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# Endoscopic Third Ventriculostomy vs. Ventriculoperitoneal Shunt for Obstructive Hydrocephalus: A Meta-Analysis of Randomized Controlled Trials

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## ABSTRACT

**AIM:** To conduct a meta-analysis for investigating the safety and efficacy of endoscopic third ventriculostomy (ETV) and extracranial shunting for patients with obstructive hydrocephalus.

**MATERIAL and METHODS:** Randomized controlled trials (RCTs) of ETV and ventriculoperitoneal shunting (VPS) for obstructive hydrocephalus were analyzed systematically by using MEDLINE, EMBASE, and the Cochrane Controlled Trials Register. The reference lists of the retrieved studies were also perused. Postoperative infection, postoperative cerebrospinal fluid (CSF) leakage, mortality and surgical success were the main outcomes of the analysis.

**RESULTS:** Among 841 selected studies, 6 RCTs evaluated ETV and VPS. Compared to VPS, ETV had lower postoperative infection incidence (risk ratio [RR]: 0.19, 95% confidence interval [CI]: 0.08-0.43, p=0.0001), postoperative CSF leakage (RR: 5.10, 95% CI: 1.19-21.89, p=0.03) VPS. VPS had no mortality as compared to ETV (RR 0.64, 95% CI: 0.26-1.56, p=0.32).

**CONCLUSION:** While VPS had no mortality in comparison to ETV, the latter showed lower incidences of major complications, such as postoperative infection and CSF leakage, than those of the former for patients with obstructive hydrocephalus.

**KEYWORDS:** Ventriculoperitoneal shunt, Endoscopic third ventriculostomy, Obstructive Hydrocephalus, Meta-Analysis

**ABBREVIATIONS: CI:** Confidence interval, **CSF:** Cerebrospinal fluid, **ETV:** Endoscopic third ventriculostomy, **OR:** Odds ratio, **RCT:** Randomized controlled trial, **RR:** Risk ratio, **VPS:** Ventriculoperitoneal shunting

## INTRODUCTION

Obstructive hydrocephalus is a common neurological condition that can affect patients at any ages, with a higher prevalence in newborns and adults (10,33). This congenital anomaly could occur alone or in combination with other diseases. Regardless of its different causes, similar pathological changes occur in obstructive hydrocephalus. This condition results from the blockade of the cerebrospinal fluid (CSF) during its production or circulation and absorption, leading to CSF accumulation in the patient's subarachnoid space and ventricular system. CSF accumulation causes an increase in intracranial pressure and the expansion of cerebral ventricle, creating serious complications for the brain function. There are several surgical treatments for obstructive hydrocephalus, including endoscopic third ventriculostomy (ETV) and ventriculoperitoneal shunting (VPS). Both procedures are radiologically and clinically operational.

## MATERIAL and METHODS

### Search Strategy

The PRISMA guideline has been used to conduct a systematic review of randomized controlled trials (RCTs) (28). All related studies in English were included. MEDLINE, EMBASE, and

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the Cochrane Controlled Trials Register were used for study selection from the inception date of the database to December 31, 2021. The search formula was as follows: "obstructive hydrocephalus, third ventriculostomy, ventriculoperitoneal shunt, and RCT". The references of related articles were also used for additional searches. In this regard, to identify qualified studies, the researchers used the EndNote software program to manually search the reference lists from all relevant studies.

### Trial Selection and Inclusion Criteria

The inclusion criteria for the RCTs in our study were as follows: (i) Studies of patients with obstructive hydrocephalus who underwent ETV or VPS; (ii) the entire texts of the selected publications were available; and (iii) studies with correct data that could be examined, including the total number of participants and the relevant clinical outcomes. If details of the same study were published in multiple journals or at different times, the latest study was included for the analysis. If the same research group analyzed the same patient cohort in different trials, each trial was combined. The flow diagram of the study selection process is shown in Figure 1.

### Extraction of Information

The following relevant data were retrieved separately by two researchers: (A) publication time; (B) the first author's name; (C) the study design; (D) the country where the study was conducted; (E) the number of participants in each study group; (F) intervention: the surgical procedures; (G) follow-up duration; (H) measured outcomes: complications, mortality, and the number of successful surgeries. The data were compiled into an Excel spreadsheet (Microsoft Excel; Microsoft, Redmond, Washington, USA).

