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Review Article

Is endoscopic third ventriculostomy a viable treatment option for normal pressure hydrocephalus? A systematic review

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ABSTRACT

Background: Endoscopic third ventriculostomy (ETV) is considered an alternative treatment for hydrocephalus and has become a standard of care for obstructive hydrocephalus. Recent studies have also explored its role in normal pressure hydrocephalus (NPH). We conducted a systematic review aiming to assess the outcomes of this minimally invasive endoscopic technique as a viable treatment option for NPH.

Methods: A systematic literature search was performed using PubMed and Scopus databases, using iterations of search terms "Endoscopic third ventriculostomy," "Idiopathic normal pressure hydrocephalus," and "Normal pressure hydrocephalus." To be eligible for inclusion in the review, articles had to report the usage of ETV as a primary treatment modality for NPH, report its outcomes, and be published in the English language.

Results: Out of the 13 studies selected for qualitative synthesis, nine supported the use of ETV for NPH as an effective treatment option with improvement in the preoperative symptoms. Two studies favored shunt over ETV, stating that quality of life is better with VP shunt insertion. One study reported that ETV has higher perioperative mortality rates that outweigh its benefits. One study reported it to be an ineffective surgical option.

Conclusion: The current review of evidence does not support the use of ETV for the treatment of NPH, except perhaps in a small subset of patients. These patients have a shorter duration of symptoms and a better preoperative neurological status. The lumbar infusion test and ventricular infusion test are modalities useful for selecting these candidates.

Keywords: Endoscopic third ventriculostomy, Idiopathic normal pressure hydrocephalus, Normal pressure hydrocephalus, Systematic review

INTRODUCTION

Endoscopic third ventriculostomy (ETV) is a technique that uses a rigid or flexible endoscope to perforate the floor of the third ventricle to create communication between the third ventricle, interpeduncular, and prepontine subarachnoid spaces. It is a minimally invasive procedure that is used mainly to treat obstructive hydrocephalus.[4,20] Several recent studies have shown that ETV can also be successfully used in communicating or nonobstructive hydrocephalus, including normal pressure hydrocephalus (NPH) in carefully selected patients.[5,20]

NPH is clinically characterized by the Hakim-Adams triad, which includes gait ataxia, cognitive dysfunction, and urinary incontinence.[20,21] At present, shunting of cerebrospinal fluid (CSF) using programmable ventriculoperitoneal shunts (VPSs) is considered the standard surgical

treatment option for NPH. However, a substantial number of patients do not respond to VP shunts, and despite improving outcomes through better shunt technology, complication rates remain high, and there is often a need for another surgical intervention. These complications include shunt malfunction, over-drainage resulting in chronic subdural hematomas and hygromas, ischemic/hemorrhagic events, and postoperative infections. In the US alone, the total cost of hospitalization per year due to shunt-related complications approaches $2 billion.[19] ETV, if effective, can be a desirable alternative to shunt placement. Indeed, in selected patients, it has been shown to provide good outcomes and fewer complication rates.[7,12,21]

In this review, we aim to evaluate the utility of ETV for the management of patients with NPH to determine whether it might be a suitable option in comparison to other modalities.

MATERIALS AND METHODS

This systematic review has been reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Search strategy

An electronic search of literature was conducted using PubMed and Scopus on February 02, 2023, and the following search strategies were used: (((ETV) OR (Endoscopic third ventriculostomy) OR (Third ventriculostomy) OR (Microscopic third ventriculostomy) OR (Endoscopic 3rd ventriculostomy)) AND (iNPH) OR (Idiopathic normal pressure hydrocephalus) OR (NPH) OR (Normal pressure hydrocephalus))).

Inclusion and exclusion criteria

All observational studies comprising cross-sectional, cohorts, as well as randomized control trials in which ETV was used for treating iNPH or NPH were included in the study. Case reports, conference papers, commentaries, articles other than English language, and review articles were excluded from the study. All the articles in which ETV was not used as the primary modality of treatment were excluded from the study. Articles in which ETV was used in obstructive/noncommunicating hydrocephalus or had mixed cohorts where individual data for NPH could not be determined were also excluded from the study.

Study selection

The initial results of our database search were reviewed, and duplicates were removed [Table 1]. The title screening and abstract screening were done by two authors, A.S. and A.T. independently. The articles not matching the requirement were excluded from the study. The remaining articles were assessed for full-text by the same two authors and then were compared. The included and excluded articles were discussed and approved by a third arbiter, M.H.B.

