalité rapportée au geste chirurgical. Les facteurs prédictifs d'échec étaient une

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1. Introduction

Since the 1990s [1,2], the endoscopic third ventriculostomy (ETV) has been the first-line procedure proposed for non-communicating hydrocephalus. ETV is considered superior to the internal ventricular shunt (IVS) mainly because it does not expose the patient to many of the complications observed after the implantation of a shunt system [3].

However, this procedure is not devoid of procedural complications affecting 7–12% of patients [4–6]. ETV dysfunctions occur in approximately 14–37% of patients [7,8], resulting sometimes in serious complications [9].

In non-communicating hydrocephalus, ETV efficacy has been obtained in 80% of patients, but this figure reflects patient follow-up times that were limited to 2 to 3 years following the procedure [10–14]. An analysis of long-term efficacy is necessary as very few long-term studies have been published. The aim of our study was to assess the long-term efficacy (over 4 years on average) and reasons for failure, in a retrospective series of 82 consecutive patients treated by ETV.

2. Clinical material and methods

2.1. Study design

This single centre retrospective study involved all consecutive patients treated for hydrocephalus by an ETV between June 1999 and June 2008. The primary objective was to evaluate the long-term clinical efficacy of ETV. Secondary objectives were:

- to evaluate the morbidity and mortality of the procedure;
- to quantify the reduction in the size of the ventricular system and to correlate this reduction with evolution;
- to determine the predictive factors of efficacy.

2.2. Inclusion and exclusion criteria

Inclusion criteria were:

- a preoperative diagnosis of non-communicating symptomatic hydrocephalus, e.g. tri-ventricular dilatation due to idiopathic stenosis or tetra-ventricular dilatation secondary to stenosis of the aqueduct of Sylvius with obstruction of the Luschka and Magendie foramina;
- ETV performed by a senior neurosurgeon;
- postoperative follow-up of at least 1 year.

Exclusion criteria were:

- ventricular endoscopy performed for a different indication;
- hydrocephalus first drained by an internal ventricular shunt (IVS).

Our retrospective study permitted analysis of various independent variables (age, sex, diagnostic indicators, preoperative and postoperative imaging results, aetiology, and duration of follow-up). The circumstances leading to diagnosis of non-communicating hydrocephalus were classified as: intracranial hypertension syndrome (ICH), chronic active hydrocephalus syndrome, isolated headache, isolated balance impairment, increased head circumference (HC), behavioural disorders, torticolis, visual disorders, and fortuitous. Non-communicating hydrocephalus was confirmed on magnetic resonance imaging (MRI) when a ballooning of the third ventricle revealed increased intraventricular pressure compared to the cerebellomedullary cistern. The aetiologies of hydrocephalus were classified as:

- malformations (idiopathic aqueductal stenosis, Arnold-Chiari malformation type I, ventriculomegaly, atresia of the foramina of Luschka and Magendie);
- secondary to an obstructive mass lesion;
- post-infectious (meningitis).

No post-haemorrhagic hydrocephalus was found in our series. We divided our population into two groups: paediatric, patients under 16 years of age, and adults.

2.3. Characteristics of the population

Our population (Table 1) comprising 82 consecutive patients (age range 1 month–83 years) was divided into a paediatric group (n = 26, mean age 5.9 ± 5.1 years; sex ratio: 0.86) and an adult group (n = 56, mean age 47.4 ± 17.1 years; sex ratio: 1.15).

The predominant symptom leading to diagnosis was ICH observed in both the paediatric group (42.3%) and the adult group (53.6%). An isolated increase in HC was present in 23.1% of children while 25% of adults complained of chronic hydrocephalus syndrome. More rarely, in children, the circumstances of diagnosis were isolated headache (11.5%) and behavioural disorders (7.7%); we found one case of torticolis, one case of balance disorders and a chronic hydrocephalus syndrome. In the adult group, few people reported isolated balance disorders (12.5%) or isolated headache (7.1%). In our series, visual disturbances were objectified in 5 children (19.2%) and 20 adults (35.7%), but very rarely isolated (1 case adult).

The aetiologies of hydrocephalus were divided into 3 groups: malformations (52.4%), secondary to a mass lesion (42.7%) or an infectious process (4.9%). Idiopathic stenosis of the aqueduct of Sylvius dominated all aetiologies: 50% of children and 41.1% of adults. The nature of bacterial post-infectious hydrocephalus was variable: group 8 Streptococcus in 2 patients, methicillin sensitive Staphylococcus in 1 patient and methicillin-resistant Staphylococcus for the last patient.

