Comparison of sitting position vs. non sitting position the resection of brain metastases in the posterior fossa. Surgical and functional outcome in a contemporary cohort.

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Research Article

Keywords:

Posted Date: March 17th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1435719/v1

Abstract

For surgery of brain metastases, good immediate postoperative functional outcome is of utmost importance. Improved functional status can enable further oncologic therapies and adverse events might delay them. Pros and cons of either sitting or supine positioning for resective surgery of the posterior fossa are debated but contemporary data on direct postoperative outcome is rare. Aim of our study was to compare the functional outcome and adverse events of surgery for brain metastases in sitting vs. non sitting position in the direct postoperative setting. We retrospectively compared surgery of metastases located in the posterior fossa over a 3-year period in two level-A neurosurgical centers. Either center performed surgery exclusively in sitting or non-sitting positioning respectively. Worse functional outcome (Karnofsky Performance scale) and functional deterioration was seen in the “sitting” group (coming from higher functional scores). We found significantly more “sitting” patients to deteriorate to a KPS ≤60% including four deaths (vs. one in non-sitting position). In this study, treating patients with brain metastases in sitting position resulted in a number needed to harm (NNH) of 2.3. In this study, we found sitting position for surgery of brain metastases to be associated with worse outcome and more adverse events. Therefore, we tend to recommend non-sitting over sitting position for surgery of brain metastases of the posterior fossa.

Introduction

Resection of brain metastases is an accepted therapeutic strategy for up to three large or symptomatic lesions. Masses in the cranial posterior fossa (PF) can cause a severe symptom burden due to vertigo, cranial nerve palsy, occlusive hydrocephalus or direct compression of structures within the brainstem[10, 4, 3]. Therefore, safe resection to maintain good postoperative functional status is of utmost importance to enable optimal comprehensive oncologic treatment[11]. Surgery of the PF can be performed either in sitting position (SP) or non-sitting position (NSP), e.g. prone or supine. The choice of positioning is often made according to the surgeon’s preferences, whereas SP is claimed to enable superior anatomic orientation and two handed dissection because of clear situs for gravitational blood drainage and easier more convenient opening of cranial fissures due to gravity, with a non-negligible risk of air embolism and a more complex anesthesiologic set up[4, 8, 6]. NSP is often regarded less complex with the risk of higher venous pressure with consecutive swelling and venous bleeding[9, 5]. Aim of this study is to compare surgical parameters and functional short-term outcome along with adverse events in a contemporary cohort of patients undergoing resection of brain metastases in the PF.

Methods

Ethics approval

The study protocol was approved by the local ethics committee (TUM: 459/21 S-KH) in accordance to the Declaration of Helsinki.

Study design

We performed a retrospective two-center (two academic neurooncological/surgical centers) study by analysis of patient-specific clinical records. Center one performed surgery exclusively in SP, center two only in NSP according to a local standard protocol. All data was collected, encrypted, processed, and analyzed according to the study protocol. Patients were dichotomized according to patient positioning during surgery (SP vs. NSP). NSP included prone and supine patient positioning. The analyzed parameters included age, gender, ASA score, Karnofsky Performance Scale (KPS) before and after surgery as well as KPS deterioration, length of surgery (LOS), length of anesthesia (LOA), length of hospitalization (LOH) and adverse events during hospitalization according to the Clavien Dindo Grading system (CDG) [11, 2, 7].

Patient selection

Electronic data files of all adult patients who underwent resection of brain metastases in the posterior fossa between January 2018 and December 2020 were screened. Patients younger than 18 years of age and patients that underwent stereotactic biopsy were excluded.

Statistics

Statistical analysis was performed using the software SPSS Statistics™ (version 25, IBM Corp, Armonk, New York, USA). Normal distribution was assumed for continuous data according to the central limit theorem. An unpaired 2-tailed student's t-test was used to compare the significance of means between two groups. Pearson's or Spearman's correlation was used respectively. Ordinal data war analyzed with an unpaired Mann- Whitney U-test, dichotomous by means of Chi^2-test. Data in text and graphs are shown as mean and standard deviation (SD) for continuous data and as median and interquartile range for ordinal data. A p value ≤ .05 was considered significant and indicated by "*", p values ≤ 0.01 were indicated by "**," and values ≤ 0.001 by "***."

