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Incidence of Postoperative Pulmonary Complications in Patients with Brain Tumors: A Systematic Evaluation and Meta-analysis

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Abstract

Background: The incidence of postoperative pulmonary complications in patients with brain tumors currently varies widely among studies worldwide. The aim of this study was to clarify the occurrence of postoperative pulmonary complications in patients with brain tumors worldwide. Methods: We searched all relevant studies published before December 31, 2023 from PubMed, Embase, Web of Science, Cochrane Library and four Chinese databases (CNKI, SinoMed, VIP and Wanfang databases). We screened these studies according to the inclusion and exclusion criteria. Two graduate nursing students screened the studies, extracted data, and independently assessed the risk of bias. Study quality was assessed using the Newcastle-Ottawa scale for study quality and meta-analysis was performed using stata 15.0 software. Results:A total of 27 studies were included. The overall incidence rate of postoperative pulmonary complications in patients with brain tumors is 7.5% [95%CI(0.063, 0.087)]. Subgroup analyses based on region, tumor type, and type of pulmonary complication revealed the highest overall incidence rates as follows: 10.1% [95%CI(0.082, 0.119)] in Asia, 12% [95%CI(0.075, 0.166)] for gliomas, and 15% [95%CI(0.109, 0.191)] for specific pulmonary complications. Conclusion: Our findings indicate that the incidence of postoperative pulmonary complications in patients with brain tumors is notably high, underscoring a significant clinical concern. It is imperative to comprehensively monitor various types of pulmonary complications and prioritize the prevention of these complications in patients with malignant brain tumors.

Keywords

Brain tumor, Pulmonary complications, Incidence.

1. INTRODUCTION

According to statistical data, the incidence rate of brain tumors account for 1.6% of all cancers worldwide, ranking 18th. However, its mortality rate is significantly higher than that of other cancers, ranking 12th and accounting for 2.5% of all cancer-related deaths globally[1]. Surgery is one of the primary methods for treating brain tumor patients, but due to the high difficulty, extended duration, and highly traumatic nature of the procedure, patients often suffer from various complications[2-4]. Among these, postoperative pulmonary complications (PPCs) are the most typical, including respiratory infection, respiratory failure, pleural effusion, atelectasis, pneumothorax, bronchospasm, and aspiration pneumonitis[5]. Research indicates that 68.1% of PPCs occur within the first week following brain tumor surgery. The occurrence of PPCs can delay postoperative recovery, extend the perioperative period, increase hospitalization costs,

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and significantly impact the quality of life and long-term survival outcomes for brain tumor patients[6,7]. Patients may experience symptoms such as dyspnea, chest tightness, shortness of breath, and excessive sputum. Additionally, they may require high-flow oxygen, non-invasive or invasive mechanical ventilation, and reintubation[8-12].The incidence of unplanned reintubation in brain tumor patients following surgery can be as high as 6%[13].Furthermore, PPCs are an independent risk factor for 30-day postoperative mortality in patients with malignant brain tumors.[14]. Therefore, our focus on preventing PPCs in patients with brain tumors assists clinical healthcare workers in providing precise care measures. On the other hand, by studying and publishing the incidence rates of postoperative complications, patients and their families can better understand the potential risks of surgery, aiding them in making more informed decisions preoperatively and cooperating better with the medical team during postoperative rehabilitation. However, the incidence of such complications in these patients remains inadequately understood, with studies worldwide reporting widely varying rates. Consequently, the aim of this systematic review and meta-analysis was to assess the incidence of PPCs in adults diagnosed with brain tumors. The results of this study may enhance clinical healthcare providers' understanding and management of PPCs in these patients, provide foundational data and insights for future research on postoperative complications in brain tumor patients, and promote further research and clinical practice improvements in this field.

2. METHODS

This systematic review and meta-analysis were developed and conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [15]. The protocol for this review was previously developed and registered on the International Prospective Register of Systematic Reviews Platform (PROSPERO CRD42023494641).

