



# Endoscopic Third Ventriculostomy versus Ventriculoperitoneal Shunt in Patients with Obstructive Hydrocephalus: An Updated Systematic Review and Meta-Analysis

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## Abstract

Endoscopic third ventriculostomy (ETV) and ventriculoperitoneal shunt (VPS) are surgical methods for treating obstructive hydrocephalus. However, there is still disagreement regarding the most effective technique, in terms of both operative success and postoperative complications. Therefore, we performed a systematic review and meta-analysis to compare the efficacy and safety of these two methods in patients with obstructive hydrocephalus. We performed a systematic search of the PubMed, Scopus, and Cochrane Library databases. Randomized clinical trials (RCTs) comparing ETV and VPS in pediatric or adult patients with obstructive hydrocephalus were included. The outcomes included were operative success, postoperative cerebrospinal fluid leak, postoperative infection, postoperative or intraoperative bleeding, blockage rate, and mortality. The risk ratio (RR) was calculated with a 95% confidence interval (CI). Heterogeneity was evaluated with  $I^2$  statistics. We used a fixed-effects model for outcomes with  $I^2 < 25\%$  and DerSimonian and Laird random-effects model for other conditions. The Cochrane collaboration tool for assessing the risk of bias in randomized trials was used for risk-of-bias assessment. R, version 4.2.1, was used for statistical analyses. Of the 2,353 identified studies, 5 RCTs were included, involving 310 patients with obstructive hydrocephalus, of which 163 underwent ETV. There was a significant difference in favor of ETV for postoperative infection (risk ratio [RR]: 0.11; 95% confidence interval [CI]: 0.04–0.33;  $p < 0.0001$ ;  $I^2 = 0\%$ ) and blockage rate (RR: 0.15; 95% CI: 0.03–0.75;  $p = 0.02$ ;  $I^2 = 53\%$ ). Meanwhile, there was no significant difference between groups for the postoperative or intraoperative bleeding (RR: 0.44; 95% CI: 0.17–1.15;  $p = 0.09$ ;  $I^2 = 0\%$ ), postoperative cerebrospinal fluid leak (RR: 0.65; 95% CI: 0.22–1.92;  $p = 0.44$ ;  $I^2 = 18\%$ ), operative success (RR: 1.18; 95% CI: 0.77–1.82;

## Keywords

- ▶ endoscopic third ventriculostomy
- ▶ ventriculoperitoneal shunt
- ▶ obstructive hydrocephalus

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$p = 0.44$ ;  $I^2 = 84\%$ ), and mortality (RR: 0.19; 95% CI: 0.03–1.09;  $p = 0.06$ ;  $I^2 = 0\%$ ). Three RCTs had some concerns about the risk of bias and one RCT had a high risk of bias due to the process of randomization and selection of reported results. Thus, this meta-analysis of RCTs evaluating ETV compared with VPS demonstrated that although there is no superiority of ETV in terms of operative success, the incidence of complications was significantly higher in patients who underwent VPS. Our results suggest that the use of ETV provides greater benefits for the treatment of obstructive hydrocephalus. However, more RCTs are needed to corroborate the superiority of ETV.

## Introduction

Hydrocephalus is defined as an abnormal state of production, flow, or absorption of cerebrospinal fluid (CSF), resulting in ventricular dilatation, and increased intracranial pressure (ICP).<sup>1</sup> The last one, however, may not always occur, as in hydrocephalus with normal pressure found in adults.<sup>2</sup> Hydrocephalus can be divided into two categories that present different pathophysiologies: communicating and noncommunicating.<sup>1–3</sup> The causes of noncommunicating hydrocephalus involve, in general, abnormalities in CSF flow due to mechanisms such as infections, tumors, hemorrhages, and surgeries, among others, leading to partial or complete flow obstruction.<sup>1,3</sup>

The treatment of obstructive hydrocephalus for decades has been done by performing a shunt communicating the cerebrospinal system with the peritoneal cavity, a procedure called ventriculoperitoneal shunt (VPS).<sup>1,4,5</sup> However, this procedure is associated with several complications, such as infections and obstructions, which require surgical intervention.<sup>4</sup> In recent years, a debate has arisen regarding the comparison of the risks and benefits of VPS and endoscopic third ventriculostomy (ETV), due to the lower risk of infections, which has already been shown in a previous meta-analysis.<sup>5,6</sup> Thus, the objective of this systematic review and updated meta-analysis is to compare these methods, evaluating clinical results, complications, and mortality associated with both treatments of obstructive hydrocephalus.

