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Impact of Intracranial Pressure Monitoring on Prognosis of Patients With Severe Traumatic Brain Injury

A PRISMA Systematic Review and Meta-Analysis

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Abstract: To evaluate the influences of using intracranial pressure (ICP) monitoring on the prognosis of patients with severe traumatic brain injury.

Systematic search were conducted in PubMed, Embase, Cochrane Library, Wanfang, and CNKI. The eligible studies were identified for pooling analysis under fixed- or random effects model. Hospital mortality, functional outcomes, length of hospital stay, and the related complications in patients were extracted.

Six randomized controlled trials with 880 cases and 12 cohort studies with 12,606 cases were included. Combined analysis found that ICP monitoring was effective for reducing the risk rate of electrolyte disturbances (RR = 0.47, 95% confidence interval (CI): 0.63–0.90), rate of renal failure (RR = 0.50, 95% CI: 0.30–0.83), and for improving favorable prognosis (RR = 1.15, 95% CI: 1.00–1.35). However, ICP monitoring was not significant for hospital mortality (RR = 0.91, 95% CI: 0.77–0.1.06), decreasing rate of pulmonary infection (RR = 0.93, 95% CI: 0.76–1.14), rate of mechanical ventilation (RR = 1.02, 95% CI: 0.86–1.09), and duration of hospital stays (weighted mean difference (WMD) = 0.06, 95% CI: −0.03, 0.16).

ICP monitoring may not reduce the risk of hospital mortality, but plays a role in decreasing the rate of electrolyte disturbances, rate of renal failure, and increasing favorable functional outcome. However, effect of other outcomes need to be further confirmed in the future randomized controlled trials (RCTs) with larger sample size.

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Abbreviations: AIS = Abbreviated Injury Scale, CI = confidence interval, CT = computed tomography, GCS = Glasgow Coma Scale, ICP = intracranial pressure monitoring, NOS = Newcastle-Ottawa scale, OR = odd ratios, RCT = randomized controlled trial, RR = relative risk, SMD = standardized mean difference, TBI = traumatic brain injury, WMD = weighted mean difference.

INTRODUCTION

Despite the fact that the morbidity and mortality have declined every 10 years, traumatic brain injury (TBI) is still a significant cause of death and disability during emergency room visits and hospital stays.[1,2] One severe complications of moderate or severe TBI is the acute increased intracranial pressure (ICP). Approximately 50% of TBI comatose patients with abnormal computed tomography (CT) scan also suffer from high ICP.[3] The ICP elevation could cause interference of blood circulation, decline of perfusion pressure, obstruction of venous reflux, delay of intracranial blood flow, and even brain damage, brain shift, and cerebral hernia.[4] Finally, patients usually died from the secondary brain stem injury.[5] Therefore, early diagnosis and treatment of ICP could significantly improve the prognosis of TBI patients. The ICP monitoring is a method that records the dynamic change of ICP by a pressure monitor or sensor and play it out through a digital signal and image.[6] As ICP cannot be predicted through routine clinical examinations and its dynamic change after severe TBI, ICP becomes an effective tool for its diagnosis and treatment.[7] Several lines of evidences reported that the ICP monitoring could improve the prognosis after severe TBI. A study with 2134 patients found that ICP monitoring could reduce the mortality of severe TBI compared with patients without ICP monitoring.[8] Another study involving 10,628 severe TBI patients confirms that ICP monitoring is associated with lower mortality.[9] A prospective study also suggests that patients managed according to the Brain Trauma Foundation ICP guidelines experienced significantly improved survival.[10] However, some studies report negative reports. A study with a sample size of 1646 shows a higher mortality and worse neurological dysfunctions occurred after ICP monitoring.[11] A retrospective analysis did not find significant difference between the ICP monitoring group and the control group.[12] It is clear that the effectiveness and safety of ICP monitoring remains controversial.

A recent meta-analysis gave a negative finding that TBI patients did not benefit from ICP monitoring.[13] We read this meta-analysis with great interest and found it did not include several important studies, which may reduce the convincingness of this conclusion. Thus, we retrieved the relevant databases, made stricter inclusion and exclusion and conducted a more comprehensive analysis with the aim to provide stronger evidence for clinical practice.