Data extraction

The selected articles were reviewed, and data describing the authors of the study, year of publication, type of study, total number of patients, demographics of patients, presented pathology (type of hydrocephalus), number of patients who underwent ETV, presenting symptoms, outcomes of the procedure, factors defining ETV success, postoperative complications, number of patients who had to undergo re-intervention, and factors contributing in better ETV outcome were extracted. Due to heterogeneous data present between cohorts, meta-analysis was not possible. A qualitative assessment of all the articles was conducted using the National Institutes of Health (NIH) Quality Assessment Tool for Cohorts, Cross-Sectional Studies, and Randomized Controlled Trials.

RESULTS

A total of 358 articles were identified (176 on Scopus and 182 on PubMed) from the search algorithm from which duplicates were removed, titles and abstracts were screened, and 13 articles were selected that met all inclusion criteria for subjective analysis. Table 1 shows the study selection process according to the PRISMA statement criteria.

Risk of bias within studies

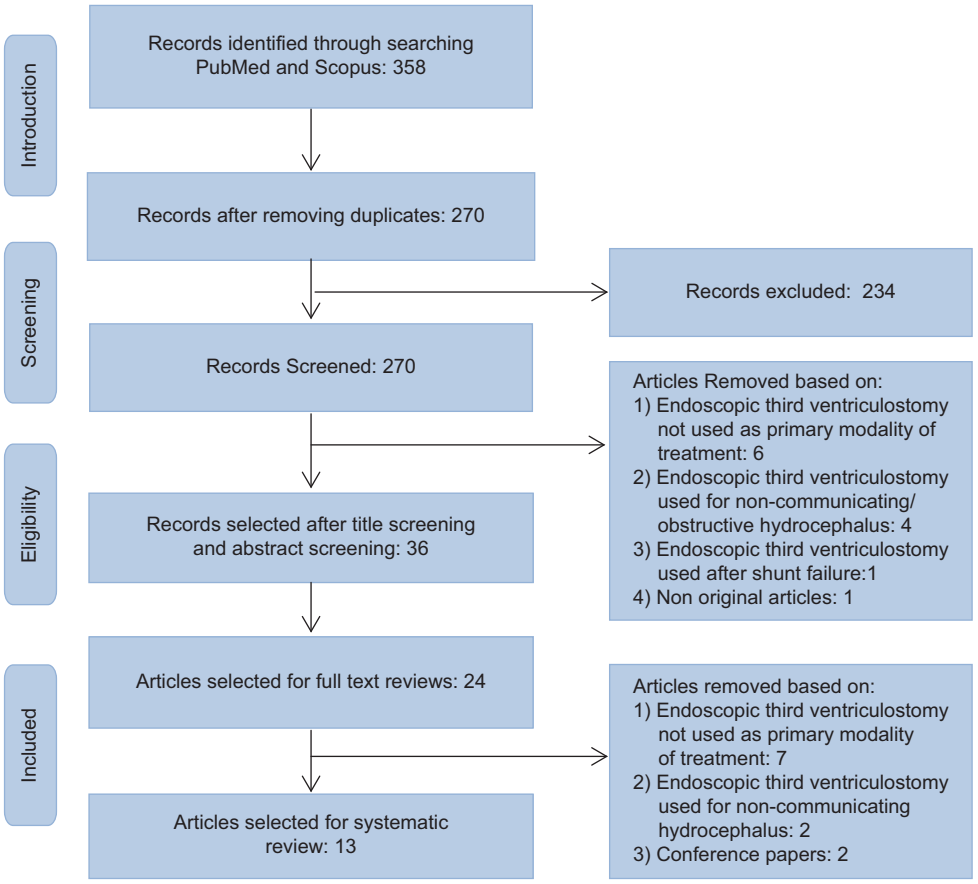
The NIH Quality Assessment Tool for Cohorts, Cross-Sectional Studies, and Randomized Controlled Trials was used by two authors, A.S. and Q.V., independently and the results were then compared. All of the 13 studies were reported as fair-quality studies, as shown in Tables 2a-c.

ETV as a primary treatment modality in NPH

ETV success in NPH patients is defined by the improvement in the patient's neurological status and preoperative symptoms, that is, gait, urinary incontinence, and dementia post-procedure, whereas ETV failure is defined by the worsening of preoperative symptoms and deterioration of the neurological status necessitating the need for another endoscopic procedure or shunt insertion later on.

