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Can TMT predict overall survival in patients with brain metastases from different primary malignancies as an indicator of sarcopenia?

Is TMT a predictor of OS in metastatic brain disease?

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Abstract
Aim: The present study aimed to examine the accuracy of temporal muscle thickness (TMT) in predicting overall survival (OS) of brain metastases from different primary malignancies utilizing a publicly available database.
Material and Method: A total of 75 patients with metastatic brain tumors with different primary malignancies, whose data were obtained from open data sets, were included in the study. TMT was analyzed on axial thin section postcontrast T1-weighted images. Median TMT MMT was employed to establish the cut-off point.
Results: Evaluation of the median TMT measure (7.47 mm) served as the basis for establishing a survival threshold. Median overall survival was higher in the group with greater muscle thickness for TMT value (TMT<7.47 mm: 608 days TMT>7.47: 919 days). According to these results, there was no significant difference between the groups. Cox regression analysis indicated that TMT values less than median muscle thickness were negatively associated with overall survival (TMT<7.47: HR 1.63 CI 1.01-2.64, p = 0.044).
Discussion: We suggest that TMT is a promising marker for predicting the survival in patients with metastatic brain tumors with different primaries.

Keywords
Brain Metastases, Sarcopenia, Survival, Indicator, Primary Malignancies

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Introduction

The highest occurrence rate within intracranial malignancies can be attributed to metastatic brain tumors [1]. Although there have been advancements in different treatment approaches, the average lifespan after the initial treatment for brain metastasis is around 7 months [2]. When designing personalized treatment plans for cancer patients, clinicians need to take into account different factors such as age, tumor characteristics on molecular and histological levels, tumor size and location, and the overall physical health of the individual. Objective assessment of most parameters is feasible, yet the attending physician's subjective evaluation of patients impacts the determination of their clinical status, resulting in substantial variability among observers and an inability to reliably predict survival [3].

Sarcopenia is characterized by a gradual and widespread reduction in skeletal muscle mass, which is associated with an increased probability of experiencing harmful outcomes such as fractures, physical limitations, and mortality [4]. Sarcopenia has important clinical significance within the realm of surgical oncology, rendering patients more susceptible to adverse outcomes such as complications, prolonged hospital stays, and mortality. This occurs because sarcopenia signifies patients' limited capacity to withstand the physiological stress response triggered by surgery, thereby adversely affecting their overall well-being [5, 6]. Sarcopenia is identified as an adverse forecasting determinant in diverse solid malignancies. [7]. To determine the amount of skeletal muscle mass, it is customary to examine the cross-sectional area of skeletal muscle near the level of the lumbar third vertebra on a computed tomography (CT) scan [7]. Due to the infrequent use of abdominal CT scans, the conventional technique does not allow for the assessment of skeletal muscle mass in the majority of neuro-oncology patients. Consequently, there has been a lack of comprehensive evidence of the connection between sarcopenia and clinical implications for individuals with brain tumors, especially when compared to other types of cancer. A significant correlation has been discovered in recent research between the thickness of the temporal muscle (TMT) and the cross-sectional areas of the lumbar skeletal muscles visualized in routine diagnostic brain MR images. This indicates that estimating skeletal muscle mass can benefit from considering not only lumbar muscles, but also craniofacial muscles [8]. There are several studies analyzing the relationship between temporal muscle thickness and survival in GBM patients [9]. However, there are fewer studies on metastases, which are the most common intracranial malignancies.

The main aim of this study was to analyze the predictive power of temporal muscle thickness in estimating the lifespan of individuals with brain metastases of different primary malignancies using a publicly available database.

Material and Methods

Patient Selection

Open source images of 75 brain metastases with different primers from the University of Castilla-La Mancha were analyzed (Available at: https://molab.es/datasets-brain-metastasis-1/?type=metasrd.) [10]. Clinical data of the patients, including age, gender, primary malignancy, and survival time, were obtained from open sources. The system data did not contain any personal identifying information, and informed consent was obtained from patients in the reference study.