2.1. Literature search

PubMed, Embase, Web of Science, Cochrane Library, and four Chinese databases (CNKI, SinoMed, VIP, and Wanfang) were searched to identify studies published up to December 31, 2023, related to the incidence of postoperative pulmonary complications in patients with brain tumors.The search terms included “nervous system OR Central nervous system OR brain tumor OR brain neoplasm OR astrocytoma OR glioma OR glioblastoma OR gliosarcoma OR glioneuronal OR oligodendroglioma OR meningioma OR skull base OR pituitary adenoma OR craniopharyngioma OR prolactinoma OR Cushing disease OR Cushing's disease OR acromegaly OR chordoma OR chondrosarcoma OR nervous system lymphoma OR subependymoma OR ependymoma OR medulloblastoma OR brain metastasis OR brain metastases OR choroid plexus papilloma OR vestibular schwannoma OR acoustic neuroma OR neurilemmoma OR pineal OR germinoma OR hemangioma OR hemangioblastoma OR hemangiopericytoma OR neurocytoma OR xanthroastrocytoma” And “Pulmonary complications OR pulmonary infection OR pneumonia OR atelectasis OR acute respiratory distress syndrome OR pleural effusion OR respiratory failure OR bronchospasm” And “risk factors OR risk factor OR relevant factors OR influencing factor OR incidence OR predictor.” Table 1 shows the search strategy in the PubMed database.

2.2. Inclusion and exclusion criteria

The inclusion criteria were as follows: participating population—patients with a definitive diagnosis of a brain tumor, aged ≥18 years; type of study—observational, including cross-sectional, cohort, or case-control studies; outcome—a study of the incidence or factors influencing PPCs in patients with brain tumors. The following types of records were excluded: reviews, conference papers, studies with inability to extract data or incomplete data, inability

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to access full text, duplicate publications, non-Chinese and non-English literature, and studies with a Newcastle-Ottawa Scale score below 7.

2.3. Data extraction

Literature screening was independently performed by two researchers based on the inclusion and exclusion criteria. Initially, the titles and abstracts of the studies were reviewed to exclude those that did not meet the inclusion criteria. If eligibility could not be determined from the title and abstract, the full text was downloaded for further assessment, and the results were cross-checked. Data extraction was conducted independently by the two researchers using a pre-formulated Excel 2019 data extraction form. The extracted data included the first author, year of publication, study area, patient diagnosis, sample size, type of pulmonary complication, and incidence. In cases of disagreement, a third researcher was consulted to reach a consensus.

2.4. Statistical analysis

Data were analyzed using Stata 15.0. The primary outcome of the included studies was the incidence of PPCs, and the statistical results were analyzed using odds ratios (OR) and their 95% confidence intervals (CI). The heterogeneity of the included studies was assessed using the Chi-squared (X^2) test combined with the I^2 statistic, with a significance level of $\alpha=0.10$. If $P<0.10$ and $I^2>50\%$, a random-effects model was used for the meta-analysis; otherwise, a fixed-effects model was applied. To explore the sources of heterogeneity, subgroup analyses were conducted based on study area, type of PPCs, and tumor type.

2.5. Quality assessment

The risk of bias in the literature was evaluated independently by two researchers. The Agency for Healthcare Research and Quality (AHRQ) criteria were used to assess the quality of cross-sectional studies, categorizing scores of 0 to 3 as low quality, 4 to 7 as moderate quality, and 8 to 11 as high quality. The Newcastle-Ottawa Scale (NOS) was employed to evaluate the quality of case-control and cohort studies, with scores of 0 to 4 indicating low-quality literature, 5 to 6 indicating medium-quality literature, and 7 to 9 indicating high-quality literature. In cases of disagreement during the quality assessment, a third researcher was consulted to reach a consensus.

2.6. Publication bias

Publication bias was analyzed using Begg's test in combination with Egger's test, with $P<0.05$ considered indicative of a statistically significant difference.

2.7. Sensitivity analysis

Studies will be excluded on a case-by-case basis to examine the robustness of the results and to determine whether any particular study significantly impacts the overall findings or contributes to heterogeneity.

3. RESULTS

3.1. Study selection

The initial search yielded a total of 3,537 documents, from which 610 duplicates were excluded. Preliminary screening of titles and abstracts resulted in the exclusion of 2,880 articles. Subsequent full-text screening excluded an additional 20 articles, leaving 27 articles for final inclusion. The search results are illustrated in Figure 1.

