Review

Surgical resection for multiple brain metastases: a systematic review and meta-analysis of functional and survival outcomes

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Abstract

Background. Brain metastases (BMs) are the most common intracranial tumors among adults, which exceed primary brain tumors by far. Surgery and radiotherapy represent the key local management of BM. However, the exact role of surgery is still under debate.

Objective. To comprehensively evaluate the safety and efficacy of surgical management in patients with brain metastases.

Methods. We searched four electronic databases from January 2023 until September 2024 (PubMed, Scopus, Web of Science, and Cochrane Library). All the studies assessing the role of surgery in managing BM were included. Our primary search targets were survival, mortality, and postoperative Karnofsky Performance Status (KPS). The results were reported as pooled mean or proportions with 95% confidence interval (CI) for continuous and dichotomous data, respectively.

Results. Eight observational studies comprising 1010 patients met our inclusion criteria. The pooled mean of overall survival was 10.482 with 95% CI [7.651, 13.314]. While the pooled proportion of one-year and two-year survival was (0.451, 95% CI [0.320, 0.582]) and (0.240, 95% CI [0.112, 0.367]), respectively. We found the pooled proportion of overall mortality to be 0.535 with 95% CI [0.278, 0.793]. Patients with immediate postoperative KPS improvement showed a pooled estimate of 0.463 with 95% CI [0.243, 0.683].

Conclusion. Surgical resection is an effective therapeutic option for patients with BMs. Yet, careful patient selection and surgical technique are crucial for reducing postoperative complications and death.

Keywords: brain metastases, BMS, multiple metastases, surgical resection, radiotherapy

DOI: 10.15386/mpr-2927

Manuscript received: 20.07.2025
Received in revised form: 05.08.2025
Accepted: 15.09.2025

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Introduction

Brain metastases (BMs) are the most prevalent intracranial tumors in adults, significantly outnumbering primary brain tumors [1] and occurring in 20% to 40% of individuals diagnosed with cancer [2]. Advances in cancer prevention, screening, and treatment have inadvertently led to a rise in BM incidence, with nearly half of these patients presenting with multiple lesions [3–6]. Historically, the prognosis for patients with BMs has been poor, with a median survival ranging from 3 to 6 months following whole-brain radiation therapy (WBRT) [7–9]. While current evidence strongly supports the resection of a single BM followed by radiotherapy, particularly in patients with good performance status, the surgical management of multiple BMs remains a complex and evolving issue [10–12].

The role of surgery in managing multiple BMs is a subject of ongoing debate, given the generally poor prognosis,

the potential for systemic involvement of the central nervous system, and the inherent risks associated with neurosurgical procedures [10,13–15]. Surgery is typically considered for alleviating mass effect and associated neurological symptoms, obtaining tissue for histological and molecular genetic analysis, and potentially achieving cytoreduction [13,16,17].

Notably, certain tumor histological types, such as renal cell carcinoma and malignant melanoma, demonstrate limited radiosensitivity, potentially favoring surgical intervention over radiation therapy [18,19]. Furthermore, large, space-occupying lesions, particularly in the posterior fossa, can cause neurological decline and hinder the delivery of necessary oncological treatments for both CNS and systemic disease [15,20]. Therefore, reducing the mass effect of BMs can be crucial for maintaining or establishing a patient's eligibility for further treatment. However, surgical intervention carries the risk of complications, including postoperative hematoma in the surgical cavity, acute hydrocephalus, and CSF fistula [21].

Recent studies have yielded valuable but sometimes conflicting insights into the benefits and risks of surgery for multiple BMs. Several studies have suggested that surgery can lead to clinical stabilization or functional improvement, particularly when focused on reducing mass effect and facilitating further oncological treatment [22–24]. These studies highlight the potential for surgery to improve functional status and potentially prolong survival, even in patients with a low Karnofsky Performance Status [22]. However, other research emphasizes the importance of careful patient selection and acknowledges the potential risks, particularly in elderly populations [21]. These findings underscore the need for further investigation to clarify the role of surgery in this challenging patient population.

Despite valuable insights from individual studies, the optimal management of multiple BMs remains under scrutiny, with the literature demonstrating inconsistencies regarding surgical efficacy and safety. This systematic review and meta-analysis aims to address this uncertainty by comprehensively evaluate the evidence in order to determine surgery's impact on KPS score, survival and mortality outcomes across diverse patient characteristics and treatment approaches.

Methods

This systematic review and meta-analysis were performed according to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [25].