Inclusion criteria were as follows: (a) patients with primary malignancy and metastatic brain tumors, (b) patients with preoperative imaging data available on T1-weighted MR imaging with and without contrast. Exclusion criteria were as follows: (a) cranial MR images with poor quality and artifacts, and (b) patients for whom survival data were not available.

A total of 75 patients who met the criteria were included in the study. No patient was excluded from the study.

Measurement of muscle thickness

The measurements were taken by an experienced radiologist with 6 years of MRI reading expertise, and a neurosurgeon with 18 years of experience who underwent training under another independent radiologist. All statistical evaluations were conducted subsequent to the anonymized patient measurements.

All patients' images underwent a series of procedures before measuring muscle thicknesses. Bias field correction and Z-score normalization were performed using Advanced Normalization tools for Python and the Density-Normalization package [11, 12]. Images were resampled to a 1 × 1 voxel range and resized to 256 × 256 pixels. The anterior-posterior commissure line served as the redirecting path for the axial images. Slicer v 13 was employed throughout this process.

Temporal muscle thickness (TMT) was assessed using routine preoperative imaging, which included axial thin-section contrast-enhanced T1-weighted MR images. In adherence to a previously documented approach, measurements were executed perpendicular to the temporal muscle's long axis, with the orbital roof and Sylvian fissure serving as anatomical landmarks [13].

The arithmetic mean of both right and left muscle thicknesses was utilized for the analysis.

Ethical Committee

With the decision of Afyonkarahisar Health Sciences University Medical Ethics Committee dated 11-08-2023 and numbered 2023/8-353, it was resolved that there was no need to obtain ethics committee approval for the study.

Statistical analysis

The statistical analysis was conducted using SPSS version 25 from IBM Corporation based in Armonk, NY, USA. The reliability of the two observers was assessed using the intraclass correlation coefficient (ICC). To determine if there were any significant differences in TMT and OS between male and female patients, Student's t-test or Mann-Whitney U-test was employed. Pearson's correlation analysis was used to evaluate the correlation between age at diagnosis of metastasis and TMT. The patients were categorized into two groups according to median TMT values. The OS curve was calculated using the Kaplan-Meier curve, and the OS differences between the two groups were investigated using the log-rank test. To assess if there were any significant differences in TMT and OS between male and female patients, Student's t-test or the Mann-Whitney U-test was employed. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated. The variables

underwent multivariate analysis, and p-values less than 0.05 were considered statistically significant.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

Descriptive analyses were performed for the patient group. The group consisted of 28 males and 47 females. Mean survival days were calculated as 914.12±580.17. The mean age of the patients at the time of diagnosis was 56.88 ± 10.81 years.

The ICC calculated for left and right-side TMT was 0.911 and 0.921, respectively (P<0.001). The mean TMT was 7.93±1.19 mm in males and 7.89±1.32 mm in females.

No substantial disparity in average survival duration was observed between genders (p:0.911).

The median TMT (7.47mm) was found to determine a cut-off value for predicting survival. The median overall survival was higher in the group with greater muscle thickness for TMT value (TMT<7.47 mm: 608 days TMT>7.47: 919 days). The measurement of patient sample is presented in Figure 1. The log-rank test revealed a statistically significant difference between the groups (p=0.044) (Figure 2).

Cox regression analysis indicated that TMT values less than median muscle thickness were negatively associated with overall survival (TMT<7.47: HR 1.63 CI 1.01-2.64, p = 0.044).