Kang *et al*., in 2017, reported the use of ETV among 15 out of 21 patients diagnosed with NPH.[9] About 80% of those patients showed favorable outcomes at 6.4 months of mean follow-up with improvement in the preoperative symptoms, 13.3% of them remained stable with no improvement or worsening of the NPH symptoms after surgery, whereas 6.6% of them showed poor outcomes with worsening of the preoperative symptoms.[9] Gangemi *et al*., in 2008, conducted

Table 1: Study selection process according to PRISMA statement criteria.



a multicentric comparative study in which ETV was used in 110 patients with NPH.[6] The authors reported that 69.1% of those patients who showed favorable outcomes with improvement in gait disturbance at 6.5 years of mean follow-up had better preoperative neurology and had a short clinical history of not more than 3 years.[6] About 21.8% of the patients within this cohort remained stable, whereas 9.1% of patients showed ETV failure with worsening of the NPH symptoms.[6] Koutsouras *et al.*, in 2022, conducted a study on 36 patients with NPH who underwent ETV; 56% of them showed improvement in gait at 5–8.9 months follow-up.[11] Komlakh *et al.*, reported the use of ETV in 24 patients with NPH, among which 20.8% of the patients had favorable outcomes, and 50% of them reported satisfactory outcomes with improvement in dementia and movement disorders, while 29.2% of patients reported ETV failure.[10] Balevi *et al.*, in 2017, reported the results of three patients with NPH who underwent ETV.[1] About 66.7% of them had favorable outcomes, and 33.3% of them had satisfactory outcomes, with none of them needing shunt insertion after ETV at 5-year follow-up.[1] Hailong *et al.*, in 2008, reported the use of ETV in 17 out of 32 patients suffering from NPH.[8] About 64.7% of those patients had a favorable outcome at 14 months of follow-up, whereas satisfactory outcomes were observed in 17.6% of patients, and the other 17.6% showed poor outcomes.[8] Sankey *et al.*, in 2015, used ETV in seven patients diagnosed with NPH.[18] He reported a failure rate of 100% with the need for shunt insertion in all seven patients postoperatively.[18] Paidakakos *et al.*, in 2012, reported the outcomes of ETV in 16 out of 44 patients with NPH.[14] Favorable outcomes were observed in 68.7% of patients who were able to resume their pre-illness activities, whereas 31.2% of them who were not able to do so were categorized as part of the group showing ETV failure at 21.9 months follow-up.[14] Pinto *et al.*, in 2012, reported the use of ETV in 16 out of 42 patients suffering NPH.[15] The NPH scale was used at 3–12 months follow-up to categorize ETV failure and success. About 75% of the patients showed favorable outcomes with two points higher score on the NPH scale, whereas 25% of them reported ETV failure.[15] Cage *et al.*, in 2010, reported the use of ETV in four out of 252 patients with NPH in which favorable outcomes were reported in 55.6% of patients at 5–10 years follow-up.[2] Rangel-Castilla *et al.*, in 2012, reported the use of ETV in seven patients with NPH.[17] Favorable outcomes were observed in 66% of

Table 2a: Quality assessment using NIH quality assessment tool for cohorts and cross-sectional studies.

	Kang *et al*., 2017	**Gangemi *et al*., 2008**	**Koutsouras *et al*., 2022**	**Komlakh *et al*., 2022**	**Balevi *et al*., 2017**	**Hailong *et al*., 2008**
Was the research question or objective in this paper clearly stated?	✓	✓	✓	✓	✓	✓
Was the study population clearly specified and defined?	✓	✓	✓	✓	×	✓
Was the participation rate of eligible persons at least 50%?	✓	✓	✓	✓	✓	✓
Were all the subjects selected or recruited from the same or similar populations (including the same period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants	✓	✓	✓	✓	✓	✓
Was a sample size justification, power description, or variance and effect estimates provided?	×	×	×	×	×	×
For the analyses in this paper, were the exposure (s) of interest measured before the outcome (s) being measured?	✓	✓	✓	×	✓	✓
Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	×	✓	×	×	✓	✓
For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure or exposure measured as a continuous variable)?	NA	NA	NA	NA	NA	NA
Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓	✓	✓	✓	✓	✓
Was the exposure (s) assessed more than once over time?	NA	NA	NA	NA	NA	NA
Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓	✓	✓	✓	✓	✓
Were the outcome assessors blinded to the exposure status of participants?	×	×	×	×	×	×
Was the loss to follow-up after baseline 20% or less?	✓	✓	✓	NA	✓	✓
Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure (s) and outcome (s)?	×	×	×	×	×	×
Overall rating	Fair (8/14)	Fair (9/14)	Fair (8/14)	Fair (6/14)	Fair (8/14)	Fair (9/14)

NIH: National Institutes of Health, NA: Not applicable

patients with improvements in gait and urinary incontinence at 9.2 months follow-up[17] [Tables 3, 4, and 5a].