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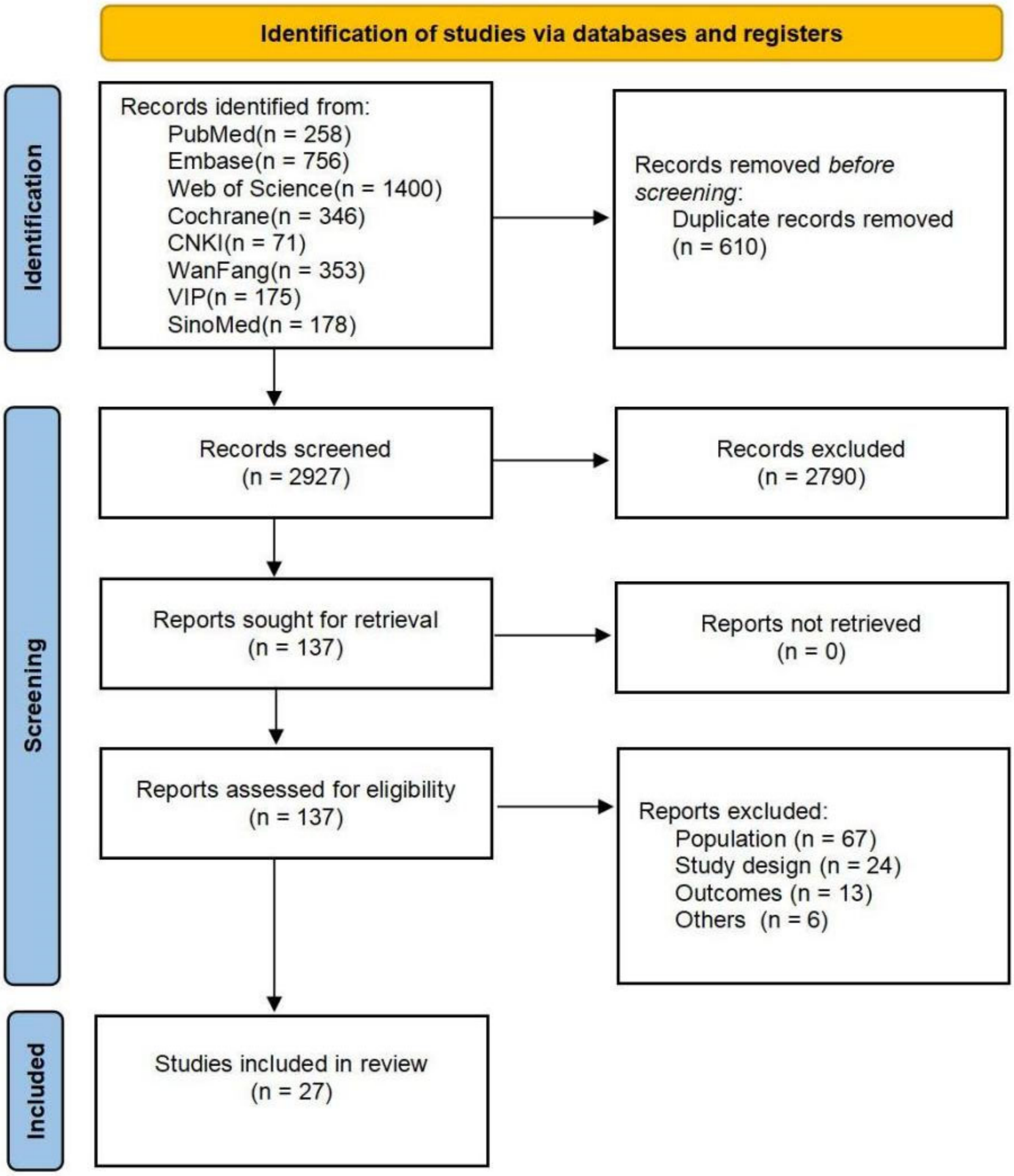

Figure 1. Search results

3.2. Characteristics of the studies

The included studies were published between 2010 and 2023. Eighteen studies were conducted in China, four in the United States, two in Germany, one in Norway, one in Canada, and one in India. The sample sizes of the included studies ranged from 82 to 28,700 participants. The study and participant characteristics are detailed in Table 1.