MATERIALS AND METHODS

The ethical approval is not needed because this is a systematic review and meta-analysis of published studies.

Search Strategy

We systematically searched the following electronic databases from initial to May 31, 2015: PubMed, Web of Science,

and 2 Chinese databases (China National Knowledge Internet and Wangfang). The following keywords were used: "ICP monitoring" OR "intracranial pressure monitoring" OR "brain injury" OR "head injury" OR "severe traumatic brain injury." We also retrieved the references in the publications so as not to miss any relevant studies. The search language was limited to English and Chinese.

Inclusion and Exclusion Criteria

All included studies should meet the following criteria: the study design is a randomized controlled trial (RCT), case–control study or cohort study; subject are these patients diagnosed with severe TBI within Glasgow Coma Scale (GCS) < 8 within 24 hours after injury, or in case of no GCS scores, the Abbreviated Injury Scale (AIS) ≧ 3; ICP monitoring was used for severe TBI, and other clinical intervention was used for the control group. One of the following outcome indices for pooled analysis: hospital mortality, functional outcomes, length of hospital stay, and the related complications in patients. These patients (the ICP monitoring group) with GCS > 8 or AIS > 3 or who died within 24 hours were excluded. These studies without enough information were also excluded.

Data Extraction and Quality Assessment

From the studies included in this meta-analysis, we extracted the following information: the first author, publication years, study design, number of patients, age range, sex ratio, in-hospital mortality, favorable outcomes (GOS ≥ 4 or GOS-E ≥ 5), length of hospital stay and related complications. Two researchers collected the above information, and cross-check was conducted to guarantee its accuracy. Any disagreement between them was resolved via judgment from the third researcher. The chance-adjusted interrater agreement for data extraction was substantial (kappa statistic = 0.82; 95% confidence interval (CI): 0.67–0.93).

We used the Newcastle-Ottawa scale (NOS) to evaluate the quality of included cohort study according to Cochrane bias assessment criterion.[14] The NOS scale includes selection (3 questions), comparability (1 question), and outcome (3 question) with 10 cores. We used to Cochrane Collaboration tool to evaluate the quality of RCT. The evaluation tool consisted of the following items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Study with or without 1 or more items was considered to have high-risk bias, low risk and unclear, respectively.

Statistical Analysis

The whole analysis was conducted on Stata 11.0 (College Station, TX). The indices included here was in-hospital mortality, functional outcomes, length of hospital stay, and related complications. The heterogeneity among the studies was evaluated by Cochran Q test and I^2 statistic. $I^2 < 25\%$ is considered low, 25% to 50% is moderate, and >50% is treated as high-level heterogeneity, respectively.[15–17] A random-effect model was used if heterogeneity existed and otherwise, a fixed-effect model was applied. For continuous data, pooled estimation was calculated using the weighted mean difference (WMD) or standardized mean difference (SMD). Odds ratio (OR) was used for categorical variable. Both of them were followed by 95% CI. Sensitivity analysis was also conducted to explore the potential factors of heterogeneity and pooled

estimated stability. Publication bias was evaluated by testing funnel plot asymmetry, Begg test and Egger test. Significance was set at a P-value of less than 0.05. This is a meta-analysis and do not apply the ethic stamens.

RESULTS

Study Selection Flow

Our initial search returned 930 records, of which 595 articles went through abstract screening after exclusion of repetitive publications and reviews, and 62 studies went through full-text review. We got 2 studies from the cited records. Finally, 18 studies, including 6 RCTs[18–23] and 12 cohort studies[8,11,24–33] met the inclusion criteria. The flow chart of screening literatures is presented in Figure 1 and checklist is given, http://links.lww.com/MD/A713 in Table S2, http://links.lww.com/MD/A714.

General Characteristics of Included Studies

All included studies were published from 2000 to 2013. The 6 RCTs included 880 TBI patients (ICP+: 435 and ICP−: 445), 12 cohort studies consisted of 12606 TBI patients (ICP+: 4303 and ICP−: 8303). The rate of men from the included studies ranged from 61% to 95.8%. Although some studies used different criteria for TBI patients, they all used GCS ≦ 8 as the ICP monitoring criteria. All studies report in-hospital mortality. Favorable outcome was presented in 9 studies,[18,21–23,27,30–33] occurrence of renal failure was recorded in 4 studies,[19,21–23] electrolyte disturbance was reported in 3 studies,[19,21,22] pulmonary infection was found in 4 studies,[18,19,21,23] 2 cohort studies gave hospital stays,[11,30] and 2 cohort studies shown the use of mechanical ventilation.[24,25] The general characteristics of the included studies are provided as supplementary materials (Table S1, http://links.lww.com/MD/A714).