Results

Patient population

In this study, 60 (n = 25 female) patients were identified and met the inclusion criteria (n = 30 per center) according to the study protocol. Patients undergoing surgery in SP had significantly better ASA Scores and KPS before surgery. Age, surgical approach (lateral vs. median) and side of lesion were equally distributed in both groups. (Table 1 and Fig. 1).

Surgery and outcome

Mean LOS was 161 min., with a trend towards longer mean LOS in SP vs. NSP without reaching significance (p = .42). LOA, as well as LOH were significantly longer in patients undergoing surgery in SP vs. NSP (p = .03; p = .02). Starting from a significantly higher pre-operative level of physical fitness

(measured by means of ASA classification ($p < 0.01$) and KPS($p = 0.30$)) patients undergoing surgery in SP had significantly more important deterioration ($p = .03$) in functional outcome (KPS) without difference in absolute outcome scoring ($p = .38$) (Table 2 and Fig. 1). Patient age inversely correlated significantly with LOS ($p = .02$; $r = -.29$) and LOA ($p = .02$; $r = -.29$). Patients with more important functional deterioration (KPS) had significantly longer LOH ($p = .001$; $r = .43$). Regarding functional outcome, 6 / 30 (20%) patients that were operated in SP deteriorated from KPS > 60% to ≤ 60% compared to 2 / 30 (7%) in NSP ($p = .13$). One patient in each group 1 / 30 (3%) improved from KPS ≤ 60% to > 60%.

Adverse events

In this study, 16 / 60 patients experienced 23 adverse events during the direct postoperative course resulting in a number needed to harm (NNH) of 2.3 patients to experience adverse events in SP. Significantly more patients undergoing surgery in SP experienced adverse events ($p = .04$) and patients undergoing surgery in SP experienced significantly more adverse events ($p = .03$) per patient. According to the CDG system, median grading of adverse events did not significantly differ ($p = .39$). 4 / 30 patients undergoing surgery in SP died during hospitalization compared to 1 / 30 patient in the NSP group (Table 2). Patients in the SP group experienced CSF leak (n = 1), surgical site infection (SSI) (n = 1), cerebral ischemia (n = 3), air embolism (n = 2) and hydrocephalus (n = 3), while none of these complications occurred in the NSP group. Furthermore, cranial nerve (CN) deficit occurred in 4 patients (n = 2 SP; n = 2 NSP) and rebleeding in four patients (n = 2 SP; n = 2 NSP). Four SP group patients died during the direct postoperative course versus one in the NSP group. Despite their lower pre-operative fitness level and functional status, patients operated in NSP did not show higher occurrence rates in any type of complication.

Discussion

In this study we compared surgical parameters, functional outcome and adverse events in a contemporary cohort undergoing surgery for brain metastases in the posterior fossa in either sitting or non-sitting position.

Baseline parameters

In our cohort, patients undergoing surgery in SP had a significantly better status according to ASA and KPS compared to patients in the NSP group. No relevant differences in age, sex or the number of lateral vs. median craniotomies was found. Functional baseline status is known to affect long term outcome in cancer, which has been shown as well in intraparenchymal lesions of the posterior fossa[1].

Surgical parameters

In our study, LOA was significantly shorter in NSP compared to SP. In SP, transesophageal echography is necessary, which might be an explanation for the longer time of anesthesiologic preparation prior to the skin incision. LOS was slightly but not significantly longer in SP, questioning the advantage of possible

superior anatomic orientation or atraumatic dissection during surgery. Whether lateral or medial approaches harbor higher complication risks per se is not systematically investigated, but did not show significant correlation to outcome in our population.

Functional outcome

Functional status is of utmost importance regarding the outcome in cancer treatment[11]. Therefore, the aim of surgical interventions is to improve the functional status or not deteriorate it towards low KPS, limiting further systemic therapy. In our cohort, postoperative KPS was not significantly different in both groups, but patients undergoing SP deteriorated significantly more often. In the SP group 20% of patients compared to 7% in the NSP group deteriorated to a KPS ≤ 60%, coming from better functional status and therefore possible limiting or delaying adjuvant therapy. Only one patient in each group improved to a KPS > 60% after surgery enabling further therapy. Therefore, SP approach can be regarded as less favorable regarding short term functional outcome. Whether this affects actual overall survival or progression free survival cannot be answered sufficiently from this sample. Nevertheless, overlooking the hospitalization of mean 19 days, reduction in functional status might already delay necessary adjuvant therapy. Postoperative functional outcome also affected LOH, leading to significantly longer hospitalization in the SP group.