### Statistical Analysis

RevMan v.5.1.0 was used to generate applicable data for the meta-analysis (Cochrane Collaboration, Oxford, UK) (12,26). To indicate event probabilities, RCT results were given as the odds ratio (OR) or risk ratio (RR) with a 95% confidence interval (CI) for dichotomous variables to reflect event probabilities. The $I^2$ and $\chi^2$ values were used to determine heterogeneity. A fixed-effect model (Mantel-Haenszel method) was used for data with $I^2 < 50\%$. Otherwise, a random-effects model (DerSimonian and Laird method) was selected.

## RESULTS

### Study Selection Outcome

The database search yielded 841 publications for our study. Among these, 803 articles were excluded after examination of their titles and abstracts, based on eligibility criteria. Thirty-two publications were not RCTs. Finally, 6 articles that reported results of six RCTs (9,11,15,21,27,30) were included in the meta-analysis of ETV and VPS for obstructive hydrocephalus.

### Study Characteristics

The baseline characteristics of the six RCTs from different countries are listed below Table I (9,11,15,21,27,30). A total of 398 patients, with 203 in the ETV group and 195 in the VPS group, were included. The numbers of successful surgeries were provided in 5 RCTs (9,11,21,27,30). Sixteen deaths were documented in all studies. The following complications were observed in three RCTs (9,11,30): 11 patients with CSF leakage (ETV group: 10; VPS group: 1), and 37 patients with postoperative infection (ETV group: 5; VPS group: 32).

### Quality Assessment

The randomization and double-blinding techniques were employed in all RCTs. The Cochrane criteria were used to evaluate the risk of bias for each outcome. In each of the six RCTs, the randomization procedures were discussed. We noted that blinding could not influence the study results since the blinding procedure for key researchers and participants was challenging, given that patients had to provide written

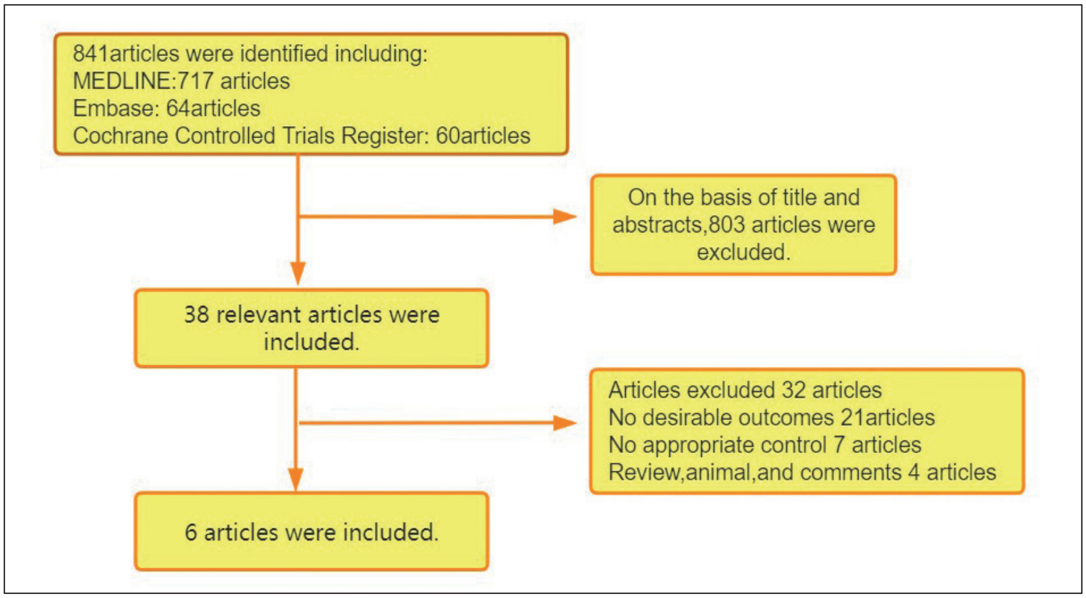


**Figure 1:** Eligibility of studies for inclusion in metaanalysis.

preoperative informed consent. Two RCTs (21,30) were of excellent quality, with a negligible risk of bias in all dimensions, whereas the remaining four (9,11,15,27) lacked information on random sequence generation and allocation concealment. Without data of successful operations, one RCT, reported by Kamikawa et al. (15), faced a considerable danger of reporting bias. The summary data of the risk of bias of all studies are shown in Figure 2.