Quality of Assessment

Different evaluation criteria were used as the different design. The cohort studies refer to the NOS (see Supplementary materials 3, http://links.lww.com/MD/A714). The score of 12 cohort studies ranged from 6 to 8, and the mean score is more than 7. One study is lack of outcome of ascertainment of exposure, 7 study were lack of length of follow-up, and none have adequacy of follow-up. We used to Cochrane Collaboration tool to evaluate the quality of RCT. The risk bias of 6 RCTs is shown in Figure 2. Two trials were considered to have high-risk bias, and 4 studies were judged to be at unclear risk of bias. Among 6 RCTs, none were double-blinded. But, it is quite difficult to conduct a double-blinded in these trials, and we thought that the lack of blinding may not have effect on the primary outcome. The evaluation results were limited in our opinion.

Pooled Analysis

Different from previous studies that provided the whole rate in all patients or total sample, we also conducted a meta-analysis to estimate different types of rates. Table 1 lists out the occurrence rates of different outcomes, and Table 2 shows the risk difference of different outcomes between the ICP monitoring group and the non-ICP group.

In-Hospital Mortality

Mortality was observed in all studies with 13,486 patients. The meta-analysis shows that the in-hospital mortality rate is 24.6% in all TBI patients, but it is not significantly different
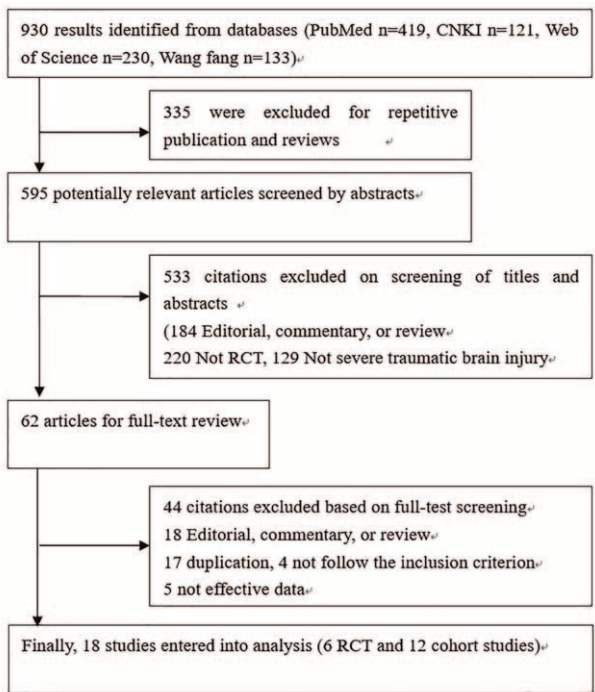
930 results identified from databases (PubMed n=419, CNKI n=121, Web of Science n=230, Wang fang n=133)

335 were excluded for repetitive publication and reviews

595 potentially relevant articles screened by abstracts

533 citations excluded on screening of titles and abstracts
(184 Editorial, commentary, or review
220 Not RCT, 129 Not severe traumatic brain injury)

62 articles for full-text review

44 citations excluded based on full-test screening
18 Editorial, commentary, or review
17 duplication, 4 not follow the inclusion criterion
5 not effective data

Finally, 18 studies entered into analysis (6 RCT and 12 cohort studies)

FIGURE 1. Flow diagram of the study selection process.

between the ICP group and the non-ICP group (22.9% vs 27.2%), with pooled RR = 0.91 (95% CI: 0.77–1.06, Figure 3) in the random-effect model ($I^2 = 71.1\%$, $P = 0.000$). The mortality rates are significantly different between groups in the RCTs (RR = 0.71, 95% CI: 0.86–0.90), but not significant in the cohort studies (RR = 0.98, 95% CI: 0.81–1.19). The heterogeneity within studies and selection of effect model is shown in Table 2.