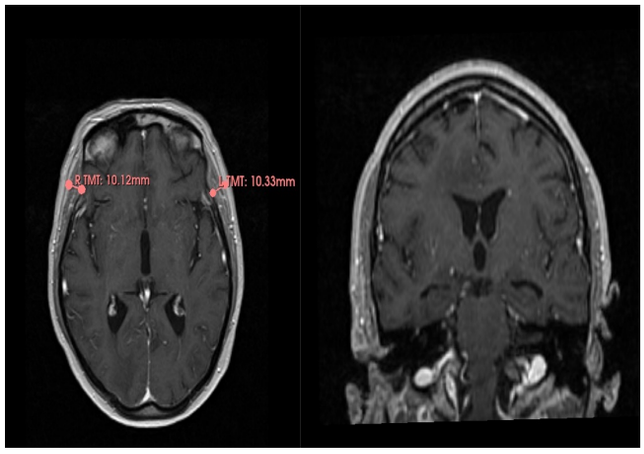

Figure 1. TMT measurement of the sample patient

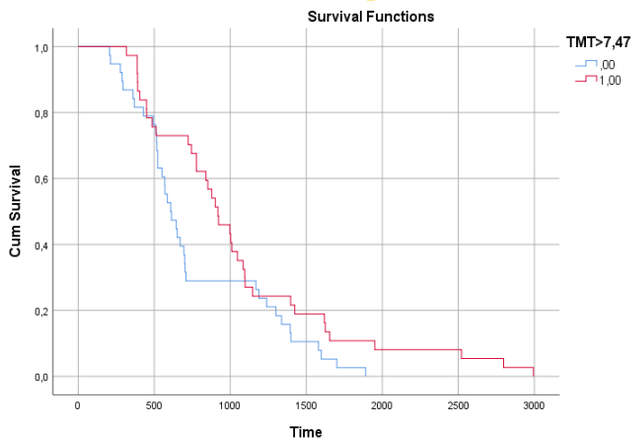

Figure 2. Kaplan-Meier analysis of overall survival based on median temporal muscle thickness (TMT)

Discussion

This single-center, retrospective open datasets study revealed that muscle thickness below the median value was associated with lower survival in patients with brain metastases that developed in patients with different primary malignancies

Sarcopenia, identified as muscle mass deterioration, has been specifically suggested as a crucial and autonomous indicator for clinical consequences, complications after surgery, and toxicity induced by chemotherapy among different cancer patients [14, 15]. The relationship between the prognosis of brain tumors and sarcopenia was greatly advanced by the work of Furtner et al. Multiple brain cancer types, including glioblastoma (GBM), melanoma, and metastatic tumors, have been recorded in this association [16-18].

Cho et al. [19] and Kim et al. [20] found that lower TMT thickness than median muscle thickness was associated with lower canal survival in patients with brain metastases whose primary disease was small cell lung cancer. The present study, in contrast, revealed that sarcopenia may be helpful in predicting overall survival, even in different primary malignancies.

Individualized care has become an increasingly pertinent matter. Tailoring treatment selection and plans to each patient has been shown to enhance treatment outcomes. In the prediction of postoperative complications, in-hospital death, and length of hospitalization, the determination of patient frailty holds significant utility [21]. Patient frailty is evaluated by utilizing patient age, weight, and performance status, while sarcopenia indicates a clear parameter for frailty and an adverse prognosis. The use of TMT as indicators of sarcopenia is recommended because they are practical and applicable for this intention. To enhance the integration of radiology, oncology, and surgery into everyday practice, it is recommended that these parameters be utilized as predictors of pre- and post-operative complications, tools for individualized treatment, and means to reduce patient frailty via physical exercise and myostatin inhibitors [22, 23].

Limitation

The present study has some major limitations. It was retrospectively designed as it was a study conducted on open datasets. Data on the performance status of the majority of patients at the time of diagnosis, including ECOG and KPS, were unavailable. Since the sample was relatively small, subtype analysis based on different primary malignancies could not be performed. The assessments were based on median cut-off values and no detailed assessment was performed in terms of quartiles or quantitative values. The lack of automated segmentation in measurements gives rise to user dependency. Only the OS was examined in the assessment, excluding progression-free survival from consideration.

Conclusion

We conclude that TMT is a promising marker for predicting survival in patients with metastatic brain tumors with different primaries.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest
The authors declare no conflict of interest.

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