### Postoperative Infection

In six RCTs with a total of 398 patients (9,11,15,21,27,30), 37 patients experienced postoperative infection (ETV group: 5; VPS group: 32). The combined data revealed that the ETV group had a significantly lower postoperative infection rate than the VPS group (RR: 0.19, 95% CI: 0.08-0.43, $p$=0.0001), with no evidence of heterogeneity ($I^2$ = 14%, $p$=0.32) (Figure 3).

**Table I:** Characteristics of Included Studies

| Study | Study Design | Country | Number of Patiens ETV/VPS | Intervention operation | Follow-up Duration | Outcomes Measured |
|---|---|---|---|---|---|---|
| Kamikawa et al. (2001) (15) | RCT | Japan | 44/44 | ETV/VPS | 24 Months | Revision rates, bleeding, infection, blockage, damage to brain tissue |
| El-Ghandour (2011) (9) | RCT | Egypt | 32/21 | ETV/VPS | 27.4/25 Months | Improvement of symptoms, death, bleeding, infection, blockage, CSF leakage |
| Goyal et al. (2014) (11) | RCT | India | 24/24 | ETV/VPS | 6 Months | Infection, CSF leakage, death, cranial nerve deficit |
| Kulkarni et al. (2017) (21) | RCT | Uganda | 51/49 | ETV/VPS | 12 Months | Infection, CSF leakage, death, brain volume, survival |
| Navaei et al. (2018) (27) | RCT | Iran | 22/27 | ETV/VPS | 36 Months | Bleeding, infection, raised intracranial pressure, death |
| Rahman et al. (2018) (30) | RCT | Bangladesh | 30/30 | ETV/VPS | 30 Days | Bleeding, infection, blockage, CSF leakage, death, pseudomeningocele |

***ETV:** Endoscopic third ventriculostomy, **VPS:** Ventriculoperitoneal shunt, **RCT:** Randomized controlled trial, **CSF:** Cerebrospinal fluid.*