Favorable Prognosis

There was heterogeneity within studies, so a random-effective model was used ($I^2 = 50.8\%$, $P = 0.039$, Figure 4). The rate of favorable prognosis for all TBI patients is 55.0%, but it is significantly higher in the ICP group versus the non-ICP group (60.3% vs 47.0%). There was no heterogeneity within studies, so a fixed-effective model was used. The ICP group got a 1.15-fold higher prognosis versus the non-ICP group (RR = 1.15, 95% CI: 1.00–1.35).

Renal Failure and Electrolyte Disturbance

The occurrence rate of renal failure for all TBI patients is 12.1%, but it is lower in the ICP group versus the non-ICP group (8.3% vs 17.1%). The difference analysis shows that the risk of renal failure for the ICP group is lower versus the non-ICP group (RR = 0.50, 95% CI: 0.30–0.83, Figure 4) in the fixed-effective model ($I^2 = 0.0\%$, $P = 0.819$). The rate of electrolyte disturbance is 19.2% among all TBI patients, but it is significantly lower in the ICP group versus the non-ICP group (14.1% vs 26.2%). The risk ratio was 0.47, with 95% CI from 0.63 to 0.90 under the fixed-effective model ($I^2 = 0.0\%$, $P = 0.791$). The non-ICP patients tend to suffer from electrolyte disturbance.
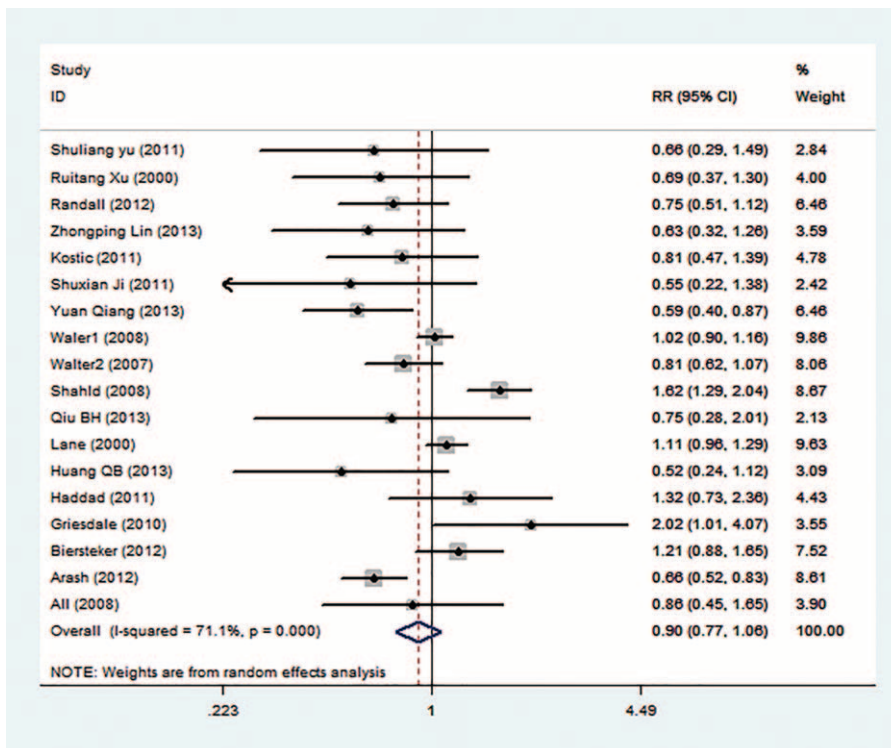