3.3. Incidence of PPCs

3.3.1 Overall incidence rate

The meta-analysis revealed that the overall incidence of PPCs in patients with brain tumors was 7.5% [95%CI(0.063,0.087), I2=96.2%,P<0.001]. Detailed meta-analysis data are presented in Figure 2.

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Table 1. Study and participants characteristics

Study	Year	Country	Type of study	N	Dypshagia/ non-dypshagia	Diagnosis	Types of Pulmonary Complications	Quality assessment
Fu[16]	2022	China	Case–control study	310	46/264	chordoma	Pulmonary Complications	8
Li[17]	2021	China	Case–control study	108	23/85	brain tumor	Pulmonary Complications	9
Hooda[18]	2019	India	Case–control study	288	35/253	brain tumor	Pulmonary Complications	7
He[19]	2023	China	cross-sectional study	8663	828/7835	brain tumor	pneumonia	7
Guo[20]	2022	China	cross-sectional study	598	77/521	meningioma	pneumonia	7
Huang[21]	2022	China	Case–control study	863	28/835	Vestibular Schwannoma	pneumonia	8
Zhao[22]	2022	China	cross-sectional study	372	18/354	brain tumor	pneumonia	7
Ahmeti[23]	2021	Germany	Case–control study	768	11/757	meningioma	pneumonia	7
Gupta[24]	2021	USA	Case–control study	3500	140/3360	brain metastases	pneumonia	8
Monden[25]	2021	Germany	Case–control study	421	18/403	meningioma	pneumonia	8
Alkins[26]	2021	Canada	cross-sectional study	1456	112/1344	Vestibular Schwannoma	pneumonia	7
Chen[27]	2020	China	cross-sectional study	282	18/264	meningioma	pneumonia	8
Deng[28]	2020	China	Case–control study	321	44/277	meningioma	pneumonia	7
Longo[6]	2019	USA	Case–control study	28700	1161/27539	brain tumor	pneumonia	7
Zuo[29]	2019	China	Case–control study	1156	51/1105	meningioma	pneumonia	9
Viken[12]	2018	Norway	Case–control study	1291	69/1222	brain tumor	pneumonia	8
Wang[30]	2017	China	Case–control study	244	29/215	Vestibular Schwannoma	pneumonia	8
Oh[31]	2014	USA	Case–control study	464	6/458	meningioma	pneumonia	7
Sughrue[32]	2011	USA	Case–control study	834	11/823	meningioma	pneumonia	7
Li[33]	2023	China	Case–control study	961	52/909	brain tumor	pulmonary infection	8
Yang[34]	2023	China	Case–control study	553	56/497	brain tumor	pulmonary infection	7
Zhang[35]	2022	China	Case–control study	273	24/249	glioma	pulmonary infection	8
Zhao[36]	2022	China	cross-sectional study	120	18/102	glioma	pulmonary infection	8
Chen[37]	2021	China	Case–control study	102	15/87	glioma	pulmonary infection	8
Ren[38]	2021	China	Case–control study	82	15/67	brain tumor	pulmonary infection	9
Zhang[39]	2018	China	Case–control study	299	48/251	brain tumor	pulmonary infection	9
Zeng[40]	2010	China	Case–control study	320	18/302	meningioma	pulmonary infection	7