## Methods

This systematic review and meta-analysis followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>7</sup> The systematic review and meta-analysis were registered to the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42023389663.

### Search Strategy and Data Extraction

A systematic search was performed in Scopus, Cochrane Central Register of Controlled Trials, and PubMed for randomized clinical trials (RCTs), with the following strategy: (“endoscopic third ventriculostomy” OR “third ventriculostomy” OR “endoscopic third ventriculostomies”) AND (“shunt, ventriculoperitoneal” OR “shunts, ventriculoperito-

neal” OR “ventriculoperitoneal shunts” OR “ventriculo-peritoneal shunt” OR “shunt, ventriculo-peritoneal” OR “shunts, ventriculo-peritoneal” OR “ventriculo peritoneal shunt” OR “ventriculo-peritoneal shunts” OR shunt) AND (“obstructive hydrocephalus” OR obstructive OR hydrocephalus). In addition, references from systematic reviews, meta-analyses, and included studies were evaluated. The selection of studies and data collection were done independently by two authors (E.P. and P.H.S.S.). The characteristics of the studies included were extracted by two independent authors (E.P. and P.H.S.S.). Disagreements were resolved by consensus between the three authors (E.P., P.H.S.S., and F.F.S.S.).

### Selection Criteria and Endpoints

The eligibility criteria for inclusion of the studies comprised were the following: (1) RCTs, (2) comparison of ETV and VPS, (3) patients with obstructive hydrocephalus, and (4) report at least one clinical outcome of interest. We excluded studies characterized by (1) overlapping populations, (2) noninterest groups, and (3) non-RCTs.

The outcomes included were (1) operative success, (2) postoperative CSF leak, (3) postoperative infection, (4) postoperative or intraoperative bleeding, (5) blockage rate, and (6) mortality.

### Data Analysis

We use risk ratio (RR), with 95% confidence intervals (CI), to compare the binary endpoints. The heterogeneity was evaluated with Cochrane  $Q$ -test and  $I^2$  statistics, and we considered  $p > 0.10$  and  $I^2 > 25\%$  for significant heterogeneity.<sup>8</sup> We used a fixed-effect model for endpoints with  $I^2 < 25\%$  and DerSimonian and Laird random-effect model for other conditions.<sup>9</sup> To perform the statistics, we used R Studio software, version 4.2.1 (R Foundation for Statistical Computing).

### Quality Assessment and Sensitivity Analysis

The risk-of-bias assessment followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions, with the Cochrane Collaboration tool, for assessing the risk of bias in randomized trials (Rob-2) with five domains (selection, performance, detection, attrition, and reporting).<sup>10,11</sup>

The RCTs were labeled very low-, low-, moderate-, or high-quality evidence based on the presence of risk of bias, inconsistency of results, imprecision, publication bias, and

magnitude of treatment effects. The quality of evidence was analyzed according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guidelines.<sup>12</sup>

We performed a leave-one-out sensitivity analysis for all outcomes to ensure the stability of the treatment. In addition, we performed a meta-regression analysis for operative success and postoperative infection to assess for any interaction with the age of patients.

## Results

### Study Selection and Characteristics

The initial search found 2,353 results. After duplicates exclusion, studies were screened by the title and abstract, resulting in 14 papers for full-text evaluation. At the end, five RCTs were included in this systematic review and meta-analysis. The selection of studies is detailed in ►Fig. 1.

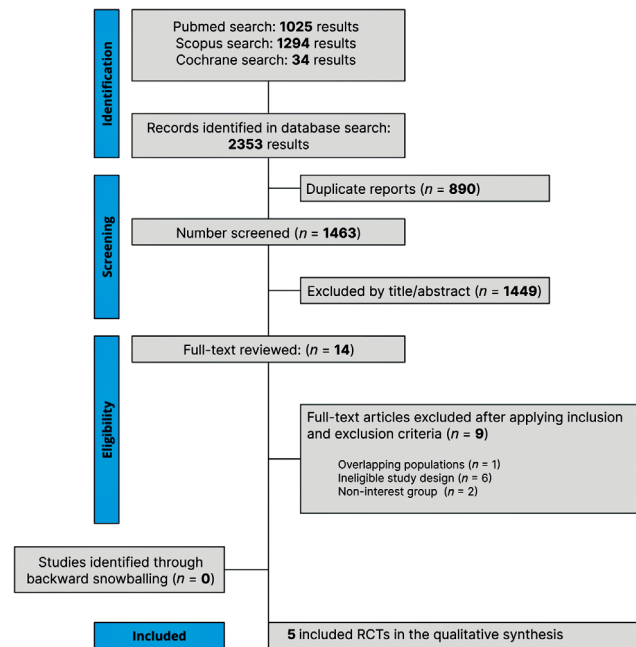
The characteristics of the included studies are reported in ►Table 1. A total of 310 patients were included in the five RCTs. Of these, 163 patients underwent ETV and 147 were treated with VPS. The mean age of the patients ranged from 3.6 months to 32.3 years in the VPS group and 3.91 months to 31.5 years in the ETV group. Only one study did not report the male-to-female ratio.<sup>14</sup> The average follow-up period ranged from 1 and 27.5 months in the ETV group, while in the VPS group it ranged from 1 to 26 months. All analyzed outcomes were reported in at least three studies.