Postoperative complications and the need for re-intervention after ETV

Gangemi *et al*., reported 1.81% intracerebral hematomas, 1.81% subdural hematomas, 1.81% CSF leak, and 0.9% wound infections postoperatively.[6] About 13.6% of patients had to undergo VP shunt, 3.6% of patients underwent a second endoscopic procedure, and 13.6% of patients refused re-intervention.[6] Koutsouras *et al*., reported no postoperative complications, but 5.5% of patients had to undergo VP shunt after ETV.[11] Komlakh *et a*l., reported that 16.7% of patients had to undergo VP shunt, whereas he reported no postoperative complications.[10] Balevi *et al*., reported 11.1% infraction/hemorrhage postoperatively.[1] Hailong *et al*., reported 3.1% stoma occlusion, transient fever, and vomiting in 12.5% of patients postoperatively, and 3.1% of patients had to undergo VP shunt.[8] Paidakakos *et al*., in their study, reported no postoperative complications, but 18.7% of patients had to undergo VP shunt, 6.25% refused re-intervention, and 6.25% of patients underwent a second endoscopic procedure after ETV.[14] Chan *et al*., conducted a population-based study comparing the perioperative safety of ETV versus VPS in iNPH. They found that ETV resulted in 0.8% intracerebral hematomas, 3.9% hemorrhage/infarction, 1.5% seizures, 2.5% mechanical complications, 11.6% urinary tract infection, and 1.7% infections due to a mechanical device postoperatively.[3] Pinto *et al*., reported that 25% of the patients had to undergo VP shunt.[15] Rangel-Castilla I *et al*., reported that 28.5% of patients had to undergo VP shunt post ETV.[8] Both of them reported no postoperative

Table 2b: Quality assessment using NIH quality assessment tool for cohorts and cross-sectional studies.

	Sankey *et al*., 2015	**Paidakakos *et al*., 2012**	**Chan *et al*., 2013**	**Cage *et al*., 2010**	**Rangel-Castilla *et al*., 2012**	**Meier *et al*., 2000**
Was the research question or objective in this paper clearly stated?	✓	✓	✓	✓	✓	✓
Was the study population clearly specified and defined?	✓	✓	✓	✓	✓	✓
Was the participation rate of eligible persons at least 50%?	✓	✓	✓	✓	✓	✓
Were all the subjects selected or recruited from the same or similar populations (including the same period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants	✓	✓	✓	✓	✓	✓
Was a sample size justification, power description, or variance and effect estimates provided?	×	×	×	×	×	×
For the analyses in this paper, were the exposure (s) of interest measured prior to the outcome (s) being measured?	✓	✓	×	✓	✓	✓
Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✓	✓	×	✓	×	×
For exposures that can vary in amount or level, did the study examine different levels of exposure as related to the outcome (e.g., categories of exposure or exposure measured as a continuous variable)?	NA	NA	NA	NA	NA	NA
Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓	✓	✓	✓	✓	✓
Was the exposure (s) assessed more than once over time?	NA	NA	NA	NA	NA	NA
Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓	✓	✓	✓	✓	✓
Were the outcome assessors blinded to the exposure status of participants?	×	×	×	×	×	×
Was the loss to follow-up after baseline 20% or less?	✓	✓	NA	✓	✓	✓
Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure (s) and outcome (s)?	×	×	✓	×	×	×
Overall rating	Fair (9/14)	Fair (9/14)	Fair (7/14)	Fair (9/14)	Fair (8/14)	Fair (7/14)

NIH: National Institutes of Health, NA: Not applicable

complications.[15,17] Meier *et al*., in their study, reported 1% pneumocephalus as their postoperative complication[13] [Table 5b].

Factors favoring the use of ETV in NPH

Kang *et al*., in their study, stated that adult NPH patients with positive aqueductal flow void on T2 sagittal magnetic resonance imaging (MRI) and aqueductal peak velocity >5 cm/s on cine MRI have better outcomes when being treated with ETV.[9] Gangemi *et al*., described that a significantly higher rate of improvement was seen in patients treated within 3 years, particularly in the 1st year after the clinical onset of NPH symptoms, compared with those with a longer clinical history.[6] Patients with lower preoperative clinical grades (according to the grading scale for NPH) showed a significantly better outcome than those with more compromised neurological conditions preoperatively.[6] Koutsouras *et al*.,[11] reported that patients of younger ages showed successful results after using ETV. In contrast, Komlakh *et al*., in their study, reported that ETV is an effective surgical procedure for the treatment of adult patients with NPH.[10,11] Balevi *et al*., stated that ETV provides good results in patients with a shorter duration of symptoms and proves to be beneficial in patients with low Japanese Cosmetic Science Society scores, which takes into account the patient's age, sex, follow-up period, and comorbidities.[1] Hailong *et al*., described that patients with comparatively milder Kiefer scores (0–10) had a favorable course after ETV. Preoperative mental state score, gait disorder, and headache severity were predictors of good outcomes after ETV.[8] Paidakakos *et al*., and Meier *et al*., reported that patients whose outflow resistance is pathologically increased in the ventricular infusion test and physiologically increased in the lumbar infusion test or those with normal lumbar route values and signs of an aqueduct stenosis in MRI/computed tomography (CT) are good candidates for ETV. However,

Table 2c: Quality assessment using NIH quality assessment tool for RCT.