Eligibility Criteria

Studies were considered eligible if they met the following criteria: (1) investigated adult patients (≥18 years old) with multiple brain metastases (BMs), regardless of primary tumor origin; (2) focused on the surgical management of multiple BMs, including any surgical technique; (3) reported at least one relevant outcome measure; (4) were original research articles including randomized controlled trials, prospective, and retrospective cohort studies.

Studies were excluded if they: (1) were published in a language other than English; (2) included patients with a single BM only; (3) were conference abstracts, case reports, case series, editorials, commentaries, letters to the editor, or review articles.

Search strategy

Our search for relevant studies encompassed four major databases: Web of Science, PubMed, Scopus, and Cochrane. We used the following search strategy: ("Brain Metastases" OR "Brain Metastasis") AND ("Surgery" OR "Operative procedures" OR Operations OR "Invasive procedures" OR "Operative therapy"). The literature search was conducted from January 2023 till September 1st, 2024.

Study selection

Retrieved studies were initially managed using EndNote X9 reference management software and then exported to Microsoft Excel for screening. We employed a two-step screening process: (1) screening of titles and abstracts, followed by (2) full-text screening of potentially eligible articles. Two independent reviewers conducted each stage. Discrepancies were settled through shared decision-making or, if necessary, consultation with a third senior reviewer.

Data extraction

To ensure consistency in data collection, a standard data extraction form, created in Microsoft Excel, was used for all eligible studies. Two different reviewers were responsible for extracting the following data: (1) general study information (e.g., authors' names, publication year, country, sample size, study methodology, and follow-up period); (2) baseline clinical characteristics (e.g., age, sex, number of BM, presenting symptoms, preoperative Karnofsky Performance Status (KPS), and postoperative adjuvant treatments); (3) relevant outcome measures e.g. postoperative KPS, proportions of immediate clinical improvement or no change in KPS, survival, and mortality outcomes.

Quality assessment

Two independent authors did the quality assessment, any disagreement was resolved by discussion or assistance from a senior author.

The Newcastle-Ottawa Scale (NOS) [26] was employed to assess the risk of bias in the included retrospective studies. The NOS utilizes a star system across three domains – selection of study groups, comparability between groups, and ascertainment of outcomes – to provide a structured assessment of methodological quality. Each domain is evaluated based on specific criteria, with a maximum of one star awarded per criterion (except for comparability, which allows for two stars).

Statistical analysis

The meta-analysis was performed using OpenMeta

[analyst] Software (version 12.11.14). Pooled mean with 95% confidence intervals (CIs) were calculated for the continuous outcomes of postoperative KPS and mean overall survival outcomes. For proportions of immediate clinical improvement or no change in KPS, survival, and mortality outcomes, pooled proportions with 95% CIs were calculated. Heterogeneity between studies was assessed using I^2, with I^2 values greater than 50% considered indicative of substantial heterogeneity, according to the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions [27]. A random-effects model was employed for analyses with substantial heterogeneity; otherwise, a fixed-effects model was used.

Results

Search results and study selection

The literature search identified a total of 2085 records. After duplicate removal, 1740 records were assessed by title and abstract screening. Of these, 1698 records were excluded, leaving only 42 articles to be evaluated by full-text screening. Finally, 8 articles met our inclusion criteria and were included in our study.

Characteristics of included studies

We incorporated eight retrospective cohort studies [22–24,28–32] comprising 1010 patients; half of them were old-age males. Four studies were conducted in Germany [22–24,29], while the rest were conducted in Belgium [32], Italy [31], China [28], and Brazil [30].