### Operative Success

Four studies reported operative success for both surgical methods, except Kamikawa et al, which showed only the results for ETV patients, which was 75%.<sup>13</sup> There was no significant difference between groups regarding operative success (RR: 1.18; 95% CI: 0.77–1.82;  $p = 0.44$ ;  $I^2 = 84\%$ ; ►Fig. 2A). Meta-regression was performed showing no significant interaction between operative success and age ( $p = 0.94$ ).

### Postoperative Infection

Considering 30 postoperative infections reported in all five RCTs, 93.3% occurred in patients with VPS.<sup>4,5,13–15</sup> There was



**Fig. 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of study screening and selection. RCT, randomized clinical trial.

a significant reduction in the total number of postoperative infections favoring ETV (RR: 0.11; 95% CI: 0.04–0.33;  $p < 0.0001$ ;  $I^2 = 0\%$ ; ►Fig. 2B). The reported infections were ventriculitis, meningitis, and peritonitis. Meta-regression did not show a significant interaction between postoperative infection and age ( $p = 0.45$ ).

### Postoperative or Intraoperative Bleeding

There was no statistical significance between the ETV and VPS groups regarding postoperative or intraoperative bleeding (RR: 0.44; 95% CI: 0.17–1.15;  $p = 0.09$ ;  $I^2 = 0\%$ ; ►Fig. 2C), in accordance with all included studies.<sup>4,5,13–15</sup>

### Blockage Rate

There was a significant increase in blockage ratio in the VPS-treated group (RR: 0.15; 95% CI: 0.03–0.75;  $p = 0.02$ ;  $I^2 = 53\%$ ; ►Fig. 3A). Blockage rate was reported in four