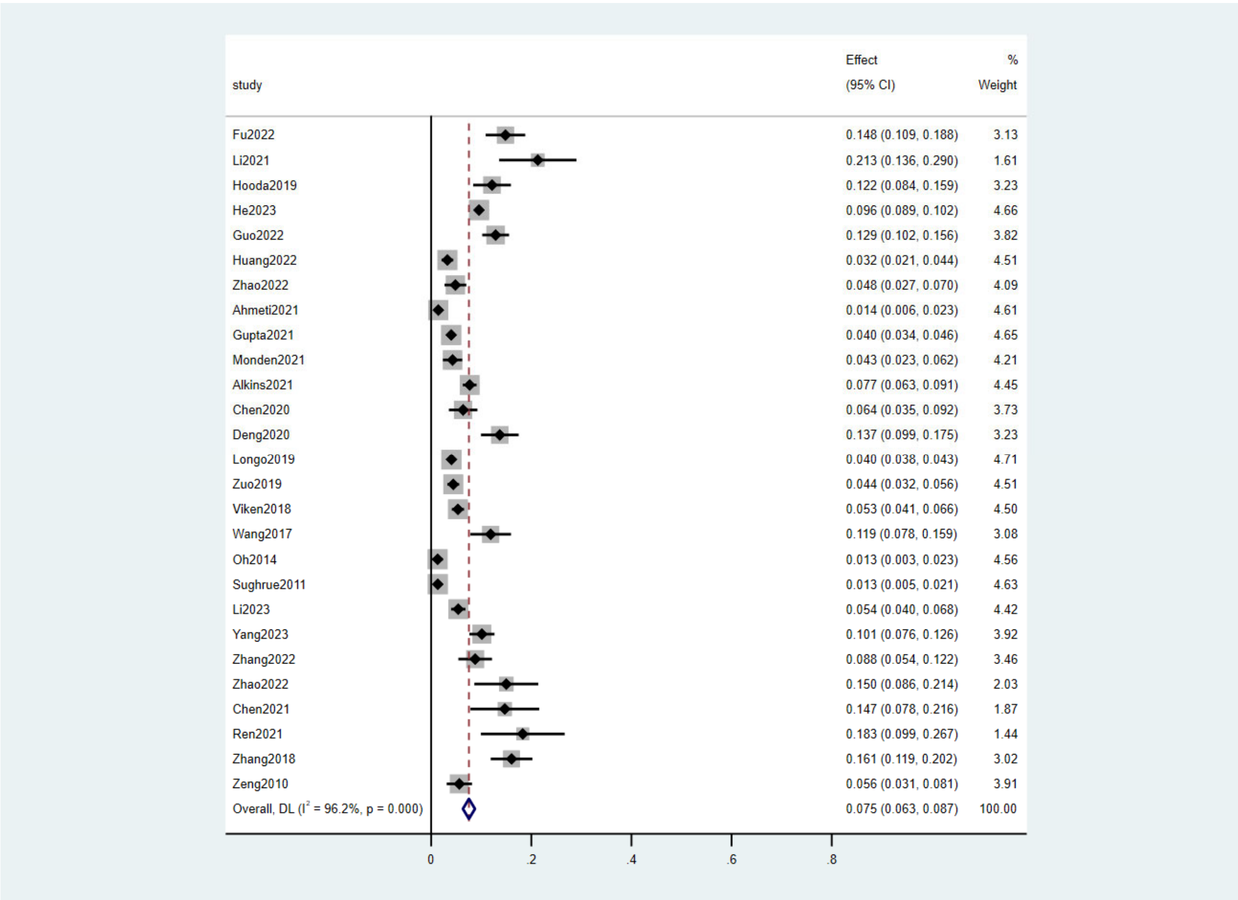

Figure 2. Incidence of postoperative pulmonary complications

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3.3.2 Incidence rate of subgroup analysis

Meta-analyses of the incidence of PPCs were performed according to the study area, type of PPCs, and tumor type. The results of the subgroup analysis are shown in Table 2.

Table 2. Subgroup analysis results

Subgroup analysis	Inclusion in the study	Results of heterogeneity test		Meta-analysis results	
		I2(%)	P	incidence(%)	95%CI
Region					
Asia	19	92.2	<0.001	10.1	(0.082, 0.119)
Europe	3	93.1	<0.001	3.6	(0.009, 0.064)
North America	5	95.9	<0.001	3.6	(0.021, 0.051)
Tumor category					
brain tumor	10	97.5	<0.001	9.3	(0.069, 0.117)
meningioma	9	94.2	<0.001	5.3	(0.033, 0.072)
glioma	3	53.2	0.118	12	(0.075, 0.166)
vestibular nerve sheath tumor	3	94	<0.001	7.2	(0.031, 0.113)
Complications category					
Pulmonary Complications	3	55.2	0.107	15	(0.109, 0.191)
pneumonia	16	97.1	<0.001	5.6	(0.042, 0.071)
pulmonary infection	8	85.1	< 0.001	10.8	(0.077, 0.138)
Region					
Asia	19	92.2	<0.001	10.1	(0.082, 0.119)
Europe	3	93.1	<0.001	3.6	(0.009, 0.064)
North America	5	95.9	<0.001	3.6	(0.021, 0.051)
Tumor category					
brain tumor	10	97.5	<0.001	9.3	(0.069, 0.117)
meningioma	9	94.2	<0.001	5.3	(0.033, 0.072)

3.4. Sensitivity analysis

Studies in which the outcome indicator was the incidence of PPCs were excluded one by one for sensitivity analysis. The results showed no significant change in the combined effect size, suggesting a relatively stable outcome. The results of the sensitivity analysis are presented in Figure 3.