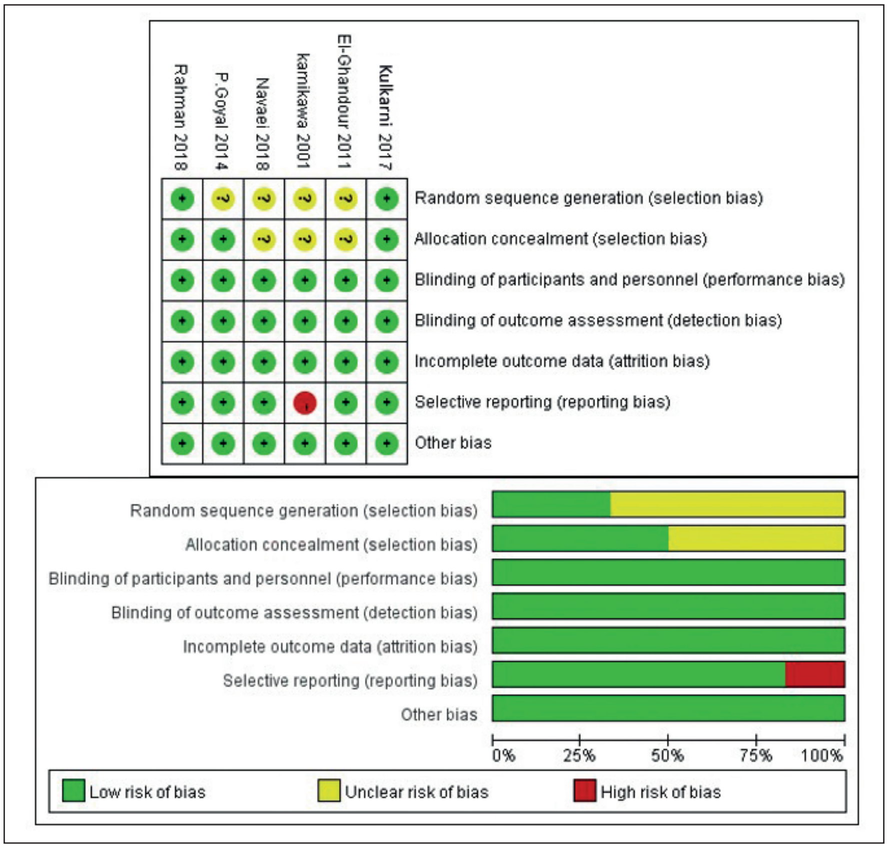


**Figure 2:** Risk of bias summary.

### Cerebrospinal Fluid Leakage After Surgery

Three RCTs (11,15,27) presented data on postoperative CSF leakage, with 11 cases (ETV group: 10; VPS group: 1) out of 161 patients being identified. In the pooled dataset, CSF leakage differed between ETV and VPS groups (RR: 5.10, 95% CI: 1.19-21.89, *p*=0.03), with no evidence of heterogeneity ($I^2$=0%, *p*=0.47) (Figure 4).

### Mortality

All six RCTs published mortality results (9,11,15,21,27,30). Six patients (3.77%) died in the ETV group, while the postoperative mortality rate of the VPS group was 6.62%. In the combined mortality dataset, there was no statistically significant difference in the overall mortality between ETV and VPS groups for patients with obstructive hydrocephalus (RR: 0.64, 95% CI: 0.26-1.56, *p*=0.32), with no evidence of heterogeneity ($I^2$ = 0%, *p*=0.44) (Figure 5).

| Study or Subgroup | ETV Events | ETV Total | VPS Events | VPS Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Kulkarni 2017 | 2 | 51 | 2 | 49 | 6.0% | 0.96 [0.14, 6.56] |
| El-Ghandour 2011 | 0 | 32 | 2 | 21 | 8.9% | 0.13 [0.01, 2.65] |
| kamikawa 2001 | 0 | 44 | 14 | 44 | 42.9% | 0.03 [0.00, 0.56] |
| Navaei 2018 | 0 | 22 | 2 | 27 | 6.7% | 0.24 [0.01, 4.82] |
| P.Goyal 2014 | 2 | 24 | 4 | 24 | 11.8% | 0.50 [0.10, 2.48] |
| Rahman 2018 | 1 | 30 | 8 | 30 | 23.7% | 0.13 [0.02, 0.94] |
| **Total (95% CI)** | | **203** | | **195** | **100.0%** | **0.19 [0.08, 0.43]** |
| Total events | 5 | | 32 | | | |

Heterogeneity: Chi² = 5.83, df = 5 (P = 0.32); I² = 14%
Test for overall effect: Z = 3.97 (P < 0.0001)

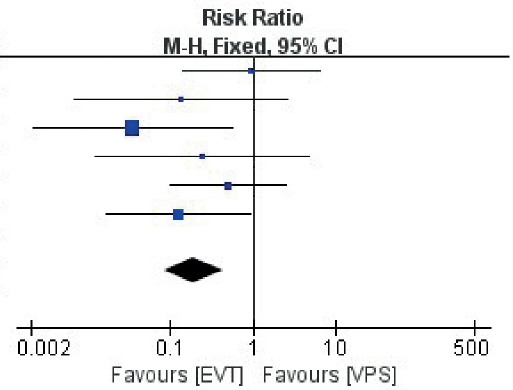


**Figure 3:** Forest plot of postoperative infection rates for endoscopic third ventriculostomy and ventriculoperitoneal.