	Pinto *et al.* 2012
Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?	✓
Was the method of randomization adequate (i.e., use of randomly generated assignment)?	✓
Was the treatment allocation concealed (so that assignments could not be predicted)?	✓
Were study participants and providers blinded to treatment group assignment?	✓
Were the people assessing the outcomes blinded to the participants' group assignments?	NR
Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, and comorbid conditions)?	✓
Was the overall drop-out rate from the study at the endpoint 20% or lower of the number allocated to treatment?	✓
Was the differential drop-out rate (between treatment groups) at the endpoint 15% points or lower?	✓
Was there high adherence to the intervention protocols for each treatment group?	✓
Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	✓
Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	✓
Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	×
Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	✓
Were all randomized participants analyzed in the group to which they were originally assigned? That is, did they use an intention-to-treat analysis?	×
Overall rating	Fair (10/14)

NIH: National Institutes of Health, RCT: Randomized controlled trial

these patients may not be strictly classified as those suffering from NPH[13,14] [Table 6]

DISCUSSION

Mechanism of ETV

Cerebral parenchyma, in normal conditions, acts as a viscoelastic tissue that adequately disperses CSF pressure. In patients with NPH, this brain elasticity is lost due to multiple factors, such as insufficient transcortical subarachnoid space, fibrosis, meningitis, and small periventricular ischemic lesions that weaken the cerebral ventricles and decrease the absorption of CSF. Fenestration of the floor of the third ventricle by an ETV is purported to decrease the intraventricular pressure and increase the cerebral blood flow and perfusion pressure.[17] The optimal site for fenestration of the floor of the third ventricle lies in the transparent area situated anterior to the basilar artery and between the mammillary bodies and the infundibular recess. The use of a microvascular Doppler probe is beneficial. When a Doppler probe is unavailable, a gentle and careful exploration using the tip of bipolar forceps can identify dorsum sellae, and fenestration is created in the midline just posterior to it.[22] The main aim of ETV in communicating hydrocephalus is to increase intracranial compliance by increasing the systolic outflow from the ventricles and decreasing the intraventricular pulse pressure and width of the ventricles. These effects help dilate the compressed vessels, restore the cerebral pulsations within the ventricles, and thus, increase the intracranial compliance and improve the CSF flow from ventricles into the subarachnoid space, which facilitates increased blood flow and CSF absorption.[8,20]

ETV success in NPH

Rangel-Castilla *et al*., in their study of 36 patients with communicating hydrocephalus, reported the use of ETV as a good surgical option in replacing malfunctioning shunts and in the treatment of NPH, allowing patients to be shunt independent.[17] In an Italian multicentric comparative study, ETV was shown to have higher rates of clinical improvement and low complication rates compared to VP shunt, especially in patients with a shorter clinical history and a better preoperative neurological status. No significant difference in outcomes was reported in younger or older patients with NPH within this cohort. Clinical improvement was seen to be greater in gait disturbances, and outcomes were reported to be better among the patients who had gait abnormalities as their first clinical complaint. Similar results were also reported in a study conducted by Balevi *et al*., in which they concluded that ETV provides good results when used in properly selected NPH patients with short duration of clinical symptoms and has lower complication rates when compared to VP shunt.[1,6] A review on ETV that summarized its indications, outcomes, complications, and limitations by Yadav *et al*., reported ETV**,** when used for communicating hydrocephalus, provides good results when there is forward bowing of the anterior wall and inferior bulging of the floor, of third ventricle preoperatively regardless of the ETV success score (ETVSS).[22] Other factors reported in the literature that can predict ETV success include measuring the depression of the floor of the third ventricle postoperatively, bowing of the lamina terminalis, distance from anterior commissure to tuber cinereum, distance from mamillary body to lamina terminalis, and width of the third ventricle. Postoperative reduction of infundibular recess angle and third ventricular height anteriorly correlated well with a successful ETV.[22] A scoring system known as ETVSS exists to predict the likelihood of early success of ETV, which considers factors such as age, etiology, and history

Table 3: Patient Demographics and follow-up period.