Study ID	RR (95% CI)	% Weight
Shuliang yu (2011)	0.66 (0.29, 1.49)	2.84
Ruitang Xu (2000)	0.69 (0.37, 1.30)	4.00
Randall (2012)	0.75 (0.51, 1.12)	6.46
Zhongping Lin (2013)	0.63 (0.32, 1.26)	3.59
Kostic (2011)	0.81 (0.47, 1.39)	4.78
Shuxian Ji (2011)	0.55 (0.22, 1.38)	2.42
Yuan Qiang (2013)	0.59 (0.40, 0.87)	6.46
Waler1 (2008)	1.02 (0.90, 1.16)	9.86
Walter2 (2007)	0.81 (0.62, 1.07)	8.06
Shahld (2008)	1.62 (1.29, 2.04)	8.67
Qiu BH (2013)	0.75 (0.28, 2.01)	2.13
Lane (2000)	1.11 (0.96, 1.29)	9.63
Huang QB (2013)	0.52 (0.24, 1.12)	3.09
Haddad (2011)	1.32 (0.73, 2.36)	4.43
Griesdale (2010)	2.02 (1.01, 4.07)	3.55
Biersteker (2012)	1.21 (0.88, 1.65)	7.52
Arash (2012)	0.66 (0.52, 0.83)	8.61
All (2008)	0.86 (0.45, 1.65)	3.90
Overall (I-squared = 71.1%, p = 0.000)	0.90 (0.77, 1.06)	100.00

NOTE: Weights are from random effects analysis

.223   1   4.49

FIGURE 2. Risk of bias summary.

TABLE 1. Summary of Prevalence for Different Outcomes in Patients With TBI

Category	Prevalence (95% CI) (%)		
	Overall	**ICP group**	**Non-ICP Group**
Hospital mortality	24.6 [20.8−29.0]	22.9 [18.5−28.0]	27.2 [22.6−32.4]
Favorable prognosis	55.0 [40.1−69.1]	60.3 [47.2−72.0]	47.0 [28.6−66.2]
Renal failure	12.1 [8.4−17.2]	8.3 [5.20−12.9]	17.1 [12.3−23.4]
Electrolyte disturbance	19.2 [9.6−34.8]	14.1 [7.0−26.5]	26.2 [12.7−46.5]
Pulmonary infection	22.5 [6.1−56.5]	21.0 [5.6−54.1]	24.0 [6.4−59.2]
Duration of hospital stays	—		—
Use of mechanical ventilation	93.9 [25.6−99.9]	99.6 [78.7−1.0]	89.3 [22.0−99.6]

ICP = intracranial pressure.

Pulmonary Infection

The rate of pulmonary infection among TBI patients is 22.5%, but it is almost equal between the ICP group and the non-ICP group (21.0% vs 24.0%). The difference analysis shows that ICP monitoring cannot relieve pulmonary infection (RR = 0.93, 95% CI: 0.76–1.14, Figure 4) in the fixed-effective model ($I^2 = 0.0\%$, $P = 0.630$).

Duration of Hospital Stays and Mechanical Ventilation

The ICP monitoring seemingly did not shorten the in-hospital duration for severe TBI patients (WMD = 0.06, 95% CI: −0.03, 0.16, Figure 4). There was no significant difference between 2 groups in the random-effective model ($I^2 = 99.4\%$, $P = 0.000$). The use rate of mechanical ventilation is 93.9% for all TBI patients, and the rates are not significantly different between the 2 groups (99.6% vs 89.3%) (RR = 1.02, 95% CI: 0.86–1.09) under the fixed-effective model ($I^2 = 59.2\%$, $P = 0.117$).

Sensitivity Analysis

We used 2 different ways to perform sensitivity analysis. First, we sequentially excluded individual studies one by one, and the summary RRs were not significantly altered, which indicated that the pooled results were stable (Figure S2, http://links.lww.com/MD/A713). Second, we purposely exclude some studies such study with few sample size, higher weight in the meta-analysis. We compare the original results with the ones with excluding studies, the results also did not change significantly (Table 3).

Publication Bias

Begg funnel plot and Egger tests were performed to evaluate the publication bias of the included articles. We treated the pooled mortality analysis with the most studies as the assessment standard. The Begg test and modified Egger linear regression test indicated that no significant publication bias ($Z = 0.08$, $P = 0.940$; $t = −0.95$, $P = 0.357$, Figure 5).