2.4. Surgical technique

The patient was placed in supine position, under general anaesthesia, with the head flexed at 5° on a horseshoe headrest. After incision behind the hairline, the surgical protocol began with a burr hole located 1 centimetre in front of the right hemi-cranial suture, on the mid-pupillary line.

A rigid neuro-endoscope (Karl Storz®) with a work shirt of 3 mm diameter and a trocar mounted on a self-static arm, was
introduced into the ventricular system using a trans-gyrual approach. The ventricles were explored with a 30° endoscope. Through the right foramen of Monroe, the tip of the endoscope was positioned to face the floor of the V3. Once the anatomical structures were analyzed (the contours of the two mamillo-motor bodies and the optic chiasm, termination of the basilar artery, the infundibular recess), fenestration of the floor of the V3 and Liliequist membrane was performed mechanically using an endoscopic microdissector.

The orifice window was then dilated using a double balloon catheter (Integra® Neurosciences (France) SA. Nice, France) to obtain a diameter of approximately 5 mm. Three criteria were used to verify the success of ETV:

- direct endoscopic visualization of the tip of the basilar artery and its perforators without interposed membrane confirming Liliequist membrane perforation;
- undulations of the floor surface of the V3 indicating cerebrospinal fluid (CSF) movements in both directions;
- flow analysis on postoperative sagittal T2-weighted MRI sequences (flow MRI), confirming ventriculostomy patency.

2.5. Endpoints

The primary endpoint was the clinical efficacy of ETV with regression of the symptoms, i.e. a final resolution of symptoms without the need for an IVS [7,10]. The permeability of the ventriculostomy was verified on postoperative flow MRI performed at 3 months [15]. On T2-weighted sequences of flow analysis in the mid-sagittal plane, we looked for the stoma opening and we objectified the flow through the stoma.

ETV dysfunction was defined by the non-resolution or recurrence of symptoms. In this instance, the inefficacy or the obstruction of the perforation of the floor surface of the V3 resulted in re-operation. In cases of dysfunction, a new MRI was performed. When the flow MRI showed a closure of the stoma, a second ETV procedure was proposed, otherwise, an internal ventricular shunt was implanted. Patients were followed-up in outpatient clinic at 3 and 6 months, then annually.

The secondary endpoints were:

- the morbi-mortality linked with the procedure by analyzing procedural complications. They concern haemorrhagic, infectious, neurological or fluid adverse events related to the ETV occurring within 3 months after surgery, and involving changes in the patient's management;
- change in ventricle size on pre- and postoperative MRI, using two MRI criteria on T1-weighted axial sections:
  - the Evans index [16,17] which is the ratio of the maximum distance between the frontal horns of the lateral ventricles and the bi-parietal maximum distance,
  - the maximum width of V3 [18] measured in millimetres.

The preoperative and postoperative MRI were compared.

2.6. Statistical analysis

Variables were analyzed using JMP software (version 6.0.3, SAS Institute Inc., Cary NC). Quantitative variables (age, Evans index, maximal V3 width, reduction of ventricular size), considered as continuous numeric variables, were expressed as average ± standard deviation and compared using a Student t-test. Qualitative variables (time to diagnosis, diagnostic circumstances, aetiology), considered as ordinal variables, were expressed as proportions and compared using a Chi² test analysis of a contingency table and a Fisher’s exact test for small samples.

The population was divided according to the need for re-operation (IVS or second ETV), into group “ETV efficiency” and “ETV dysfunction.” An univariate then multivariate analysis was correlated with these two groups using logistic regression. A survival curve based on a Kaplan–Meier test was performed for the ETV dysfunction delay. The confidence interval was 95%, and the results