Authors	Year of Study	Population (*n*)	Male/Female Ratio	Mean/Median age	Mean/median follow-up (months/years)
Kang *et al.*	2017	21	12/9	70 years	6.4 months
Gangemi *et al.*	2008	110	59/51	67 years	6.5 years
Koutsouras *et al.*	2022	36	19/17	72 years	5–8.9 months
Komlakh *et al.*	2022	24	15/9	70.85±9.1 years	-
Balevi *et al.*	2017	9	-	40 years	5 years
Hailong *et al.*	2008	32	24/8	66 years	14 months
Sankey *et al.*	2015	7	4/3	73 years	39 months
Paidakakos *et al.*	2012	44	21/23	72.2 years	21.9 months
Chan *et al.*	2013	652	386/266	72.4±1.2 years	-
Pinto *et al.*	2012	42	24/18	71 years	3–12 months
Cage *et al.*	2010	252	130/122	46–90 years	5–10 years
Rangel-Castilla *et al.*	2012	36	21/15	52 years	9.2 months
Meier *et al.*	2000	48	-	-	7 months

Table 4: Number of patients who underwent ETV for NPH.

Authors	Patients with NPH or INPH	ETV used in (n) of patients with NPH or INPH	ETV success is defined by:
Kang *et al.*	15/21	15	Improvement in the preoperative symptoms.
Gangemi *et al.*	110	110	1. Length of clinical history. 2. Preoperative clinical score. 3. Symptom of clinical onset. 4. Type of hydrocephalus on MRI. 5. Intraoperative features.
Koutsouras *et al.*	36	36	Gait improvement.
Komlakh *et al.*	24	24	1. Improvement in dementia. 2. Improvement in movement disorders.
Balevi *et al.*	3/9	3	All the patients did not have to undergo shunt placement after the ETV procedure.
Hailong *et al.*	17/32	17	1. Patient age. 2. Etiological considerations. 3. The mental state of the patient. 4. All the patients who did not have to undergo shunt placement after ETV procedure
Sankey *et al.*	7	7	-
Paidakakos *et al.*	44	16/44	Resumed pre-illness activity without deficit
Chan *et al.*	652	652	Medical comorbidity is a crucial predictor of worse short-term safety outcomes and again reinforces the importance of patient selection in ETV and VPS for INPH.
Pinto *et al.*	42	16/42	After 1 year, the late postoperative result was classified as positive if the patient had at least a 2-point higher score on the NPH Scale.
Cage *et al.*	252	Only ETV was used in 4 patients, and ETV+VPS used in 5 patients	-
Rangel-Castilla *et al.*	7/36	7	1. Improvement in gait 2. Improvement in incontinence
Meier *et al.*	48	11	-

ETV: Endoscopic third ventriculostomy, NPH: Normal pressure hydrocephalus, MRI: Magnetic resonance imaging, VPS: Ventriculoperitoneal shunt, INPH: Idiopathic normal pressure hydrocephalus

of previous shunting. However, it has not been validated for NPH patients.[16] Koutsouras *et al.*, conducted a study in which 36 patients with NPH underwent ETV and cortical biopsy for assessment of plaques consistent with dementia. He concluded

Table 5a: Presenting symptoms of patients with NPH. And outcomes after using ETV.

	Kang *et al.*[9] (%)	Gangemi *et al.*[6] (%)	Koutsouras *et al.*[11] (%)	Komlakh *et al.*[10] (%)	Balevi *et al.*[1] (%)	Hailong *et al.*[8] (%)	Sankey *et al.*[18] (%)	Paidakakos *et al.*[14] (%)	Chan *et al.*[3] (%)	Pinto *et al.*[15] (%)	Cage *et al.*[2] (%)	Rangel-Castilla *et al.*[17] (%)	Meier *et al.*[13] (%)
Symptoms													
Gait ataxia	100	87.3	11	95.8	-	87.5	100	79.5	-	50	-	38.8	-
Cognitive impairment	57	50.9	30	87.5	-	96.8	71	4.5	-	23.8	-	27.7	-
Urinary symptoms	48	60	30	33.3	-	50	100	16	-	9.5	-	22	-
Two symptoms of NPH	63.6	-	-	-	-	-	-	-	-	33.3	-	-	-
Complete NPH triad	-	-	7	-	100	-	-	38.6	-	50	-	-	-
Headache	-	-	22	-	-	87.5	14	-	-	-	-	44	-
Vertigo/Dizziness	-	-	-	-	-	100	43	-	-	-	-	-	-
Other symptoms	-	-	-	-	-	-	-	-	-	-	-	20	-
Outcomes													
Favorable outcome	80	69.1	56	20.8	66.6	64.7	-	68.7	-	75	55.6	66	-
Stable	13.3	21.8	-	-	-	-	-	-	-	-	-	-	-
Satisfactory outcome	-	-	-	50	33.3	17.6	-	-	-	-	-	-	-
Poor outcome	6.6	-	-	-	-	17.6	-	-	-	-	-	-	-
Failure rate	-	9.1	-	29.2	-	-	100	31.2	-	25	-	-	-