| Study or Subgroup | ETV Events | ETV Total | VPS Events | VPS Total | Weight | Risk Ratio M-H, Fixed, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| El-Ghandour 2011 | 1 | 32 | 0 | 21 | 28.6% | 2.00 [0.09, 46.90] | 2011 |
| P.Goyal 2014 | 7 | 24 | 0 | 24 | 23.8% | 15.00 [0.90, 248.78] | 2014 |
| Rahman 2018 | 2 | 30 | 1 | 30 | 47.6% | 2.00 [0.19, 20.90] | 2018 |
| **Total (95% CI)** | | **86** | | **75** | **100.0%** | **5.10 [1.19, 21.89]** | |
| Total events | 10 | | 1 | | | | |

Heterogeneity: Chi² = 1.52, df = 2 (P = 0.47); I² = 0%
Test for overall effect: Z = 2.19 (P = 0.03)

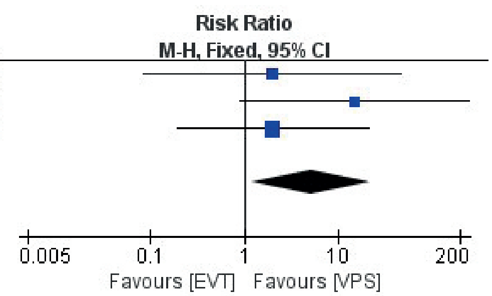


**Figure 4:** Forest plot of postoperative cerebrospinal fluid leakage rates for endoscopic third ventriculostomy and ventriculoperitoneal shunt for treating obstructive hydrocephalus.

| Study or Subgroup | ETV Events | ETV Total | VPS Events | VPS Total | Weight | Risk Ratio M-H, Fixed, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| kamikawa 2001 | 0 | 0 | 0 | 0 | | Not estimable | 2001 |
| El-Ghandour 2011 | 0 | 32 | 1 | 21 | 15.5% | 0.22 [0.01, 5.21] | 2011 |
| P.Goyal 2014 | 2 | 24 | 2 | 24 | 17.2% | 1.00 [0.15, 6.53] | 2014 |
| Kulkarni 2017 | 4 | 51 | 2 | 49 | 17.6% | 1.92 [0.37, 10.02] | 2017 |
| Navaei 2018 | 0 | 22 | 2 | 27 | 19.4% | 0.24 [0.01, 4.82] | 2018 |
| Rahman 2018 | 0 | 30 | 3 | 30 | 30.2% | 0.14 [0.01, 2.65] | 2018 |
| **Total (95% CI)** | | **159** | | **151** | **100.0%** | **0.64 [0.26, 1.56]** | |
| Total events | 6 | | 10 | | | | |

Heterogeneity: Chi² = 3.77, df = 4 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.99 (P = 0.32)

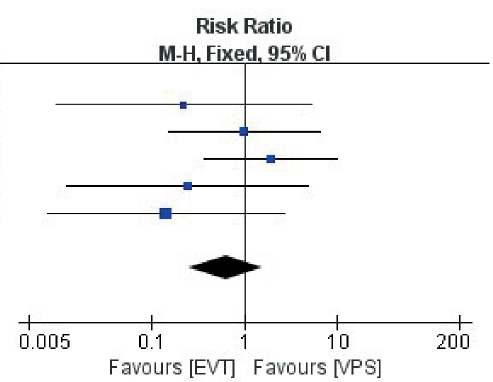


**Figure 5:** Forest plot of mortality rates for endoscopic third ventriculostomy and ventriculoperitoneal shunt for treating obstructive.

### Surgical Success

Surgical success was described as partial or total symptom alleviation or the absence of the need for additional surgery. Five RCTs (9,11,21,27,30) reported the numbers of surgical success (186 out of 285 patients), while the RCT reported by Kamikawa et al. did not (15). The overall success rate was 65.26%. In the pooled dataset, the surgical success rates were not significantly different between ETV and VPS groups (RR: 1.19, 95% CI: 0.81-1.75, *p*=0.38). However, the Chi-squared test revealed that the studies were highly heterogeneous ($I^2$ =76%, *p*=0.002) (Figure 6).