3.5. Publication bias

Stata 15.0 software was used to analyze publication bias, and the results showed significant bias as indicated by Begg's test (Z=3.23,P=0.001) and Egger's test (Z=3.056,P=0.015). These results suggest the presence of potential bias in the study. The results were corrected using the trim-and-fill method, and after three iterations using the linear method, the software estimated that nine studies were missing. The combined results, using a random-effects model, were [1.049,95%CI(1.036,1.061)], with a significant Z-value (Z=7.907,P<0.001). The heterogeneity test (Q=878.820,P<0.001) indicated that publication bias did not alter the meta-analysis results, confirming the reliability of the conclusions. The results of the trim-and-fill method are shown in Figure 4.

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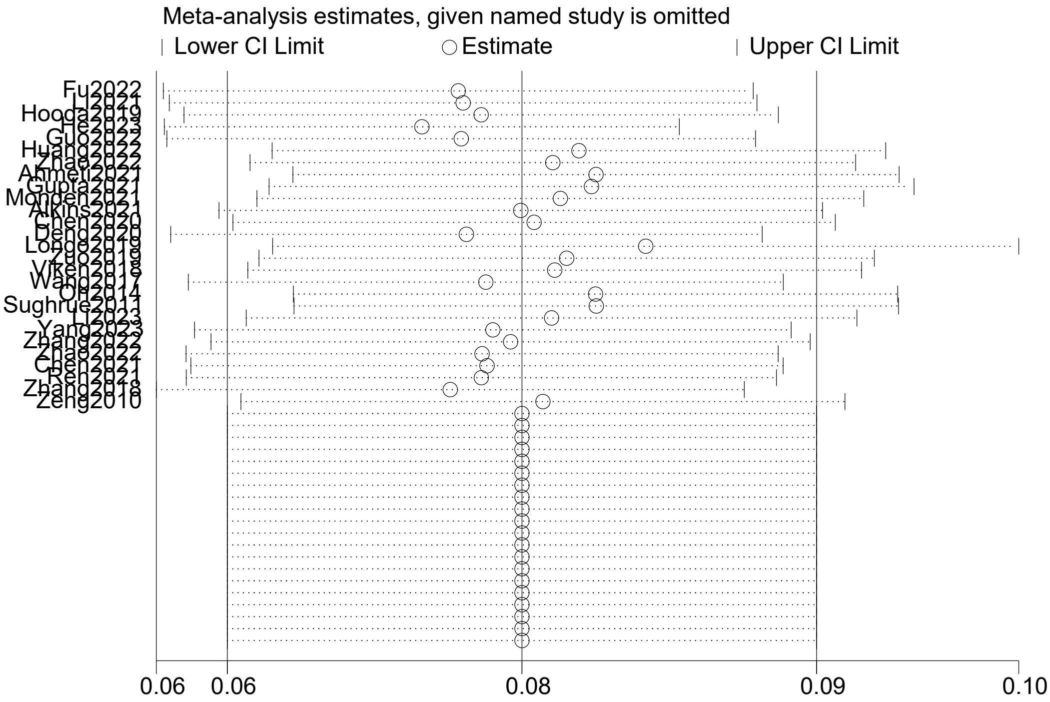