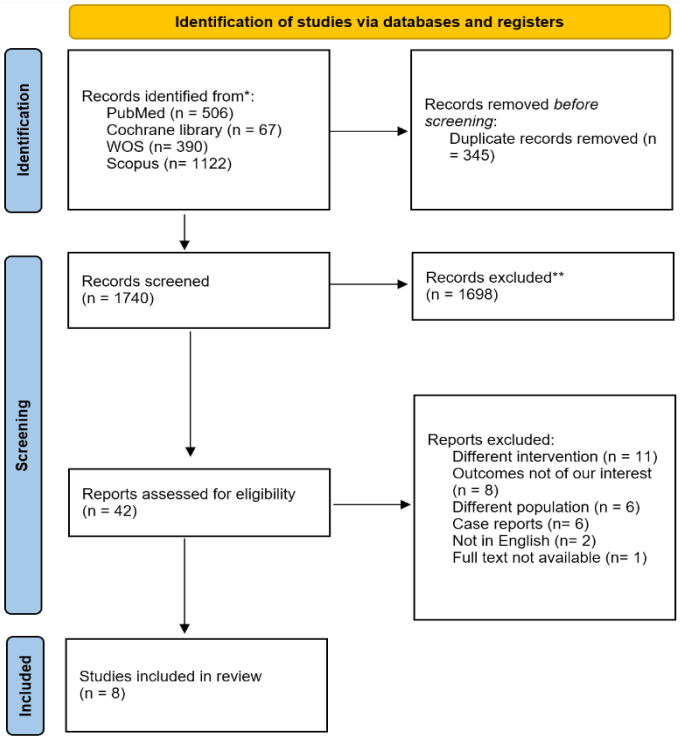

Figure 1. PRISMA flow chart.

Table I. Summary of the included studies.

Study ID	Country	Study design	Study period	Follow-up period, mean ±SD	N
Ersoy et al. 2024	Germany	Retrospective Cohort	January 2015 to July 2021	31.8 ±16.12 Months	131
Niedermeyer et al. 2024	Germany	Retrospective Cohort	January 2018 to May 2023	7 ±6.883 Months	47
Vanstraelen et al. 2023	Belgium	Retrospective Cohort	January 1, 2000, to December 31, 2019	NA	25
Telera et al. 2023	Italy	Retrospective Cohort	May 2000 to May 2021	42.33 ±90.944 Months	48
Potthof et al. 2023	Germany	Retrospective Cohort	January 2013 to December 2018	NA	353
Liang et al. 2023	China	Retrospective Cohort	1 January 2004 to 31 December 2019	NA	211
Goldberg et al. 2024	Germany	Retrospective Cohort	April 2007 to January 2020	NA	140
Botta et al. 2023	Brazil	Retrospective Cohort	June 2012 to December 2021	NA	55

SD; Standard deviation, **N;** Number.

Table II. Baseline characteristics of the included studies.

Study ID	N	Age, mean ±SD	Sex, Male N (%)	Primary tumor, N (%)	Synchronous BM diagnosis	Metachronous BM diagnosis	Number of BM		Presenting symptoms, N (%)				Preoperative KPS, N (%)		Postoperative adjuvant treatments, N (%)		
							Single	Asymptomatic Multiple	Motor/ sensory deficit	Headache	seizures		<70%	≥ 70	Radiotherapy	Chemotherapy	No radiotherapy
Ersoy et al. 2024	131	62 ±8.833	63 (48.1%)	Lung: 67 (51.1%). Breast: 26 (19.8%). Other: 38 (29.0%).	49 (37.4%)	82 (62.6%)	0 (0%)	131 (100%)	NA	NA	NA	20 (15.3%)	37 (28.2%)	94 (71.8%)	94 (72.31%)	NA	31 (24.41%)
Niedermeyer et al. 2024	47	59.333 ±16.06	NA	NSCLC: 16 (34%). Malignant melanoma: 11 (23.4%). Breast cancer: 7 (14.9%). Colorectal cancer: 4 (8.5%). Ovarian cancer: 3 (6.4%). Gastric cancer: 2 (4.3%). Others: 4 (8.5%).	11 (23.4)	NA	NA	47 (100%)	9 (19.2%)	10 (21.3%)	5 (10.6%)	7 (14.9%)	8 (17%)	39 (83%)	35 (74.5%)	18 (38.3%)	NA
Vanstraelen et al. 2023	25	NA	NA	Esophageal cancer: 25 (100%).	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Telera et al. 2023	48	70.8 ±4.6	27 (56.3%)	Lung: 20 (41.7%). Breast: 9 (18.75%). Colorectal: 8 (16.7%). Ovarian: 2 (4.2%). kidney: 2 (4.2%). Melanoma: 2 (4.2%). Bladder: 2 (4.2%). Salivary glands: 1 (2.1%). Gastric: 1 (2.1%). Uterus: 1 (2.1%).	10 (20.8%)	38 (79.2%)	NA	NA	4 (8%)	22 (45%)	7(15%)	NA	NA	NA	NA	NA	NA	NA

Table II. Baseline characteristics of the included studies.