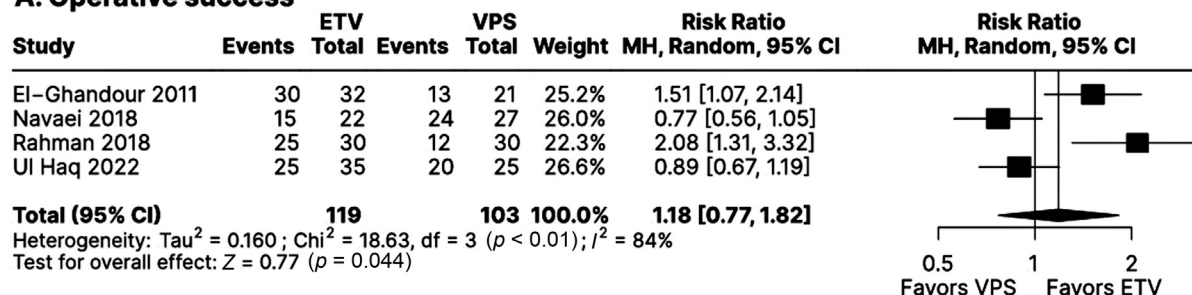
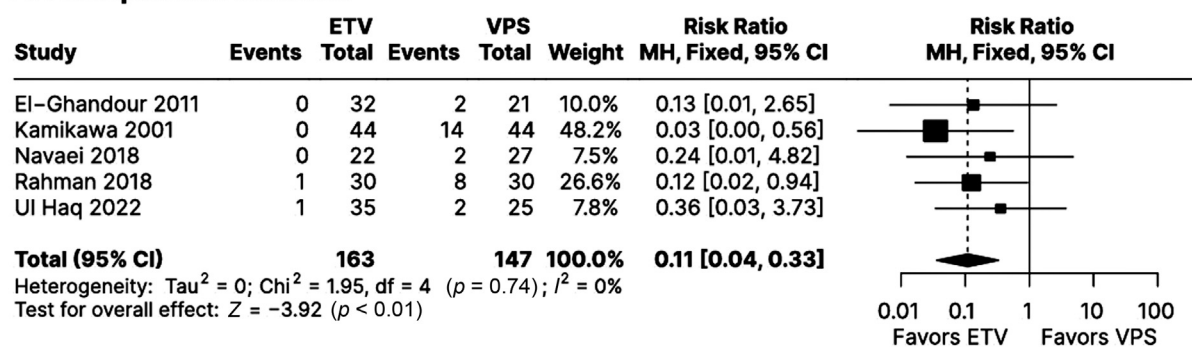
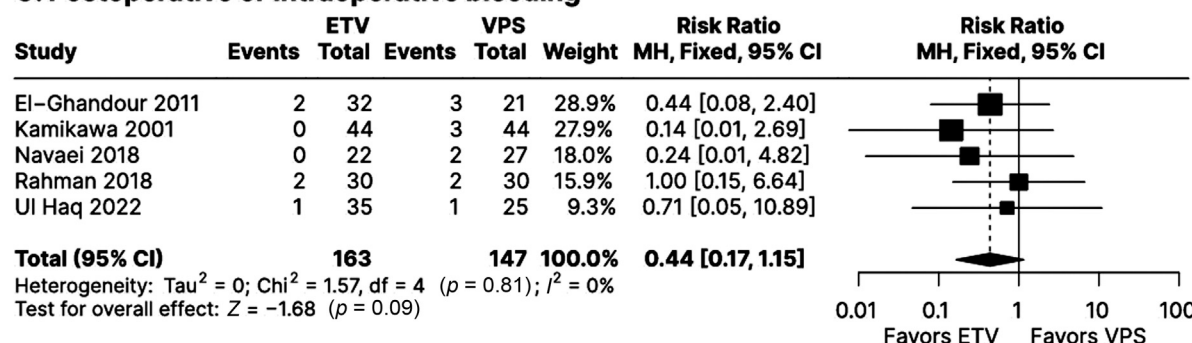
**Table 1** Characteristics of studies included in this systematic review and meta-analysis

Study	No. of patients	Age (y/mo), (mean ± SD)		Male:female		Follow-up (mo)	
	ETV:VPS	ETV	VPS	ETV	VPS	ETV	VPS
El-Ghandour <sup>4</sup>	32:21	6.5 (±2.7) <sup>a</sup>	7.2 (±2.6) <sup>a</sup>	18:14	12:9	27.4	25
Kamikawa et al <sup>13</sup>	44:44	4.47 (±0.73) <sup>a</sup>	4.48 (±0.86) <sup>a</sup>	23:21	25:19	24	26
Navaei et al <sup>5</sup>	22:27	3.91 (±3.34) <sup>b</sup>	3.60 (±2.95) <sup>b</sup>	13:9	19:8	15.22	17.12
Rahman et al <sup>14</sup>	30:30	18.29 (±19.74) <sup>a</sup>	17.24 (±18.56) <sup>a</sup>	NR	NR	1	1
Ul Haq et al <sup>15</sup>	35:25	31.5 (±6.31) <sup>a</sup>	32.3 (±5.46) <sup>a</sup>	17:18	13:12	6	6

Abbreviations: ETV, endoscopic third ventriculostomy; NR, not reported; SD, standard deviation; VPS, ventriculoperitoneal shunt.

<sup>a</sup>Years.

<sup>b</sup>Months.

**A. Operative success****B. Postoperative infection****C. Postoperative or intraoperative bleeding**

**Fig. 2** (A) Operative success. (B) Postoperative infection. (C) Postoperative or intraoperative bleeding. CI, confidence interval; ETV, endoscopic third ventriculostomy; MH, Mantel-Haenszel methods; VPS, ventriculoperitoneal shunt.

studies of this meta-analysis, with 36 cases (83.3%) in the VPS group.<sup>4,13–15</sup> Pooled data showed a 25% shunt block rate in the VPS group.

**Postoperative Cerebrospinal Fluid Leakage**

Three studies showed CSF leakage, with a total of five cases reported in the ETV group and six in the VPS group.<sup>4,14,15</sup> There was no significant difference between the groups for CSF leakage (RR: 0.65; 95% CI: 0.22–1.92;  $p = 0.44$ ;  $I^2 = 18\%$ ; ►Fig. 3B).