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the paediatric and adult populations.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent variables</td>
<td>Pediatric group n (%)</td>
</tr>
<tr>
<td>Effectives</td>
<td>26 (31.7)</td>
</tr>
<tr>
<td>Sex ratio M/F</td>
<td>0.86</td>
</tr>
<tr>
<td>Mean age in years ± SD</td>
<td>5.9 ± 5.1</td>
</tr>
<tr>
<td>Mean follow-up in months ± SD</td>
<td>59.1 ± 36.7</td>
</tr>
<tr>
<td>Circumstances of diagnosis</td>
<td></td>
</tr>
<tr>
<td>ICHT</td>
<td>11 (42.3)</td>
</tr>
<tr>
<td>Chronic hydrocephalus syndrome</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>Balance disorders</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Increased HC</td>
<td>6 (23.1)</td>
</tr>
<tr>
<td>Behavioral disorders</td>
<td>2 (7.7)</td>
</tr>
<tr>
<td>Fortuitous</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>Torticollis</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>Visual disorders only</td>
<td>0</td>
</tr>
<tr>
<td>Etiologies of hydrocephalus</td>
<td></td>
</tr>
<tr>
<td>Malformative hydrocephalus</td>
<td>16 (61.5)</td>
</tr>
<tr>
<td>Stenosis of the aqueduct of Sylvius</td>
<td>13 (50)</td>
</tr>
<tr>
<td>Arnold-Chiari malformation</td>
<td>0</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Atria of the foramina of L and M.</td>
<td>0</td>
</tr>
<tr>
<td>Hydrocephalus secondary to a mass lesion</td>
<td>8 (30.8)</td>
</tr>
<tr>
<td>Cyst</td>
<td>2 (7.7)</td>
</tr>
<tr>
<td>Benign brain tumor</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Malignant brain tumor</td>
<td>2 (7.7)</td>
</tr>
<tr>
<td>Glial dysplasia of the blade tectal</td>
<td>1 (3.8)</td>
</tr>
<tr>
<td>Post-infectious hydrocephalus</td>
<td>2 (7.7)</td>
</tr>
</tbody>
</table>

F: female; M: male; HC: head circumference; ICHT: intracranial hypertension; PF: posterior fossa.
F: femme ; M : homme ; ICHT : hypertension intracrânienne ; HC : tour de tête ; foramina of L and M : foramen de Luschka et Magendie ; PF : fosse postérieure.
were considered significant at $P<0.05$; a statistical trend was noted for $P<0.1$.

3. Results

3.1. Efficacy, complications and ETV dysfunctions

3.1.1. Efficacy

The mean follow-up was 59.1 ± 36.7 months for children and 49.3 ± 27.7 months for adults. Clinical success was obtained after an initial ETV procedure in 16 children (61.5%) and 43 adults (76.8%), for an overall efficacy in 59 patients (72%). Taking into account the success of a possible second ETV (in cases of dysfunction), 17 children (65.4%) and 47 adults (83.9%) were free of IVS (overall efficacy: $n = 64$; 78%).

Resolution of ICHT and walking disorders was obtained within the first week, but the regression of the oculomotor disorders was obtained on average three months after the ETV.

A comparative pre-and postoperative MRI was available for 35 patients. On preoperative MRI, the size of the lateral ventricles estimated by the Evans index averaged 0.40 ± 0.09 [95% CI: 0.37 to 0.42], and the mean maximum width of V3 was 18.7 ± 7.1 mm [95% CI: 16.7 to 20.5]. On postoperative MRI, the index of Evans averaged 0.36 ± 0.1 [95% CI: 0.33 to 0.39] and the maximum width of V3 13.7 ± 6.1 mm [95% CI: 11.8 to 15.6]. On postoperative MRI, performed on average 4 ± 2.9 months after the ETV, a significant reduction in the Evans index of 11.6% after the ETV ($P<0.05$) was obtained. Similarly, the maximum width of the third ventricle decreased by an average of 4.5 mm. There was a significant reduction of 25.7% of the size of the third ventricle ($P<0.05$) after ETV.

3.1.2. Surgical complications

A surgical complication occurred in 5 patients (6.1%). Three children (all under 2 years of age) had a CSF leak (11.5% of children) due to the scar during the first postoperative days, which spontaneously resolved. A limited subarachnoid haemorrhage without secondary hydrocephalus was revealed in a 48-year-old man with unusual postoperative headache. Moreover, diabetes insipidus occurred during a few days in a child with a slightly distented floor of the V3 despite tri-ventricular hydrocephalus secondary to a benign tumour of the posterior fossa. These surgical complications required longer hospital stay without further surgery. None of these patients needed a IVS. Moreover, no infectious complication occurred and the procedural mortality rate was zero.