ETV: Endoscopic third ventriculostomy, NPH: Normal pressure hydrocephalus

that even though most of the patients who showed improvement had negative biopsy results for beta-amyloid or neuritic plaques, there was no statistically significant relationship between ETV success and positive biopsy results but patients with younger age correlated with better ETV outcome. About 56% of patients showed favorable outcomes, which were defined by improvement in gait.[11] Although different MRI sequences are now used, such as T2 W Turbo Spin Echo images, 3D-SPACE sequence, time-resolved 3D MR velocity mapping, and cine phase contrast images in the postoperative evaluation of CSF flow, stoma patency, and noninvasive quantification of the flow; clinical improvement in the patient's symptoms is always considered more reliable as compared to the radiological parameters such as Evans' index, frontal horn, or third ventricular diameter.[22]

Factors contributing to ETV's success

Kang *et al.* conducted a study to determine the efficacy of ETV in older age patients with NPH. About 80% of the patients who underwent ETV for NPH showed improvement in preoperative symptoms. The group concluded that ETV is effective in carefully selected elderly patients with NPH, given that they have a positive aqueductal flow void on T2 sagittal MRI and their aqueductal peak velocity is >5 cm/s on cine MRI.[9] Komlakh *et al*., performed a descriptive cross-sectional study on 24 patients with NPH and concluded that ETV is an effective surgical procedure that can improve symptoms of dementia and gait in older patients; however, his analysis showed no statistically significant relationship between the age or gender with the success or failure of ETV.[10] As CSF outflow resistance reflects the intracranial compliance which ETV can alter, the use of an infusion test is established to determine the information for selecting ETV as a treatment option in NPH patients.[14] Ventricular or lumbar outflow resistance can confirm patency of the subarachnoid space and ensure adequate CSF absorption. A resistance below 13 mm Hg/mL/min to CSF outflow is associated with a favorable outcome.[22] A comparative study conducted by Meier *et al*., reported that the suspicion of aqueductal stenosis on CT or MRI, physiological resistance on lumbar infusion test, pathological resistance on ventricular infusion test, and baseline intracranial pressure under physiological limits indicate the use of ETV in NPH patients. Similar results were reported in a study by Paidakakos *et al*., that NPH patients with low or normal lumbar route values and higher ventricular route values are strong candidates for ETV.[13,14] A single institution-based study conducted by Hailong *et al*., reported that preoperative Kiefer score, mental state, duration of symptoms, patient's age, and etiological factors were highly correlated with the overall outcome after ETV.[8]

ETV failure in NPH patients

While some studies suggest ETV to be a reasonable option for treating NPH, several studies report that ETV has higher

Table 5b: Postoperative complications and need for re-intervention after using ETV.

	Kang *et al.*[9]	Gangemi *et al.*[6]	Koutsouras *et al.*[11]	Komlakh *et al.*[10]	Balevi *et al.*[1]	Hailong *et al.*[8]	Sankey *et al.*[18]	Paidakakos *et al.*[14]	Chan *et al.*[3]	Pinto *et al.*[15]	Cage *et al.*[2]	Rangel-Castilla *et al.*[17]	Meier *et al.*[13]
Postoperative complications													
Intra-cerebral hematoma	-	1.81%	-	-	-	-	-	-	0.8%	-	-	-	-
Subdural hematoma	-	1.81%	-	-	-	-	-	-	-	-	-	-	-
Epidural hematoma	-	-	-	-	-	-	-	-	-	-	-	-	-
Hemorrhage/ Infraction	-	-	-	-	11.1%	-	-	-	3.9%	-	-	-	-
Stroke	-	-	-	-	-	-	-	-	-	-	-	-	-
CSF leak	-	1.81%	-	-	-	-	-	-	-	-	-	-	-
Wound infection	-	0.9%	-	-	-	-	-	-	-	-	-	-	-
Stoma occlusion	-	-	-	-	-	3.1%	-	-	-	-	-	-	-
Seizures	-	-	-	-	-	-	-	-	1.5%	-	-	-	-
Mechanical complications	-	-	-	-	-	-	-	-	2.5%	-	-	-	-
Other complications	-	-	-	-	-	Transient fever and vomiting 12.5%	-	-	11.6% UTI and 1.7% infections due to mechanical device	-	-	-	1% pneumatocephalus
Re-intervention													
Ventriculoperitoneal shunt	-	13.6%	5.5%	16.7%	-	3.1%	100%	18.7%	-	25%	-	28.5%	-
Repeat endoscopic procedure	-	3.6%	-	-	-	-	-	6.25%	-	-	-	-	-
Patients who refused re-intervention	-	13.6%	-	-	-	-	-	6.25%	-	-	-	-	-