Study ID	N	Age, mean ±SD	Sex, Male N (%)	Primary tumor, N (%)	Synchronous BM diagnosis	Metachronous BM diagnosis	Number of BM		Presenting symptoms, N (%)				Preoperative KPS, N (%)		Postoperative adjuvant treatments, N (%)		
							Single	Asymptomatic Multiple	Motor/ sensory deficit	Headache	seizures		<70%	≥ 70	Radiotherapy	Chemotherapy	No radiotherapy
Potthof et al. 2023	353	64 ±12	180 (51%)	NSCLC: 153 (43%). Gastrointestinal: 48 (14%). Breast: 45 (13%). Melanoma: 37 (10%). Others: 70 (20%).	116 (33%)	237 (67%)	NA	NA	NA	NA	NA	NA	45 (12.7%	308 (87.3%)	NA	NA	NA
Liang et al. 2023	211	NA	141 (66.8%)	lung adenocarcinoma: 164 (77.7%). Others: 47 (22.3%).	121 (57.3%)	NA	143 (67.8%)	68 (32.2%)	NA	NA	NA	NA	173 (82%)	38 (18%)	79 (37.44%0	NA	132 (62.56%)
Goldberg et al. 2024	140	66.1 ±10	73 (52%)	NSCLC: 66 (47.1%). Breast cancer: 21 (15%). GI tumor: 13 (9.3%). RCC: 9 (6.4%). Prostatic cancer: 7 (5%). CUP: 6 (4.4%). Other: 18 (12.8%).	140 (100%)	NA	73 (52.1%)	67 (47.9%)	NA	NA	NA	NA	140 (100%)	0 (0%)	77 (55%)	34 (24.3%)	63 (45%)
Botta et al. 2023	55	60.9 ± 10.7	29 (52.7%)	NSCLC: 52 (94.5%). SCLC: 3 (5.5%.)	NA	NA	30 (54.5%)	25 (45.5%)	NA	20 (36.4%)	22 (40%)	13 (23.6%)	NA	NA	29 (52.7%)	31 (56.4%)	NA

N; Number, **SD;** Standard deviation, **KPS;** Karnofsky performance score, **BM;** Brain metastases, **NA;** Not available, **NSCLC;** Non-small cell lung cancer, **RCC;** renal cell carcinoma, **CUP;** Cancer of Unknown Primary, **SCLC;** small cell lung cancer.

Nearly half of the brain metastases (BM), 541 (53.6%), came from lung cancer, followed by breast cancer 108 (10.7%) and gastrointestinal tumors 101 (10%). Other data concerning the summary and baseline characteristics of the included studies are presented in tables I and II.

Quality assessment

We used NOS to assess the risk of bias in the included studies. Overall, the quality of the studies ranged from moderate [22–24,30,31] to high quality [28,29,32].

Five cohorts [22–24,30,31] were single-arm and lost 3 quality points in the selection and comparability domains. Another three studies lost 1 quality point [28,29,32] due to a lack of proper comparability between study arms. All the studies were awarded the full score in the outcome domain (Figure 2).

Outcomes

Postoperative KPS

A single-arm analysis of two studies [22,31] assessing postoperative KPS (n= 188) showed the pooled estimate to be 52.891 with 95% CI [44.006, 61.776]. The result showed a moderate heterogeneity (p= 0.138, I^2 = 54.6%) (Figure 3).

Study ID	Selection	Comparability	Outcome	Total score
Ersoy et al. 2024	★☆★★	☆☆	★★★	6
Niedermeyer et al. 2024	★☆★★	☆☆	★★★	6
Vanstraelen et al. 2023	★★★★	★☆	★★★	8
Telera et al. 2023	★☆★★	☆☆	★★★	6
Potthof et al. 2023	★★★★	★☆	★★★	8
Liang et al. 2023	★★★★	★☆	★★★	8
Goldberg et al. 2024	★☆★★	☆☆	★★★	6
Botta et al. 2023	★☆★★	☆☆	★★★	6

Figure 2. Quality assessment of the included studies.

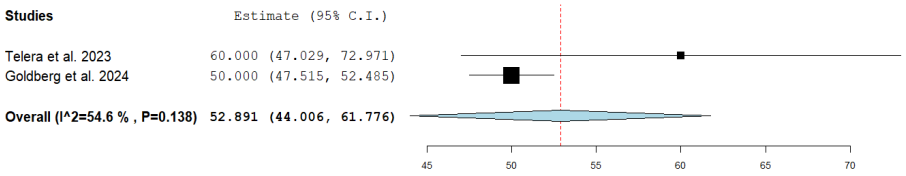

Figure 3. Forrest plot for Postoperative KPS outcome.

Immediate clinical improvement

Three studies [23,24,31] reported immediate clinical improvement in postoperative KPS (n=226). The pooled estimate was 0.463 with 95% CI [0.243, 0.683]. The result was heterogeneous (p< 0.001, I^2 = 90.57%) (Figure 4).