Adverse events

Overall adverse event rate was 30% with patients in sitting position experiencing more and more severe adverse events (according to the CDG). Four patients died after surgery in SP during the immediate postoperative course compared to one in the NSP group. In the SP group, two air embolisms occurred compared to zero events in the NSP group. This data points towards a less pronounced risk profile if surgery is performed in NSP. Surgery in SP resulted in a NNH of 2.3. Whether this is due to surgical or perisurgical/anesthesiological factors cannot clearly be distinguished. Nevertheless, direct surgical adverse events were equally distributed among both groups. Whether changing an established workflow further affects complication rates and outcome cannot be ruled out from this data. Nevertheless, if deciding on standards of care and neurosurgical training, possibly worse outcome and adverse event profile have to be taken into account.

Study limitations

This study has several limitations, that have to be clearly addressed. First, the retrospective nature of the study is inherently prone to selection bias. Second, the study was performed in two neurosurgical centers and each center performed only one single type of positioning, according to the local standard protocol, creating an inherent potential selection bias. Nevertheless, this allows us to rule out interindividual patient differences, s.a. location, size or oncological disease to account for the choice of positioning. Furthermore, the LOA can be affected by center specific differences, but we assume an attribution to a more extensive anesthesiological set up in SP. The retrospective design of the study does not allow to adequately control for various confounders and baseline parameters showed significant differences in

the KPS and ASA. Counterintuitively the SP group starting from better functional status had more severe deterioration during the postoperative course. The underlying oncologic disease was slightly different in both groups. Whether our findings ultimately affect the oncologic prognosis remains unclear, as no long-term data was collected and the focus of our study was lying on short term outcome, in which underlying oncologic disease is not assumed to play a profound role. This is due to a broad network of specialized outpatient clinics organizing further oncologic treatment with only sporadic follow up visits at the neurosurgical center. Nevertheless, as the prognostic factor of functional outcome is an established parameter, our findings implicate a favorable outcome in the cohort, that underwent surgery in NSP vs. SP.

Conclusion

In this retrospective study, patients undergoing surgery for intraaxial metastases of the posterior fossa show better short-term outcome if surgery was performed in NSP compared to SP. Significantly more patients deteriorated towards a functional status, possible delaying adjuvant cancer therapy. The number needed to harm for surgery in sitting position compared to non-sitting position was 2.3

Declarations

Funding: This research received no external funding.

Conflicts of interest/Competing interests: The authors declare no conflict of interest.

Availability of data and material: Data is availably upon request.

Code availabilit: not applicable.

Ethics approval: Study protocol approved by the local ethics committee (TUM: 459/21 S-KH).

Consent to participate: Not applicable for this retrospective analysis.

Consent for publication: All authors have read and agreed to the published version of the manuscript.

Author Contributions: Conceptualization, PK, TV, SM, MNB, JL and ES; methodology, PK, TV, SM and MNB; formal analysis, PK and SM; data curation, TV and SM; writing—original draft preparation, PK and KK; writing—review and editing, PK, TV, SM, SS, KK and ES; supervision, JL and ES.

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Tables

Table 1 | Baseline characteristics: Pre = presurgical, lat. = lateral suboccipital, med. = median suboccipital; Oncologic Disaese: NSCLC = Non-small cell lung cancer, SCLC = Small-cell lung cancer, CUP = cancer of unknown primary; (absolut counts); (mean ± SD / median [interquartile range])

	Total (n = 60)	Sitting (n = 30)	Non-Sitting (n = 30)	p-value
Age (y)	65.7 ± 10.9	65.5 ± 2.3	65.9 ± 1.6	.89
Gender (f / m)	25 / 35	12 / 18	13 / 17	1
ASA (Score)	3 [3-3]	3 [2-3]	3 [3-3]	**< .01**
Karnofsky Pre (%)	80 [60-100]	80 [80-90]	70 [60-90]	**.03**
Craniotomy (lat. / med.)	49 / 11	22 / 8	27 / 3	.18
Craniotomy (left / right)	23 / 26	11 / 12	12 / 10	1
LOS (min.)	161 ± 56	167 ± 47	155 ± 65	.42
Oncologic Disaese				
NSCLC	21	9	12	
SCLC	3	1	2	
Malignant Melanoma	2	2	0	
Colorectal cancer	8	2	6	
Breast cancer	16	10	6	
Renal cell cancer	8	4	4	