UTI: Urinary tract infection, CSF: Cerebrospinal fluid, ETV: Endoscopic third ventriculostomy

Table 6: Factors favoring the use of ETV as a treatment option for NPH.

Authors	Factors contributing to better ETV outcome.
Kang *et al*.	1. Adult NPH patients with positive aqueduct flow void on T2 Sagittal MRI. 2. Aqueductal peak velocity>5 cm/s on cine MRI.
Gangemi *et al*.	1. Significantly higher rate of improvement in patients treated within 3 years, particularly in the 1st year after the clinical onset, compared with those with a longer clinical history. 2. Patients with lower preoperative clinical grades (according to the grading scale for INPH) showed a significantly better outcome than those with more compromised neurological conditions.
Koutsouras *et al*.	Patients with younger age were correlated with successful ETV (P=0.003).
Komlakh *et al*.	Effective surgical procedure for treatment of adult patients with normal pressure hydrocephalus.
Balevi *et al*.	1. ETV in patients with less JCSS score. 2. ETV provides good results in patients with short duration of symptoms.
Hailong *et al*.	Patients with comparatively milder Kiefer score (0–10) had a favorable course after ETV. Preoperative mental state score, gait disorder, and headache severity were predictors of good out come after ETV.
Sankey *et al*.	-
Paidakakos *et al*.	Route determination could prove to be an important treatment selection element. Patients with low or normal lumbar route and high ventricular route should be strongly considered for ETV.
Chan *et al*.	-
Pinto *et al*.	-
Cage *et al*.	-
Rangel-Castilla *et al*.	-
Meier *et al*.	Patients whose outflow resistance is pathologically increased in the ventricular infusion test and physiologically increased in the lumbar infusion test and signs of an aqueduct stenosis in MRI/CT an ETV is indicated.

ETV: Endoscopic third ventriculostomy, NPH: Normal pressure hydrocephalus, INPH: Idiopathic normal pressure hydrocephalus, MRI: Magnetic resonance imaging, CT: Computed tomography, JCSS: Japanese Cosmetic Science Society

perioperative mortality and complication rates as compared to VP shunt, which outweighs its potential benefits. Sankey *et al*. studied gait outcomes in NPH patients and reported ETV to be ineffective, with a failure rate of 100% in treating NPH. Not only did ETV fail to improve gait but also all the patients ultimately had to undergo shunt placements for a better outcome.[3,18] Other factors reported in the literature that can cause ETV failure include dense adhesions of the basal cisterns and an unidentifiable floor of the third ventricle.[22] A randomized controlled trial was conducted on 42 patients with NPH by Pinto *et al*., which reported ETV to be a safe option for NPH. However, it was reported that VP shunt showed better neurological and functional outcomes at 1-year follow-up.[15] There is little data available on functional and social outcomes and quality of life in patients with NPH who underwent treatment either in the form of ETV or VP shunt insertions. Cage *et al*. conducted a study to assess the long-term functional and social outcomes after surgical intervention in patients with NPH. They reported improvement in the quality of life of 55.6% of patients who underwent ETV compared to 72.2% of patients who underwent VP shunt placements.[2]

The studies included in this review had heterogeneous data available, which was nonuniformly presented. Of the 13 studies included in this review, only one was a randomized controlled trial, two were cross-sectional studies, and the rest were cohorts. Eleven out of these 13 studies had a small sample size, which limits the generalizability of these results. Almost all the studies reported the need for further studies with a larger sample size and suggested further randomized controlled trials to confirm their results and to understand the effectiveness of ETV for NPH better.

CONCLUSION

There is inconclusive data to support ETV as an effective treatment option for NPH. Based on the literature available so far, ETV cannot be used as an interchangeable alternative to VP shunts other than in carefully selected patients. These include patients with a shorter clinical history, those with better preoperative neurological status, patients having pathologically increased outflow resistance on ventricular infusion tests, and physiologically increased outflow resistance on lumbar infusion tests.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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