DISCUSSION

The present meta-analysis consisted of 6 RCTs and 12 cohort studies with a sample size of 13,486 severe TBI patients, which ensures the reliability of the results. The comprehensive analysis found that ICP monitoring for severe TBI patients cannot reduce the mortality of hospital, pulmonary infection rate, use of mechanical ventilation and duration of hospital

TABLE 2. Summary of Different Category Results

Index	No. of Patients	RR (95% CI)	I^2 %	P_{het}*	Effective Model
In-hospital mortality					
All studies	13,486	0.91 [0.773 to 1.06]	71.1	0.000	Random
RCT	880	0.71 [0.563 to 0.90]	0.0	0.980	Fixed
Cohort study	12,606	0.98 [0.813 to 1.19]	78.1	0.000	Random
Favorable prognosis					
All studies	1755	1.15 [1.003 to 1.35]	50.8	0.039	Random
RCT	1168	1.20 [1.003 to 1.42]	0.0	0.676	Fixed
Cohort study	587	1.05 [0.943 to 1.19]	73.8	0.010	Random
Renal failure	495	0.50 [0.303 to 0.83]	0.0	0.819	Fixed
Electrolyte disturbance	324	0.47 [0.633 to 0.90]	0.0	0.791	Fixed
Pulmonary infection	695	0.93 [0.763 to 1.14]	0.0	0.630	Fixed
Duration of in-hospital stays	1911	0.06 [−0.03 to 0.16]	99.4	0.000	Random
Use of mechanical ventilation	4975	1.02 [0.863 to 1.09]	59.2	0.117	Fixed

CI = confidence interval, RCT = randomized controlled trial, RR = relative risk.
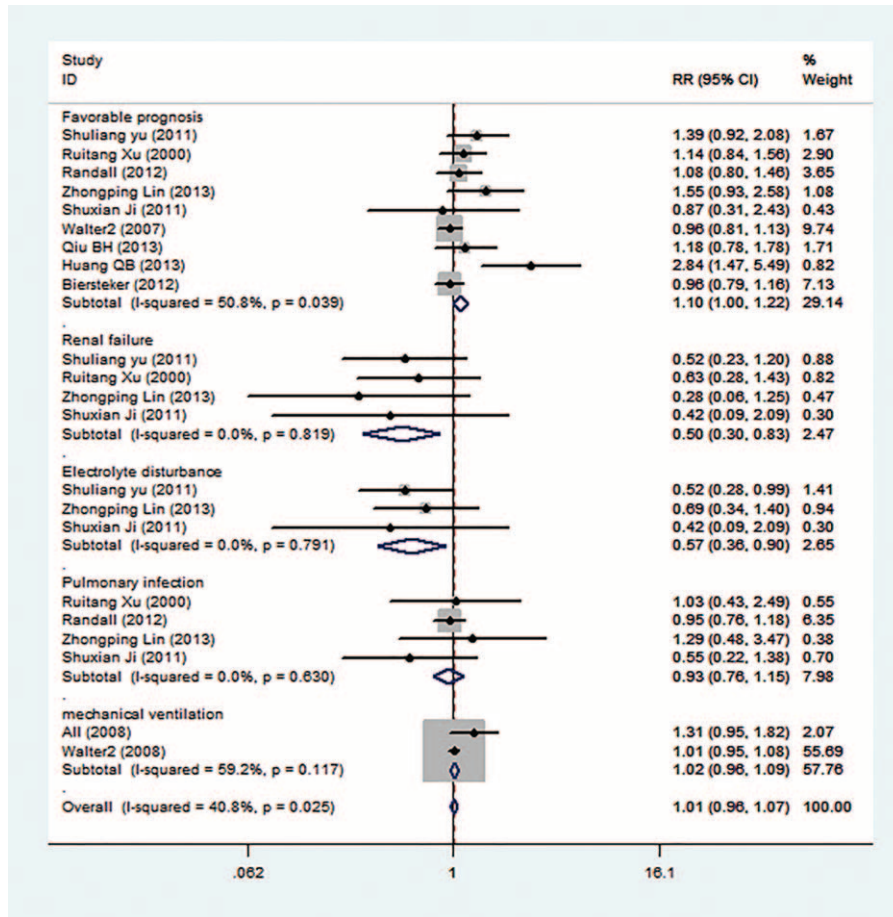* P value for heterogeneity.

FIGURE 3. Forest plot of ICP monitoring in the prevention of mortality.

stays, but lower the occurrence rate of electrolyte disturbance and renal failure and improving prognosis for these patients.