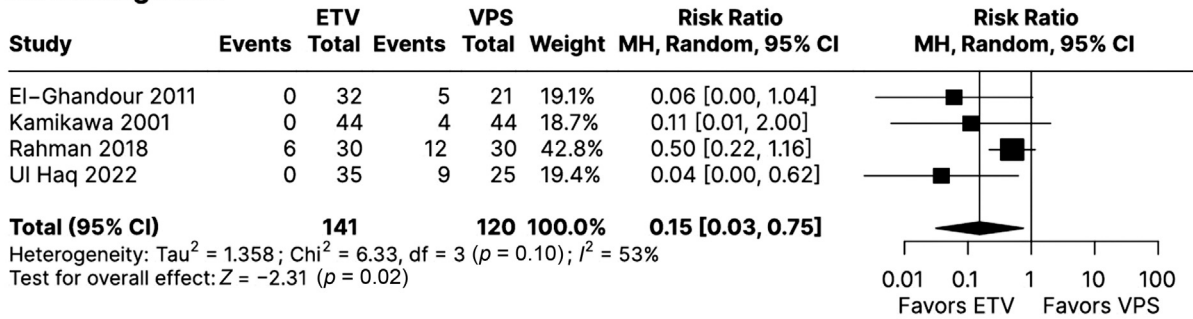
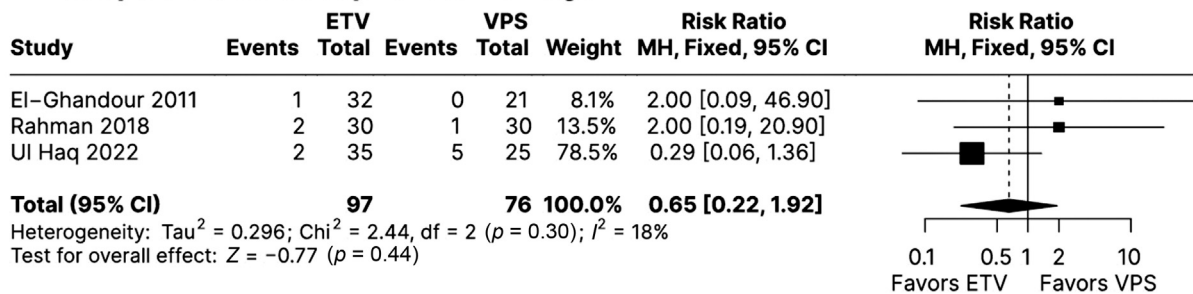
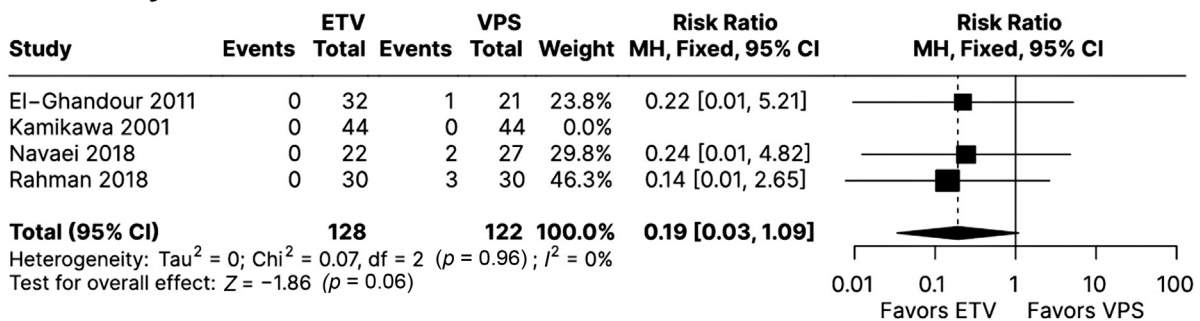
**Mortality**

Four RCTs presented the mortality data.<sup>4,5,13,14</sup> Six deaths were reported, all in the VPS group. There was no significant difference between groups for mortality (RR: 0.19; 95% CI: 0.03–1.09;  $p = 0.06$ ;  $I^2 = 0\%$ ; ►Fig. 3C), although there was a trend in favor of ETV as a protective factor for mortality.

**Quality Assessment**

The critical appraisal is reported in ►Fig. 4. All studies described randomization methods; however, four RCTs had no information about the randomization method and allocation was concealed. Only the study by Navaei et al was considered at low risk of bias for all domains.<sup>5</sup> We considered it unlikely that the absence of blinding trial professionals and participants influenced the results. The study by Kamikawa et al was considered at high risk of bias, as it did not report the complete results for operative success, although it was one of the outcomes proposed by the RCT.<sup>13</sup> The domain with the most concerns found was the randomization process.