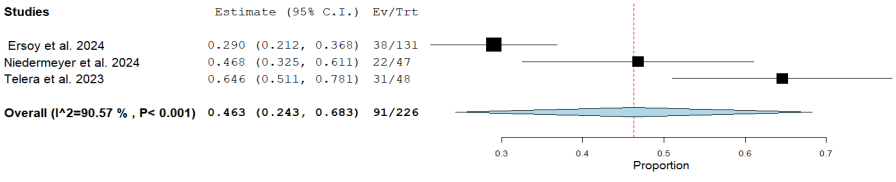

Figure 4. Forrest plot for immediate clinical improvement outcome.

KPS No change

The pooled analysis of two studies [24,31] reported no change in postoperative KPS (n= 95), showing the pooled estimate to be 0.334 with 95% CI [0.162, 0.506]. The result was heterogeneous (p= 0.066, I^2 = 70.44%) (Figure 5).

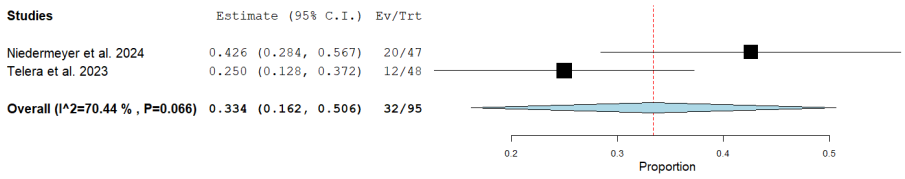

Figure 5. Forrest plot for KPS No change outcome.

KPS Worsening

Four studies [22–24,31] reported worsening of postoperative KPS (n= 366). The pooled result was 0.152 with 95% CI [0.100, 0.205], and it showed a moderate heterogeneity (p= 0.119, I^2 = 48.71%) (Figure 6).

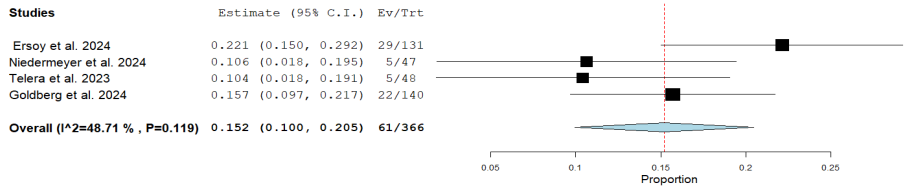

Figure 6. Forrest plot for KPS Worsening outcome.

Survival rate

Mean overall survival (mOS) in months

Six studies [22,23,29–32] reported the mOS. The pooled estimate was 8.534 with 95% CI [6.113, 10.954]. The result was heterogeneous (p< 0.001, I^2 = 85.52%) (Figure 7).

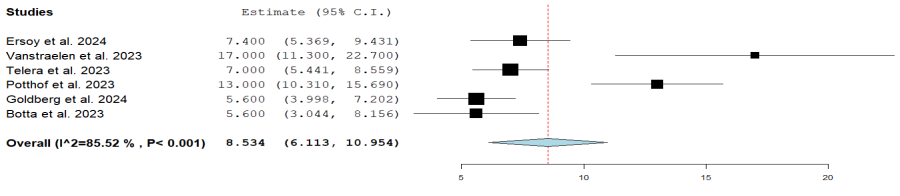

Figure 7. Forrest plot for mOS outcome.

One year overall survival

All the studies except Goldberg et al. 2024 [22] reported the overall survival rate at one year. The pooled estimate was 0.459 with 95% CI [0.312, 0.606]. The result was heterogeneous ($p < 0.001$, $I^2 = 94.82\%$) (Figure 8).

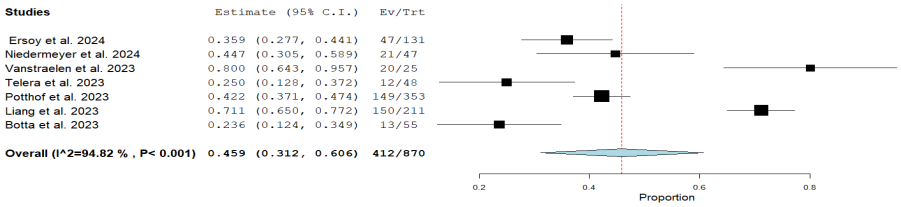

Figure 8. Forrest plot for One year overall survival outcome.