## DISCUSSION

The CSF physiology continues to be actively researched for further understanding of its role in brain function. After being produced by the choroid plexus epithelium in the cerebral ventricles, the CSF flows into the subarachnoid space, and enters the cerebral venous system via the arachnoid granulations in the conventional bulk flow concept. Hydrocephalus is a common abnormality of CSF physiology that causes aberrant enlargement and subsequent dilatation of the cerebral ventricles and/or subarachnoid space. Obstructive hydrocephalus can be of congenital or acquired origins, such as congenital malformation, infection, subarachnoid hemorrhage, tumor and traumatic head injuries, etc. The most prevalent condition addressed by neurosurgeons is hydrocephalus (6).

ETV became a popular alternate treatment for hydrocephalus in the 1990s, particularly in individuals with obstructive hydrocephalus (13). Recently, with the increased use of ventriculoscopes, ETV has become one important surgical method frequently adopted for obstructive hydrocephalus (14). Stenosis and blockage of the midbrain aqueduct as well as obstructive hydrocephalus, caused by space-occupying lesions in the midbrain, pineal region, posterior cranial fossa, or a Chiari malformation, are the most common surgical indications for ETV (5,25,31,34).

Compared to VPS, ETV has the following advantages (7,35). First, ETV has no foreign materials such as shunt, thereby avoiding intracranial infection, abdominal infection, abdominal organ injury and shunt blockage. Second, CSF can flow directly into the interpeduncular cistern after ETV, which conforms to the normal physiological state without excessive drainage. Third, the growth and development of the pediatric patient is not affected by ETV and the patient could avoid the pain caused by multiple tube replacement operations. Fourth, the operation time is short. However, ETV has some limitations, which may cause further obstruction and hydrocephalus. Additionally, complications, such as bleeding, infection, and seizures, may occur during surgery (6,19).

Despite of the aforementioned advantages of ETV and the long history of VPS, the latter currently represents an important treatment for hydrocephalus. VPS is suitable for the majority of hydrocephalus patients, except for hydrocephalus caused by infection and acute hemorrhage (8,36). The procedure is based on the principle that excess CSF in the ventricle could be drained to the abdominal cavity through an artificial silicone tube and absorbed by the strong absorption capacity of the peritoneum.

The optimal treatment for hydrocephalus remains controversial. To date, while many neurosurgeons have performed a large number of clinical procedures and trials, including RCTs, there are not enough trials to determine whether EVT or VPS is more efficacious. Our systematic review and quantitative meta-analysis of six RCTs highlighted the evidence supporting the efficacy and safety of ETV and VPS in patients with obstructive hydrocephalus. In this regard, both surgical methods were widely used to treat obstructive hydrocephalus. In terms of operational mortality and postoperative success rate, our meta-analysis revealed that there were no statistical differences between ETV and VPS. However, each surgical approach has its own benefits in terms of postoperative infection and CSF leakage. In patients receiving ETV, the incidence of postoperative infection was significantly higher than that of patients receiving VPS. In the six RCTs, there were 32 incidences of infection in the VPS group compared to 15 in the ETV group.

The use of implantation materials in VPS, which poses a higher risk of bacterial infection, might be the most plausible