3.1.3. ETV failure

ETV failure, occurred in 23 patients (28%) after a mean of 9.5 months [95% CI 3.8 to 15.2; extremes: 15 days–40 months]. The Kaplan–Meier survival analysis (Fig. 1) shows the dysfunction curve: acute during the first 2 months and then a sloping plateau until 40 months. Thus 50% of ETV dysfunction was diagnosed in the first 6 weeks and 75% within 15 months following the ETV. Based on MRI flow, 12 patients underwent implantation of an IVS and in 11 a second ETV was performed. However, in this subgroup of 11 patients, the mean age of 5 patients treated successfully by a second ETV (38.2 ± 7.9 years) was significantly different from the 6 patients (15.5 ± 5.2) in which an IVD was eventually implanted in third intention ($P = 0.03$). Thus, in cases of dysfunction, and after a possible second procedure of ETV, an IVS was implanted in 18 patients (22%).

3.2. Predictive factors for ETV failure

Among the independent variables, only the aetiology of hydrocephalus and patient age showed a statistical correlation to the ETV dysfunction.

The infectious aetiology was significantly associated with an efficacy rate and ETV dysfunction. If the success rate of ETV was 81.4% for hydrocephalus malformations and 80% for hydrocephalus secondary to an obstructing lesion, this proportion decreased significantly to 25% for post-infectious hydrocephalus ($P = 0.03$).

We did not find any relationship between age and ETV dysfunction. In the paediatric group ($n = 26$), the efficacy rate of ETV was 65.4% as compared to 83.9% in our adult population ($n = 56$), which was not significantly different ($P = 0.06$). Considering children under 2 years of age ($n = 10$), the efficacy ratio decreased to 60%, but the small sample size did not demonstrate an association with dysfunction ($P = 0.15$) compared to the adult population.

The morphological characteristics of the ventricular system, such as reducing the size of the LV and V3, either pre- or postoperatively, did not correlate with ETV efficacy.

Similarly, the multivariate analysis, using a nominal logistic regression, revealed the infectious aetiology as the only independent variable significantly associated with ETV dysfunction and implantation of an IVS.

4. Discussion

In our patient population, after a mean follow-up of 52.4 ± 31 months, the percentage of ETV efficacy was 72% after an initial endoscopic procedure, and 78% after a second procedure avoiding IVS implantation. The only predictive factor of ETV dysfunction was post-infectious hydrocephalus.

4.1. The limitations of the study

This was a retrospective study evaluating long-term (over 4 years) ETV efficacy. The eligible population, non-communicating hydrocephalus, can only present a descriptive analysis. To reduce selection bias, we established a consecutive cohort. The method used for the collection of variables was based on hospital records and therefore there exists a possible information bias. This was offset by the simplicity of the primary endpoint (clinical resolution in the absence of valve implantation). Furthermore, if the clinical and procedural variables were all obtained, postoperative imaging studies were collected in a random fashion. Also, the limited number of postoperative MRI available could not provide sufficient significant statistical power regarding the evolution of ventricular
size as a possible predictor. The measurements, however, can still provide valuable information for daily practice. Furthermore, this study was able to provide an analysis of ETV dysfunction in time using the Kaplan–Meier method. In addition, an analysis of the predictive factors of the ETV failure was performed in this cohort.

4.2. Surgical complications

The rate of surgical complications after ETV was estimated in the literature to be between 7.2 and 12.3% [5,6,8,19–21]. Numerous complications have been described and may be classified in order of decreasing frequency i.e.: CSF leakage, bleeding complications (from a subdural haematoma to an arterial lesion of the vertebrobasilar system), parenchymal injuries (fornix or hypothalamus) and trauma of ocular motor nerves. Infectious complications, seizures or neurovegetative manifestations were rarer. In our series, we observed 6.1% of complications, that spontaneously resolved, dominated by CSF leakage. Preoperative images of the 3D-CISS sequence on MRI could help to predict the difficulty to puncture in ETV [22].