Two-year overall survival

Six studies [23,24,28,30–32] reported the two-year overall survival rate. The pooled estimate was 0.244 with 95% CI [0.094, 0.394]. The result was heterogeneous ($p < 0.001$, $I^2 = 94\%$) (Figure 9).

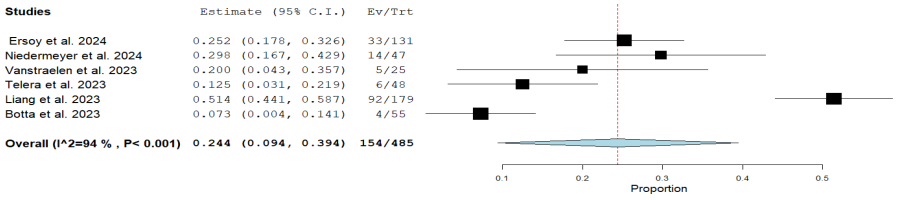

Figure 9. Forrest plot for Two-year overall survival outcome.

Mortality

Mortality rate during the postoperative first three months

Only two studies [23,31] reported that outcome. The pooled estimate was 0.156 with 95% CI [0.038, 0.273], and the result showed a moderate heterogeneity ($p = 0.065$, $I^2 = 70.52\%$) (Figure 10).

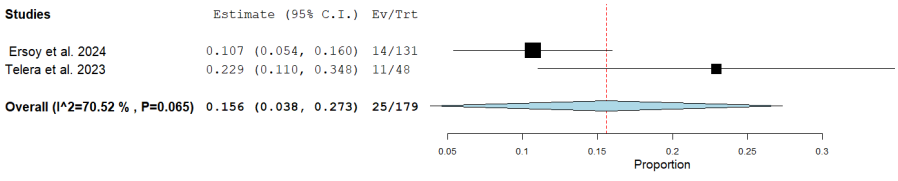

Figure 10. Forrest plot for Mortality rate during the postoperative first three months outcome.

Mortality rate at one year

Only Potthof et al. 2023 [29] and Liang et al. 2023 [28] reported the mortality rate at one year.

The pooled estimate was 0.434 with 95% CI [0.151, 0.717], and the result showed a high heterogeneity ($p<0.001$, $I^2 = 98\%$) (Figure 11).

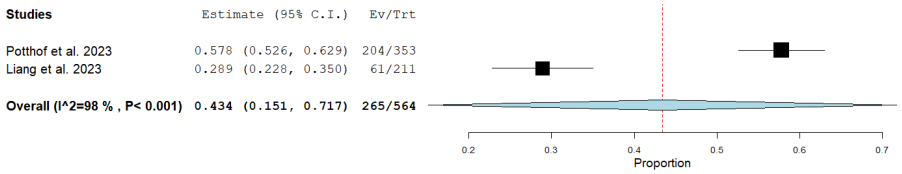

Figure 11. Forrest plot for Mortality rate of one year outcome.

Overall mortality rate

Five studies [22,23,28–30] reported the overall mortality rate. The pooled estimate was 0.490 with 95% CI [0.204, 0.775], and the result showed a high heterogeneity ($p<0.001$, $I^2 = 99.11\%$) (Figure 12).

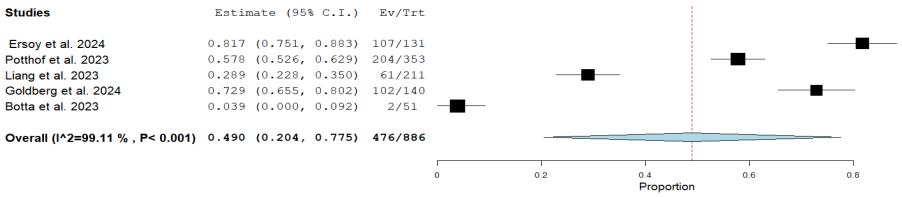

Figure 12. Forrest plot for Overall mortality rate outcome.

Disscussion

This systematic review and meta-analysis, encompassing a substantial cohort of 1010 patients across eight studies, aimed to clarify the role of surgical resection in the management of patients with multiple brain metastases (BMs). Although surgical intervention for a solitary BM is supported by robust evidence, the optimal approach for multiple BMs remains controversial, with the literature offering mixed conclusions regarding its benefits and risks [10,13–15]. This comprehensive review specifically focused on evaluating the impact of surgery on both functional outcomes, as measured by the KPS, and overall survival in this complex patient population.