According to the GRADE assessment, five outcomes evaluated in this study were classified as very low-quality evidence: CSF leak, postoperative infection, postoperative or intraoperative bleeding, blockage rate, and mortality. The main domains responsible for reducing the quality of

**A. Blockage rate****B. Postoperative cerebrospinal fluid leakage****C. Mortality**

**Fig. 3** (A) Blockage rate. (B) Postoperative cerebrospinal fluid leakage. (C) Mortality. CI, confidence interval; ETV, endoscopic third ventriculostomy; MH, Mantel-Haenszel methods; VPS, ventriculoperitoneal shunt.

evidence of the endpoints were the risk of bias, inconsistency, and imprecision. Quality assessment is detailed in **Supplementary Table S1** (online only).

**Sensitivity Analysis**

We performed a leave-one-out sensitivity analysis. There was no significant difference in blockage rate when omitting El-Ghandour,<sup>4</sup> Kamikawa et al,<sup>13</sup> or UI Haq et al.<sup>15</sup> Sensitivity analysis is reported in **Supplementary Fig. S1** (online only).

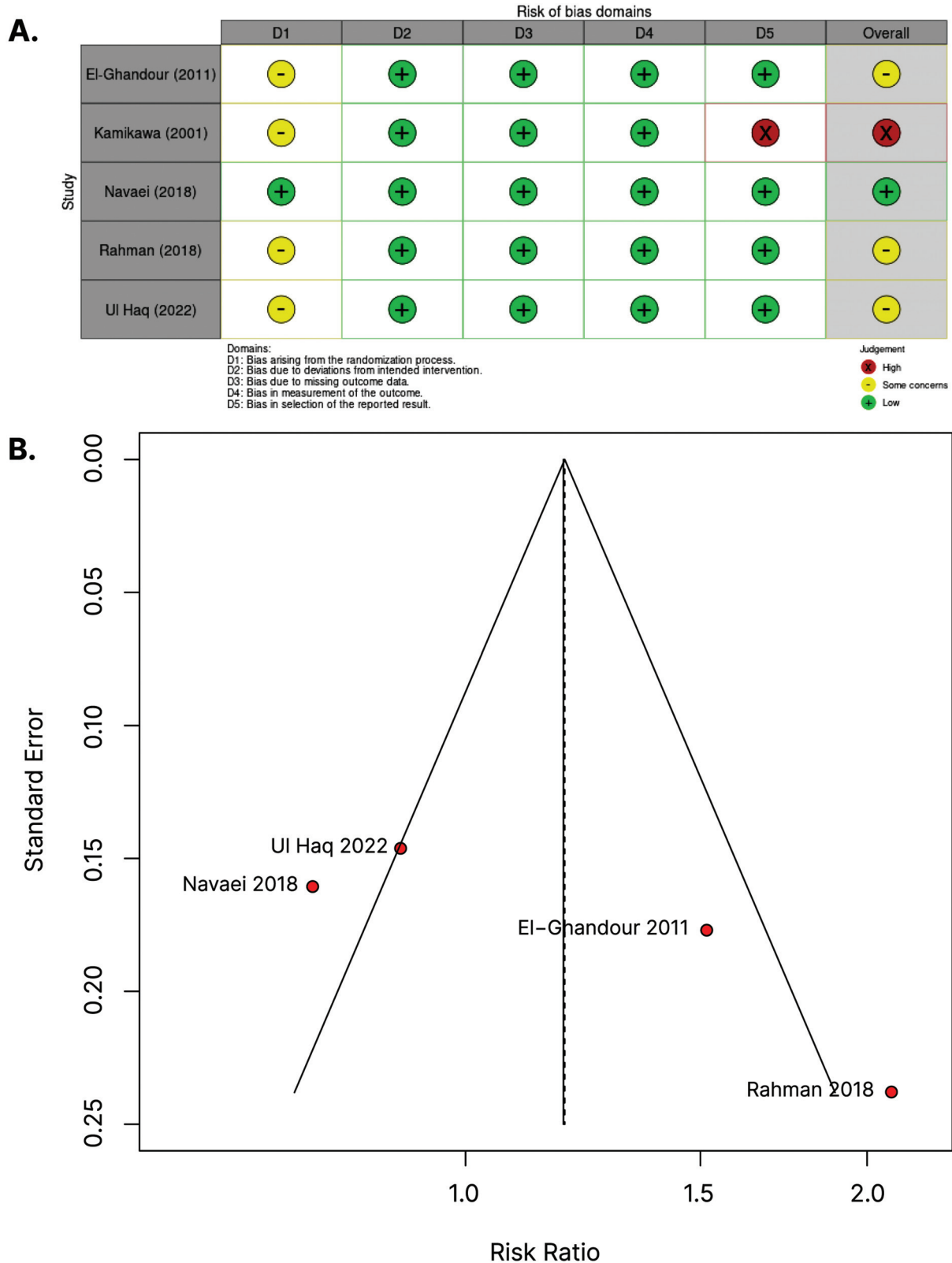
There was a significant reduction in the heterogeneity for the outcome of blockage rate with the removal of Rahman et al,<sup>14</sup> with a reduction in I<sup>2</sup> from 53 to 0%, or UI Haq et al,<sup>15</sup> with a reduction in I<sup>2</sup> from 53 to 36%. This is probably due to the shorter follow-up of these studies. In addition, there was a significant increase in the heterogeneity for the postoperative CSF leakage when omitting El-Ghandour,<sup>4</sup> with an increase in I<sup>2</sup> from 18 to 46%.