Table 2 | Surgical parameters and outcome: LOS = length of surgery, LOA = length of anesthesia, LOH = length of hospitalisation, Deter. = deterioration; Adverse Events: Adv. Event = Adverse Event (absolut counts / median [interquartile range])

	Total (n = 60)	Sitting (n = 30)	Non-Sitting (n = 30)	p-value
LOS (min.)	161 ± 56	167 ± 47	155 ± 65	.42
LOA (min.)	248 ± 250	268 ± 54	228 ± 81	**.03**
LOH (d)	19 ± 15	24 ± 18	15 ± 8	**.02**
Karnofsky Post (%)	80 [60-100]	70 [70-80]	80 [60-90]	.38
Karnofsky Deter. (%)	0 [0-10]	0 [0-20]	0 [0-0]	**.03**
Adverse Events				
Patients with Adv. Event (n)	16	12	4	**.04**
Adv. Event (n)	23	18	5	
Adv. Events per patient (mean)		0.6	0.16	**.03**
CDG (worst)	4 [3-5]	4 [4-5]	2.5[1-5]	.39
CSF Leak (n)	1	1	0	1
SSI (n)	1	1	0	1
CN deficit (n)	4	2	2	1
Cerebral ischemia (n)	3	3	0	.24
Rebleeding (n)	4	2	2	1
Air embolism (n)	2	2	0	.49
Hydrocephalus (n)	3	3	0	.24
Death (n)	5	4	1	.35

Figures

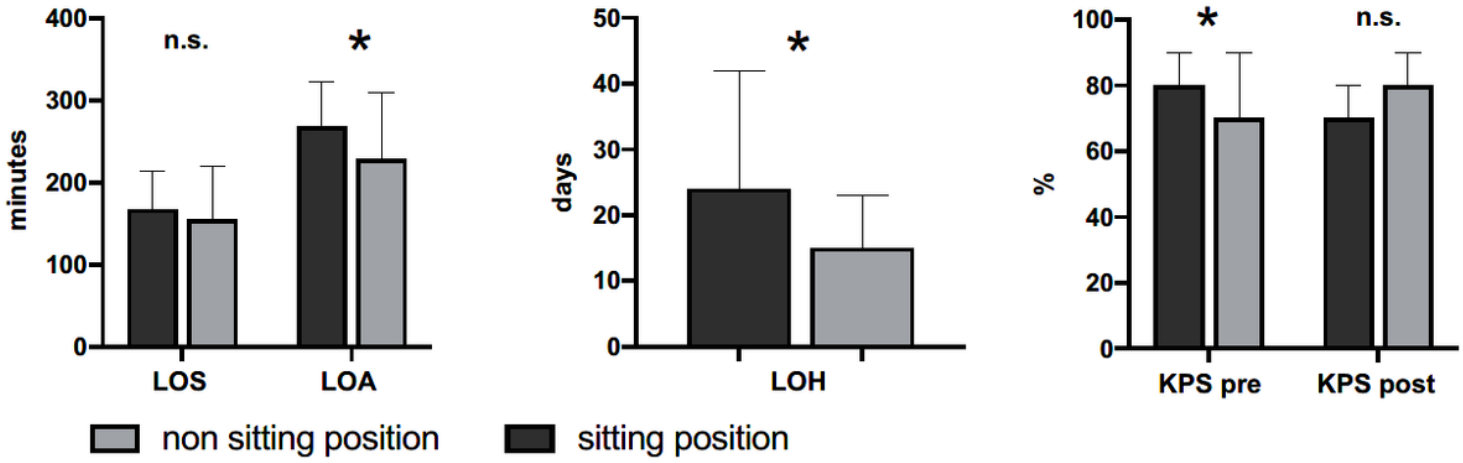

Figure 1

Comparison of sitting (light grey) vs. non sitting position (dark grey) according to LOS = length of surgery, LOA = length of anesthesia (both left) and LOH = length of hospitalization (middle). Pre- and Postsurgical KPS = Karnofsky Performance Scale (right); “n.s.” = non significant, “*” = $p < .05$.