Our analysis of postoperative KPS revealed a pooled mean score of 52.9, indicating a moderate level of functional independence. However, moderate heterogeneity was also observed. This is likely due to diverse patient factors and treatment approaches employed across the included studies. For instance, Telera et al. (2023) reported a mean postoperative KPS of 60 in an elderly population [33]. In contrast, Goldberg et al. (2024), focusing on a cohort of 140 patients with poor preoperative KPS (<70), observed a lower mean postoperative KPS of 50 [22]. This difference may be partially explained by the lower baseline functional status of Goldberg et al.'s cohort, as patients with limited functional reserve may experience less improvement after surgery. Furthermore, the lack of information regarding tumor location in Goldberg et al.'s (2024) study hinders direct comparison.

The pooled analysis of immediate clinical improvement in KPS indicated a promising rate of 46.3%. However, we observed substantial variations in the reported

rates of immediate improvement. Telera et al. (2023), focusing specifically on 48 elderly patients undergoing cerebellar metastasis resection, found a higher rate of immediate improvement (64.6%) compared to the 29.0% reported by Ersoy et al. (2024), whose study encompassed a broader cohort of 131 patients with multiple BMs [23,31]. This discrepancy might be attributed to the potentially more dramatic functional gains achievable with surgical decompression of cerebellar metastases, particularly those causing brainstem compression. Additionally, variations in how "improvement" was defined and measured across studies may have contributed to these differing results.

While the worsening of KPS observed in our pooled analysis was generally low (15.2%), the rates reported in individual studies varied. The highest rate of KPS worsening (22.0%) was reported by Ersoy et al. (2024), whose study did not provide sufficient data on surgical complications, limiting our understanding of the factors contributing to functional decline in their cohort [23]. In contrast, Telera et al. (2023) observed a lower rate of deterioration (10.4%) in their cohort of elderly patients [31], possibly reflecting meticulous surgical technique and careful patient selection to minimize risks in this vulnerable population.

Our meta-analysis revealed a pooled mOS of 8.5 months, suggesting a modest but potentially meaningful survival benefit associated with surgery for multiple BMs. However, we observed a wide range of reported mOS across studies. Telera et al. (2023) and Ersoy et al. (2024) reported comparable mOS of 7 and 7.4 months, respectively, in their predominantly lung cancer cohorts [23,31]. On the other hand, Vanstraelen et al. (2023) reported an even longer mOS of 17 months in their cohort of patients who developed BMs after undergoing esophagectomy with curative intent [34]. This finding underscores the importance of primary tumor type and its inherent responsiveness to treatment when assessing survival after surgery for multiple BMs.

The pooled one-year overall survival rate of 45.9% was characterized by significant variability. This wide range, with reported rates from 23.6% in Botta et al. (2023) to 80.0% in Vanstraelen et al. (2023) [30,32], likely reflects the impact of several factors. These include disparities in access to advanced therapies and variations in the use and availability of adjuvant therapies. Notably, Botta et al. (2023) reported that postoperative chemotherapy and whole-brain radiotherapy were administered to 31 (56.4%) and 28 (50.9%) patients, respectively [30,32]. In contrast, Vanstraelen et al. (2023) documented adjuvant therapy utilization in 15 (21%) of their sample and perioperative radiotherapy in 45 (63%) of the population [30,32]. These variations in adjuvant treatment approaches may have contributed to the observed differences in one-year survival rates.

The pooled analysis of two-year overall survival rates revealed a pooled estimate of 24.4% with a wide range of reported survival rates across studies. For instance, Botta et al. (2023), investigating a cohort of 55 lung cancer BM patients in a Brazilian public tertiary teaching hospital, reported a 7.0% two-year survival rate, highlighting the potential influence of prognostic score variability and the need to consider the impact of limited access to targeted therapies and immunotherapy in this context [30]. Conversely, the higher rate (29.8%) reported by Niedermeyer et al. (2024) [24] emphasizes the influence of primary tumor type, as well as differences in patient selection criteria, adjuvant treatment protocols, and definitions of outcome measures, on long-term survival. Variations in surgical approaches, such as the number of craniotomies performed, are also likely to contribute to the observed variations in two-year survival outcomes. Unfortunately, there was limited information about the surgical strategies that were used in the studies regarding the extent of the resection, the surgical technique, whether one craniotomy or more, the number of resected lesions, and the use of intraoperative neuronavigation, MRI, or not. This surely can also affect the surgical success rate, the incidence of adverse events, and overall outcomes

Overall mortality rates varied significantly across studies, highlighting the diverse clinical courses and prognoses of patients with multiple BMs. Our pooled analysis of six studies showed a high overall mortality rate of 49% with significant variability. This variation likely stems from factors such as patient age, comorbidities, primary tumor type, extent of systemic disease, and access to adjuvant treatments. For example, Ersoy et al. (2024) reported high overall mortality rates of 81% [23,33], whereas Potthoff et al. (2023) observed a lower rate of 57% [29]. Notably, Botta et al. (2023) reported the lowest overall mortality rate of 3.9% [30]. Further research is crucial to pinpoint the factors driving these wide variations and develop strategies for improving long-term survival in this complex patient population.