**Discussion**

In this systematic review and meta-analysis, we were able to find five eligible RCTs comprising 310 patients with obstructive hydrocephalus submitted to ETV or VPS interventions. Key findings were lower risk of postoperative infections and lower blockage rate in the ETV compared with the VPS group. In addition, there was an 18% relative increase in the risk of operative success with ETV compared with VPS technique, a 56% relative reduction in postoperative or intraoperative bleeding, a 35% relative reduction in the risk of CSF leakage, and an 81% relative reduction in the risk of death in patients who underwent ETV.

Obstructive hydrocephalus refers to obstruction of CSF in the ventricles most commonly due to occlusion of the cerebral aqueduct, colloid cysts, and tumors.<sup>16-18</sup> The obstruction may be proximal (aqueduct or third ventricle) or distal (fourth ventricle and its outflow tracts or foramen





**Fig. 4** (A) Risk of bias according to the Cochrane collaboration tool for assessing risk of bias in randomized trials. (B) Funnel plot analysis of the operative success shows evidence of publication bias.

magnum).<sup>17</sup> Clinically, the symptoms of hydrocephalus are nonspecific and are not necessarily related to the etiology. In children, clinical presentations mainly involve headache, nausea, developmental delay, drowsiness, lethargy,

and behavioral changes, while in adults, papilledema also has clinical importance.<sup>18</sup>

Despite advances in endoscopic techniques and VPS hardware, CSF diversion in the treatment of hydrocephalus

remains one of the greatest challenges in neurosurgery.<sup>19</sup> Shunt techniques were popular in the 1960s, due to the worse morbidity and mortality of endoscopic techniques, with a large number of postoperative complications.<sup>20</sup> Recently, endoscopic techniques involving ETV were developed and improved, becoming the first-line procedure in the treatment of noncommunicating hydrocephalus.<sup>18,20</sup>

The purpose of VPS or ETV is to reduce ICP to improve neurological function.<sup>18,21</sup> ETV is a minimally invasive neurosurgical procedure involving creating a small hole in the floor of the third ventricle, allowing for the CSF to bypass the point of obstruction and flow freely.<sup>18,22</sup> Successful ETV is defined as symptom improvement without the need for new shunts.<sup>18,23</sup> Additionally, advances in endoscopic technology have made the procedure safer and more efficient, with lower complication rates and shorter recovery times.<sup>20</sup> Meanwhile, the VPS is a surgical procedure that involves the placement of a catheter that drains CSF from the ventricles of the brain into the peritoneal cavity, where it is reabsorbed.<sup>20,21</sup> Although there have been significant technological improvements in the VPS, there is still no perfect shunt system available, and managing hydrocephalus in the long term continues to be a major concern due to the various drawbacks associated with shunt malfunction and infection.<sup>20,21,24–26</sup> It is estimated that approximately 40% of shunts fail within 2 years and 98% of shunts fail within 10 years in VPS.<sup>21</sup> However, device type and surgeon or hospital experience do not appear to reduce failure rates.<sup>21</sup>

The main complications of VPS are postoperative infection, bleeding, shunt blockage, and CSF leakage. Of note, in our meta-analysis, significant differences were observed in favor of ETV for postoperative infection and shunt block. These outcomes had already been significantly in favor of ETV in a previous meta-analysis; therefore, our updated meta-analysis strengthens the suggestion of the superiority of ETV compared with VPS in the treatment of obstructive hydrocephalus.<sup>6</sup> The mortality outcome remained with the same result already described in the literature, as the RCT included in this update did not present mortality data.<sup>6</sup> The trend in favor of ETV for postoperative or intraoperative bleeding and mortality possibly reflects a reality that cannot yet be proven due to the limited number of patients in the RCTs. However, the result points toward a better outcome for patients submitted to the ETV procedure.