Our results are different from the previous meta-analysis involved fewer studies and smaller sample size.[13] The previous meta-analysis failed to find any benefit in TBI patients from ICP monitoring. Compared with this finding, our study has several strengths. First, we include more comprehensive studies and a

FIGURE 4. Forest plots of ICP monitoring in the prevention of different complications.

larger sample size while the previous study missed 4 RCTs[19,21–23] and 5 cohort studies.[8,30–33] Second, the previous meta-analysis had some shortcomings in statistic methods as it used odds ratio (OR). However, OR is inappropriate for RCTs or cohort studies, which should be evaluated by relative risk (RR).[34] Moreover, the previous meta-analysis directly calculated the mortality of in-hospital and occurrence rates of other outcomes by using the sums of the inputted data. Actually, there are special methods of meta-analysis. The estimator assumes a model of the form: $x[i] = mu + b[i] + e[i]$ in which $b[i]$ is drawn from $N (0, tau^2)$ and $e[i]$ is drawn from $N (0, sigma[i]^2)$. The estimator forms a direct calculation of tau, and uses this to form revised estimates of standard error sqrt $(s[i]^2 + tau^2)$ in x, calculates weights as the inverse of these and in turn calculates a weighted mean, allowing for any calculated excess variance tau^2.[35] Third, the previous meta-analysis found that ICP monitoring could not lower the mortality while we give an opposite result. Although the total synthesis shows no significance, the results only included RCTs found that TBI patients could benefit from ICP monitoring. Considering that RCT is the optimum design to evaluate the effect of intervention, we supposed that the present results are quite reliable. Finally, our study shown some outcome indices that were not mentioned in the previous meta-analysis, and the findings further broaden the potential benefits and support of ICP monitoring. We also noticed that a recent study also reported the Impact of ICP on
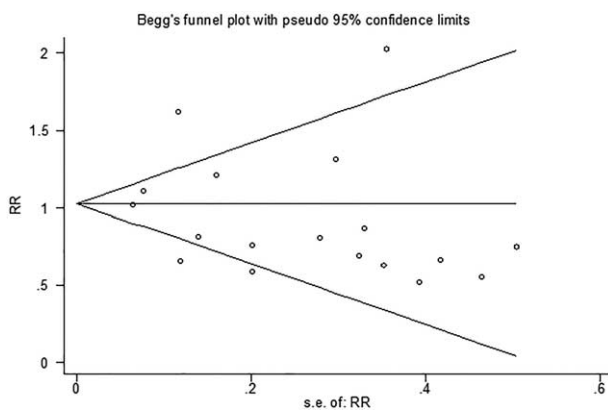
TABLE 3. Sensitivity Analysis of Different Category for Various Outcomes

Index	Excluded Studies	RR (95% CI)	I^2 %	P_{het*}	Effective Model
In-hospital mortality					
All studies	[19–21]	0.94 [0.79–1.11]	74.5	0.000	Random
RCT	[18]	0.68 [0.50–0.92]	0.0	0.60	Fixed
Cohort study	[24,28,30]	1.00 [0.74–1.37]	76.5	0.000	Random
Favorable prognosis	[27]	1.18 [1.04–1.33]	49.4	0.054	Fixed
Renal failure	[19]	0.51 [0.30–0.88]	0.0	0.648	Fixed
Electrolyte disturbance	One by one	No change	—	—	—
Pulmonary infection	[18]	0.88 [0.52–1.49]	0.0	0.431	Fixed
Duration of in-hospital stays	—	—	—	—	—
Use of mechanical ventilation	One by one	No change	—	—	—

CI = confidence interval, RCT = randomized controlled trial, RR = relative risk.

prognosis of patients with brain injury.[36] Our study is different from the recently published studies. The population of published study was limited in all TBI patients, and ours included severe TBI patients. The difference in study population could affect the results. Actually, it indeed has some effects. The published study found no evidences that ICP monitoring overall is significantly superior to no ICP monitoring in terms of the mortality of TBI patients. However, our RCT results found ICP could reduce the mortality of severs TBI patients. Besides, the published only consisted of one outcome (mortality) and the present study reported more comprehensive results.