Analysis of perioperative mortality rates further demonstrated variability across studies. The pooled mortality rate during the first three months after surgery was 15.6%, with Telera et al. (2023) reporting the highest rate of 22% in their elderly patient cohort [31]. This finding is consistent with the increased perioperative risks associated with advanced age, potentially due to reduced physiological reserve and a higher incidence of comorbidities. Variations in surgical experience and institutional protocols for perioperative care may also contribute to the variability in mortality rates.

Integrating multimodal treatment strategies, such as combining surgery with systemic therapies or radiotherapy, or combining the three approaches together, may modulate the outcomes in patients with multiple BMs. Considering the advantages of each modality, multimodal treatment approaches may improve tumor local control, reduce the possible chances of distant brain failure, and enhance the overall survival rate. Indeed, surgical resection provides

a quick relief from tumor mass effect and subsequently alleviates the symptoms; whereas, adjuvant radiotherapy can attack microscopic lesions and lower the local recurrence rate. On the other hand, systemic therapies like immunotherapies can manage extracranial diseases and enhance the therapeutic effects of local treatments.

Our findings underscored several key factors to consider during surgical decision-making and patient selection. Our results indicate that preoperative KPS might be a major predictor of postoperative improvement, highlighting the potential benefits of using KPS as a criterion to assess patients' eligibility for surgery. Furthermore, we emphasize the impact of the original tumor type and its inherent responsiveness to treatment on survival outcomes, which may potentially influence decisions regarding treatment protocols and adjuvant therapies. Also, the clinicians must consider the patient's characteristics, such as age and comorbidities, and the availability of adjuvant therapies, before deciding on surgery.

Strengths, limitations, and recommendations

This meta-analysis represents a comprehensive assessment of the available evidence on the role of surgical resection in managing multiple BMs, encompassing a substantial cohort of patients and addressing critical outcome measures such as KPS and survival. The systematic methodology, adherence to PRISMA guidelines, and rigorous quality assessment enhance the reliability and validity of our findings. However, several limitations inherent to meta-analyses of retrospective studies need to be acknowledged. The included studies varied in their methodologies, patient characteristics, and definitions of outcomes, source of the metastases.

Furthermore, they varied in the preoperative adjuvant therapies as some patients took chemotherapy, radiotherapy, or both; all these factors have contributed to the observed variability in results. Additionally, the lack of data on specific surgical techniques, tumor molecular profiles, and long-term functional outcomes limits the generalizability of our findings and underscores the need for future prospective studies.

We recommend that future research focus on prospective, multi-center studies with standardized protocols for patient selection, surgical technique, and outcome measurement. Incorporation of molecular profiling data and assessment of long-term functional outcomes and quality of life after surgery are crucial to further refine our understanding of the optimal role of surgical resection in the management of multiple BMs.

Conclusion

Despite the limitations inherent in meta-analyses of retrospective studies, our findings provide valuable insights into the role of surgery in the management of multiple BMs. Surgical resection can lead to rapid functional improvement in a substantial proportion of patients, potentially enhancing their quality of life and facilitating further oncological treatment. However, careful patient selection and meticulous surgical technique are crucial to minimize the risk of postoperative complications and mortality, particularly in elderly patients and those with infratentorial BMs. The integration of surgery with appropriate adjuvant therapies, including radiotherapy, chemotherapy, and targeted therapies, is essential for improving long-term survival outcomes. Also using the precison medicine which include other molecular techniques like epigenetics and immunophenotyping, and the evaluation of personalized drugs combination will hopefully increase the clinical utility. In order to determine the best treatment approach multidisciplinary discussions should be held. These teams of specialists collaborate, share information, and leverage diverse expertise to ensure accurate diagnosis, personalized treatment plans, improved outcomes, and better resource utilization. Future prospective, multi-center studies are needed to further refine patient selection criteria and investigate the role of personalized medicine in optimizing surgical outcomes for this complex patient population.

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