In our meta-analysis, there were no significant differences between the ETV and VPS groups for postoperative or intraoperative bleeding. El-Ghandour reported two intraoperative minor arterial bleeding in patients who underwent ETV, ceasing without the need to stop the procedure.<sup>4</sup> In the VPS group, two subdural collections (one bilateral and requiring surgical evacuation) and one epidural hematoma were observed, which also required surgical evacuation, totaling three patients with considerable bleeding.<sup>4</sup> Kamikawa et al reported no bleeding in the group that underwent ETV, while there were three intraventricular bleedings in the VPS, without specifying the size, severity, or moment of these bleedings.<sup>13</sup> Navaei et al referred to the occurrence of two intraoperative bleeding in patients who underwent

VPS, resulting in anemia and requiring irrigation and blood transfusion.<sup>5</sup> However, this bleeding occurred due to abnormalities in the dura mater's venous drainage system, with venous sinus under the perforation site.<sup>5</sup> Rahman et al reported that the patients who underwent VPS had one epidural and one subdural bleeding (the latter resulted in death), while in the group that underwent ETV, only two unspecified intraoperative bleedings were observed.<sup>14</sup> Ul Haq et al reported the occurrence of one bleeding in each group of patients.<sup>15</sup> Even though we found no significant difference in intraoperative or postoperative bleeding events, patients who underwent VPS had clinically more severe bleedings, due to a higher occurrence of subdural and epidural hematomas, the need for new interventions, and even one death reported by Rahman et al.<sup>14</sup>

In the previous meta-analysis, there was a significant difference regarding postoperative bleeding.<sup>6</sup> However, some bleedings that were considered postoperative for the previous statistical analysis are inconsistent: the bleeding reported in the VPS group in Navaei et al was intraoperative; the bleeding reported in the ETV group in El-Ghandour was intraoperative and the bleeding reported in the VPS group in Kamikawa et al was not specified.<sup>4–6,13</sup> Since our evaluations were made using intraoperative and postoperative bleeding simultaneously, we found different results in our meta-analysis.<sup>4–6,13</sup>

The RCTs included in this meta-analysis showed differences in the definition of operative success, which may explain the lack of significant results and the high heterogeneity observed for this outcome. El-Ghandour considered the surgery successful if it was fully completed.<sup>4</sup> Kamikawa et al considered success if the patients were not dependent on shunts, had average head growth and CSF flow in the ventricular system, and had no evidence of ICP elevation within 2 years from the procedure.<sup>13</sup> Similarly, Navaei et al considered an operation successful if the patient had no signs of raised ICP within 6 months.<sup>5</sup> Meanwhile, Rahman et al<sup>14</sup> defined success as when the patient had partial or complete relief of symptoms or no need for further surgery, and Ul Haq et al<sup>15</sup> did not present a definition for surgical success.

In our meta-analysis, 5% of patients had CSF leak in the ETV group and 8% in the VPS group. Similar rates of CSF leak have been observed in the management of hydrocephalus in pediatric patients with posterior fossa tumors.<sup>27,28</sup> In addition, previous meta-analyses comparing ETV to VPS have also shown similar rates of CSF leak for the two groups.<sup>6,29</sup>

Our study has limitations: (1) the reduced number of RCTs comparing ETV and VPS, with a small sample, which could lead to potential biases; (2) lack of information regarding the specific causes of obstructive hydrocephalus, which makes it impossible to assess subgroups; (3) different criteria for evaluating outcomes; and (4) heterogeneous age groups included in the meta-analysis, making it unfeasible to assess the effectiveness of a method according to the age of the patients.

Despite the limitations, our systematic review and meta-analysis was able to show that both ETV and VPS procedures are reasonable techniques for the treatment of obstructive hydrocephalus. Nevertheless, although there

was no superiority of ETV concerning operative success, the incidence of complications such as infection and blockage was significantly higher in patients who underwent VPS. Hence, our results suggest that the use of ETV provides greater benefits for the treatment of obstructive hydrocephalus. However, more RCTs are needed to corroborate the superiority of ETV.

#### Author Contributions

All the authors contributed to the design, conduct/data collection, analysis, and writing of the manuscript.

#### Conflict of Interest

None declared.

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