Different technical principles should be considered to prevent the occurrence of these complications:

- an entry point, on the mid-pupillary line. 1 centimetre in front of the right coronal suture, provides an orthogonal path to the floor of the V3, obliquely forwards. Its interest is threefold: to avoid the trauma of a frontal vein running along the roof of the frontal horn of the lateral ventricle, avoid the weight of the endoscope on the fornix, avoid trauma of the ocular motor nerves and arteriorial structures of the inter-peduncular cistern with a route to the dorsum sellae;
- the perforation of the floor of the V3 is located behind the vessels converging from the tuber cinereum. Several methods have been described: thermal or mechanical. In our experience we prefer the mechanical method allowing to adapt as required the strength of the perforation on the floor of the V3;
- the irrigation should be carefully performed with warm saline at low outflow in order to limit the risk of intracranial hypertension, vegetative dysregulation, or postoperative confusion;
- during endoscope removal, the walls of the channel created by the endoscope are carefully checked for bleeding;
- the shifted closure of the various plans and the replacement of bone powder can, especially in paediatric patients, prevent CSF leakage reflecting the temporary ICTH the first 2 weeks.

For the population younger than one year, the ETV combined with choroid plexus cauterization has been described by Warf [23]. This technique would be superior to ETV alone but a longer follow-up with neurocognitive assessment is required to definitely determine the superiority of this procedure.

4.3. Dysfunction at long-term

The time of occurrence of the dysfunction is different depending on the cause involved. Studies with a long-term follow-up (i.e. more than 4 years) reported a rate of 14% to 32.6% of ETV dysfunction [5,7,19,24,25]; the average time of occurrence of a ETV dysfunction was between 5 and 7 months. They are classified into early (<3 months) or late. The causes of early dysfunction could be of several types: failure of CSF absorption, insufficient fenestration or Lilliequist membrane unseen and not perforated. Delayed dysfunctions should be associated with a re-closing of the window in the floor of the V3, sometimes responsible for serious complications, even lethal [9]. These late failures should consider the benefits of a new endoscopic perforation, which reduces the malfunction rate to approximately 20% [11]. However, in children, the establishment of an IVS is more readily proposed.

This rate of significant dysfunction prompted us to analyze the role of this procedure compared to IVS. Indeed, the malfunction rate of IVS, in longitudinal studies using the Kaplan–Meier test, was estimated at between 20% and 40% the first year, 50% at 2 years and 60 to 75% at 5 years [3,26–28]. For Kulkarni et al. [29], the risk of ETV failure is higher than for a shunt within 3 months after the procedure. After this period of 3 months, the relative risk of failure becomes progressively lower for ETV. Furthermore, the risk of infection, which varies between 4% and 8% [28] after implantation of IVS is virtually nonexistent after ETV.

4.4. Predictors of ETV failure?

Three determinants of the ETV efficacy, age, aetiology and presence or not of a previous shunt, are conventionally discussed in the literature. With these 3 determinants, Kulkarni et al. determined a score to predict ETV success at 6 months [30]. Other determinants have been reported in the literature, i.e. the third ventricular “bowing” (deformation of the third ventricular floor) seen on the cerebral MRI, which could be predictive of ETV success [31,32]. While some authors suggest that aetiology or age as being a predominant factor, others believe that this combination may contribute to dysfunction [4,12,33] (Bognar et al., 2005). Nevertheless, for children under 2 years of age, only 50% efficacy has reported in ETV [34,35]. The immaturity of the CSF traffic routes has frequently been mentioned. Oi and Di Rocco proposed an evolution theory in CSF dynamics based on a significant role for the transepiphymal intraparenchymal CSF pathway (“the minor pathway”) [36]. This minor pathway could be dominant in human fetuses and neonates, which could explain the high rate of ETV failure in this population [36]. The results of the implantation of a shunt system were similar, or 43% efficacy during the first year and 4.5% of annual review [28].

Also the recommendation that we propose: ETV is the recommended first-line approach for non-communicating hydrocephalus regardless of age despite a dysfunction rate higher in children [35]. This recommendation is justified due to the almost complete absence of infectious complications. In addition, the correctly indicated ETV, exposes the patient to a dysfunction rate lower than the IVS but requires a prolonged clinical and iconographic approach which suggests a possible new procedure in cases of late ventricular dilatation. Moreover, the education of the patient and the family are dramatically important. They must be aware of the possibility of serious complications and the necessity of consulting in emergency in case of suspect clinical signs. In fact Drake et al. mention the possibility of serious, even lethal complication of ETV, even several years after the procedure [9].

5. Conclusion

The efficacy of ETV has been demonstrated in 72% of patients with non-communicating hydrocephalus. However, this procedure does not solve all of hydrodynamic problems, in particular in children in the context of cerebro-meningeal infection. It is offered as first-line therapy in non-communicating hydrocephalus, the ETV is only single alternative to this treatment.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