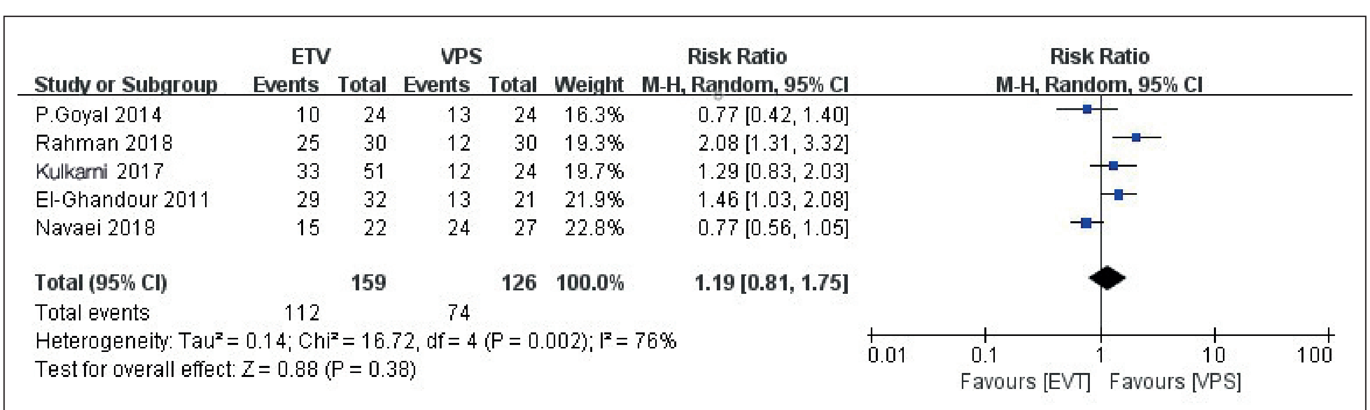


**Figure 6:** Forest plot of postoperative success rates for endoscopic third ventriculostomy and ventriculoperitoneal shunt for treating obstructive hydrocephalus.

explanation for the aforementioned finding. Shunt infection is most common within 3 months following surgery (20,22,24). In a study of nosocomial intracranial infection, van de Beek et al. (38) noted that the detailed planning before, during, and after surgery could reduce the probability of infection after surgery. Shunt fittings, including any implants, should not be placed directly under the normal scalp, which could help reduce the occurrence of infection. Furthermore, some studies (20,37) suggested that double-layer gloves should be considered by the surgeons upon the placement of the shunt tube and the surgeons should not touch the shunt tube with bloody gloves. Such practices are helpful to decrease the occurrence of infection. Antibiotic-containing or hydrophilic-coated catheters could also help reduce the infection risk (16,18,23,29).

Besides the surgical procedures, the immune status of the patient is a major determinant of postoperative infection (39). Infection is less prevalent after ETV than after shunt operations (3). Therefore, the routine use of ventriculoscopes in shunting surgery greatly reduced shunting complications, such as meningitis (15,17). Three RCTs revealed 11 incidences of postoperative CSF leakage that ceased on its own without surgical requirement. The analysis of the pooled data showed that CSF leakage was significantly different between EVT and VPS groups. While neuroendoscopic operations have been highly successful in treating obstructive hydrocephalus, we observed one major neuroendoscopic complication, which is CSF leakage. For example, shunt obstruction is a common cause of VPS failure (32,40). Since the shunt fittings, including related implants, are not involved in EVT, we did not analyze these parameters further in this study. However, our research showed that ETV might minimize the risk of complications in the VPS group, but not in the ETV group, such as slit-like ventricles, skull deformation, excessive drainage, and intestine perforation (15,30). Intraventricular hematoma, subdural hematoma, and epidural hematoma are all types of postoperative hemorrhage that can cause neurological complications (1,2,4,41). Because postoperative hematoma is uncommon, this complication is significantly influenced by many factors, such as the experience of the surgeon and the surgical conditions, which represents a limitation of this study.

There are some other limitations in our meta-analysis. First, the data from the RCTs were extracted from a relatively small sample. Second, due to differences in the etiology, severity, surgical specificity and other subjective and objective factors of hydrocephalus, it is difficult to generate completely randomized double-blind groups in clinical studies. Consequently, the selection biases in these RCTs could not be avoided. Additionally, the interpretation of the results of this study is affected by the absence of publication of studies with negative findings. Therefore, further research is warranted to address these issues. Despite of these flaws, the findings of our study are reliable and may be used to guide future research.

## CONCLUSION

This meta-analysis revealed that there are no significant differences in mortality and surgical success rates between ETV and VPS for obstructive hydrocephalus. However, compared to VPS, ETV has significantly lower incidences of serious complications, such as postoperative infection and CSF leakage, in patients with obstructive hydrocephalus.

**AUTHORSHIP CONTRIBUTION**

Study conception and design: YW, WK, YL, WZ

Data collection: YW, WK, CY

Analysis and interpretation of results: WK

Draft manuscript preparation: WK, CY, YL, WZ, GT

Critical revision of the article: YW, WK, CY, YL, WZ, GT

Other (study supervision, fundings, materials, etc...): YW, WK, CY, WZ, GT

All authors (WK, CY, YL, WZ, GT, YW) reviewed the results and approved the final version of the manuscript.

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