Figure 3. Sensitivity analysis

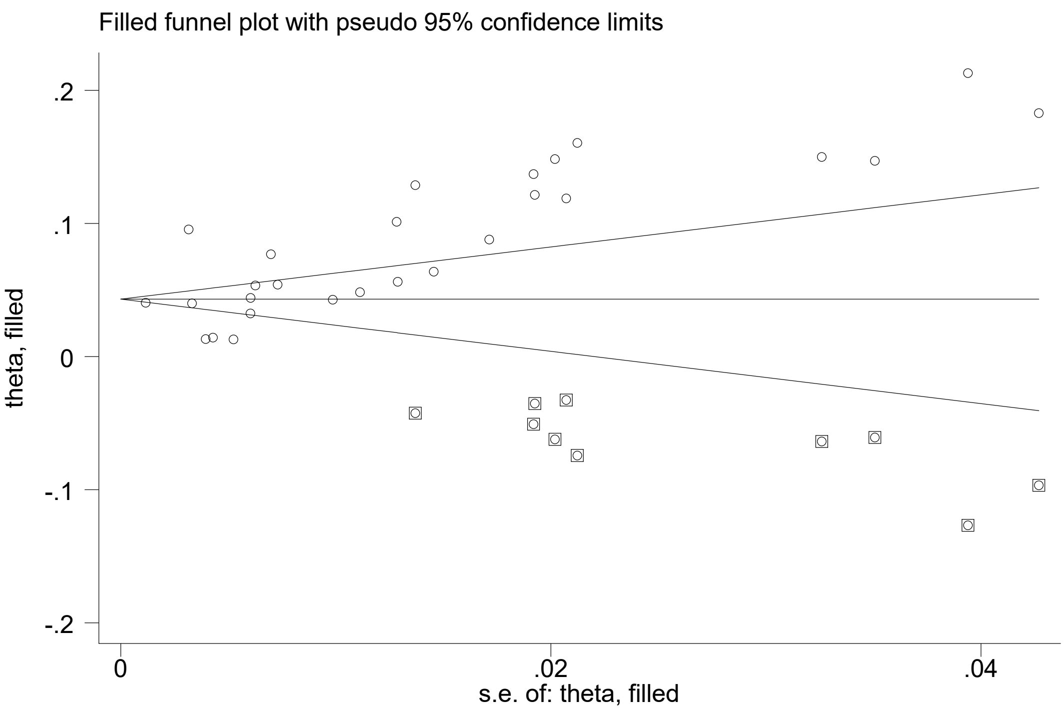

Figure 4. The results of the shear-patch method

4. CONCLUSION

Among postoperative brain tumor patients, the overall incidence rate of PPCs is relatively high, ranging from 1.3% to 21.3%.[17,31]. Through the collection and analysis of data, the overall incidence of PPCs in postoperative brain tumor patients was determined to be 7.5%, which is higher than the incidence rates of other postoperative complications.[41]. The high incidence rate of PPCs is associated with various factors. Firstly, the specific location of the brain

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tumor and the complexity of the surgery may increase the risk of complications. In particular, infratentorial neurosurgery, due to its unique anatomical location and potential impact on the brainstem, is often linked to delayed extubation, respiratory failure, and even death[42,43].Additionally, the duration of surgery is correlated with the occurrence of PPCs in patients with brain tumors. Among neurosurgical patients whose procedures exceed 300 minutes, the incidence of PPCs is 28.4%[44].Numerous studies have demonstrated that intraoperative lung-protective ventilation strategies effectively reduce the incidence of PPCs. However, due to the need to control elevated intracranial pressure following brain surgery, these strategies are cautiously implemented to ensure they do not compromise cerebral oxygenation or cause fluctuations in intracranial pressure[45,46].

The region-based subgroup analysis results indicate that the incidence of PPCs in brain tumor patients is significantly higher in Asian countries compared to European and North American countries. China (n=18,66.7%), the United States (n=4,14.8%), and Germany (n=2,7.4%) have published the highest number of studies on this topic. The higher number of studies from China can be attributed to the specific inclusion of Chinese databases in this research. Since 2009, the Central Brain Tumor Registry of the United States (CBTRUS) has been updating its survey results on primary brain and other central nervous system tumors diagnosed in the United States.[47]. However, a report from 17 cancer registries across China, covering a decade (2003 to 2013), recorded only 10,391 cases of brain tumors[48]. The first multi-hospital-based Chinese Brain Tumor Registry was established in January 2018, reporting 12,768 brain tumor cases in just the period from 2019 to 2020[49]. Consequently, the establishment of this registry represents a significant advancement in brain tumor monitoring and research in China, thereby facilitating related studies by Chinese scholars. Additionally, other developing countries have analyzed the treatment and care of their brain tumor patients, discovering that extended hospital stays, ICU admissions, and postoperative complications significantly increase treatment costs. The implementation of digital referrals through multidisciplinary neuro-oncology triage teams can mitigate postoperative complications and reduce overall treatment expenses[50].