The previous study has reported that ICP monitoring have good accuracy. The mean error has few influences on ICP measuring results although there are some errors. This may be one of the reasons that ICP monitoring is widely used in clinical practice, especially for TBI patients.[37] Severe TBI usually causes the increase of ICP and reduction of cerebral perfusion pressure[38] The traditional nerve function examination could not predict ICP because of its dynamic change over time. In the past 30 years, we found that the ICP elevation is directly associated with unfavorable outcomes, which highlights the importance of consecutive ICP monitoring.[39] Most scholars agree on the following criteria: IPV = 5 to 15, 15 to 20, 20 to 40, and >40 mmHg indicate normal, slight elevation, moderate elevation, and severe elevation, respectively.[40] In clinical practice, ICP > 20 mmHg is usually treated as the cutoff value of pressure reduction. The Guidelines for Severe TBI Management

VI list the following indications for ICP monitoring: 3 < GSW < 8 after injury, abnormal findings on skull CT; 3 < GSW < 8 after injury, normal skull CT, but meeting 2 or more of the following criteria: age > 40, unilateral or bilateral decorticated syndromes, systolic pressure < 11.97 kPa.[41] The criteria in China are a little different from the above criteria. The Chinese scholars treat ICP ≤ 2.66 kPa as the target for treatment. In spite of the controversy since its appearance, ICP monitoring has been widely used in clinical practice. The rate of ICP monitoring is 77.4% in America, 44.5% in Australia, and 57% in UK.[24,42,43] However, the rate is less than 5% according to the Chinese TBI data from December 2008 to August 2009.[44] Therefore, China has a long way to standardize diagnosis and treatment.

The morbidity and mortality of TBI patients are significant causes of death and disability among the emergency room visits and hospital stays. The present study finds no evidences that ICP could reduce the hospital mortality. The reasons could be the following. First, it is known that patients with ICP monitoring could receive increased treatment interventions according to the acquired information such as oxygen supply. It is possible for these patients to improve outcomes. However, some clinical therapy such as sedation could be related to adverse outcomes. Lack of knowledge could be a confounding factor on the negative results. Second, it is likely that ICP monitoring could benefit a special type of TBI patients. It is a pointcut that the future study should focus on the more specific patterns of TBI patients. Third, it should arouse our attention that there is still a gap from information from ICP monitoring to clinical practice. The interventions usually change with ICP or cerebral perfusion pressure.[45] However, the cutoff values of cerebral perfusion pressure have not been built. The TBI patients could benefit from these regardless of the current findings. Finally, there are some differences between results from observational and RCT. The latter obtained obvious significant findings, but the results still need to be confirmed in the future research because the number of RCT only have 6 studies.

FIGURE 5. Funnel plots of publication bias for mortality.

LIMITATIONS

There are still some limitations in this study. First, our literature search was limited in the online electronic databases and did not include some unpublished data. These unpublished may exert some effect on the results. Second, the study number of electrolyte disturbance and pulmonary infections indeed are
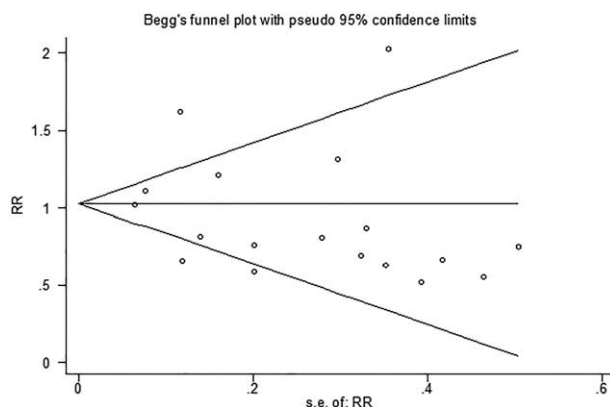
in limited quantities and we admit that there may weaken the reliability of results to some extent. But it is still stronger than a single study. We should be more cautious when explain this point. Third, the sample size of several RCTs was small, and study with larger sample size is needed in the future. Finally, in spite that Begg test and modified Egger linear regression test and indicated that no significant publication bias, the funnel plot shows slight asymmetry. It shown that there existed some publication bias.

CONCLUSION

In conclusion, ICP monitoring may play a role in decreasing the rate of electrolyte disturbances, rate of renal failure, and increasing favorable functional outcome. However, there was no significant effect for reducing the risk of hospital mortality, lowering occurrence rate of pulmonary infection, use of mechanical ventilation, and duration of hospital stays. RCTs with larger sample size are necessary to further support the current results.

ACKNOWLEDGMENT

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