Subgroup analysis of brain tumor types revealed that the overall incidence of PPCs in glioma patients is 12%, a rate higher than that observed in patients with other types of tumors. According to the fifth edition of the World Health Organization Classification of Tumors of the Central Nervous System, gliomas are typically graded between 2 and 4, while meningiomas are graded between 1 and 3[51]. Investigative studies found that gliomas accounted for 26.3% of all brain tumors. Glioblastomas, a subtype of gliomas, represented 61.5% of gliomas and 50.9% of all malignant brain tumors. Meningiomas accounted for 40.8% of all brain tumors and 56.2% of all non-malignant brain tumors.[47,52]. Vestibular Schwannoma account for 9.09% of all brain tumors, and more than 90% of patients with these tumors experience ipsilateral sensorineural hearing loss.[49,53].Concurrently, a prospective study revealed that surgeries for meningiomas and gliomas constituted 31.1% and 28.2% of brain tumor surgeries, respectively[54]. The malignancy of brain tumors, along with their high incidence and pronounced symptoms, has garnered significant attention from scholars worldwide towards gliomas, meningiomas, and Vestibular Schwannoma. The meta-analysis results indicate that, due to the highly invasive and malignant nature of gliomas and the high incidence of pulmonary complications, it is essential to address and prevent postoperative pulmonary complications in glioma patients from multiple perspectives. Besides surgical factors, the study identified an association between serum biomarkers (including lactate dehydrogenase, matrix metalloproteinases, and insulin-like growth factors) and postoperative pulmonary infections in glioma patients[35,36].Additionally, the substantial treatment costs, poor quality of life, and low survival rates of glioma patients are critical issues that necessitate the attention of clinical healthcare professionals.

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Subgroup analysis of PPCs types indicated that the overall incidence of PPCs is 15%, a rate higher than that of any single type of PPCs. This may be attributed to the inclusion of a broader range of PPCs. Furthermore, two of the included studies involved tumors located at the skull base, where tumor compression of cranial nerves can lead to preoperative neurological dysfunction, resulting in swallowing difficulties and weakened pharyngeal reflexes[16,18]. As the definition of PPCs becomes increasingly clear, it is evident that while pneumonia is widely recognized as a postoperative adverse event significantly impacting patient prognosis, other types of PPCs may also have important effects on patient recovery and long-term outcomes[5]. Prolonged intraoperative anesthesia and the use of mechanical ventilation can result in alterations in respiratory muscle function and reduced lung capacity. This is particularly evident with endotracheal intubation, which can impair mucociliary clearance in the airways. Atelectasis occurs in 75% of patients following the administration of neuromuscular blocking agents, with respiratory function potentially taking up to six weeks to return to preoperative levels[55,56]. Research has found that during anesthesia for brain tumor surgery, individualized positive end-expiratory pressure (PEEP) ventilation, while ensuring adequate cerebral oxygenation, effectively reduces the incidence of postoperative atelectasis[57]. Existing literature on the incidence of PPCs primarily focuses on pneumonia and other infections. If these conditions worsen, they can lead to respiratory failure or even death[55]. Early identification, intervention, and prevention of PPCs are therefore crucial in reversing adverse outcomes in patients with brain tumors.

5. LIMITATIONS AND FUTURE IMPLICATIONS

Despite a comprehensive review of the literature on PPCs in patients with brain tumors, this study has several limitations. First, the study included only literature in Chinese and English, predominantly from studies conducted by Chinese researchers, which may introduce bias. Additionally, variations in diagnostic criteria for PPCs across studies and the limited types of complications considered may affect the results. Finally, factors such as sample size, location, research methods, and specific variables or conditions may also influence the outcomes. Future research should aim to include a broader range of databases and larger sample sizes to address the limitations of this meta-analysis.

6. CONCLUSION

Our findings indicate that the incidence of PPCs in patients with brain tumors is notably high, underscoring a significant clinical concern. These subgroup analyses elucidate differences in PPCs among various populations and form a basis for developing more targeted prevention and treatment strategies. It is imperative to comprehensively monitor various types of pulmonary complications and prioritize the prevention of these complications in patients with malignant brain tumors.

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