



## Temporal muscle measurements as predictor for outcome in a cohort of IDH-wildtype glioblastoma patients

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### ABSTRACT

**Background:** Temporal muscle thickness has been suggested as an independent prognostic marker for glioblastoma patient outcome. Various cohort studies show however conflicting results. This study therefore aims to reevaluate the prognostic value of different types of temporal muscle measurements in glioblastoma patients.

**Methods:** A retrospective cohort study was performed including 137 patients diagnosed with IDH-wildtype glioblastoma. Temporal muscle thickness (TMT) and volume (TMV) were measured on preoperative MR-imaging. Next, these measurements were used in a multivariate Cox survival analysis to identify their possible prognostic value. These results were compared to the literature after systematic review of the Medline database.

**Results:** TMT has a moderate to strong linear correlation with total muscle volume (Pearson  $r = 0.6$ ;  $P < 0.001$ ). Glioblastoma patients “at risk for sarcopenia” show similar outcome compared to controls (median overall survival time: 13 months vs 11 months;  $P = 0.775$ ). In a covariate Cox regression model, none of the temporal muscle measurements (TMT, TMV or sex-specific cut-off points) showed prognostic value for outcome in glioblastoma patients.

**Conclusion:** Temporal muscle measurements show no independent relation to clinical outcome in IDH-wildtype glioblastoma patients. There seems adequate linear correlation of temporal muscle thickness and overall muscle volume. The literature on temporal muscle measurements lacks methodological consistency and should be interpreted with caution.

### 1. Introduction

IDH-wildtype glioblastoma is the most frequently occurring malignant intrinsic brain tumor in adults affecting 4–6 patients per 100.000 person-years (Pinson et al., 2024). Its prognosis is dismal with a median overall survival time of 14.6 months after optimal treatment (Stupp et al., 2005). In real world registries however, survival of glioblastoma patients outside trial protocol seems far inferior with an estimated median overall survival time of only 9.3 months (Pinson et al., 2024). Current standard-of-care treatment for glioblastoma includes maximal safe surgical resection followed by radiotherapy with concomitant and adjuvant temozolomide (Stupp et al., 2005).

Different prognostic factors for outcome in glioblastoma patients have been identified. Age and clinical performance scale at diagnosis are important patient related predictors (Lamborn et al., 2004). Surgically,

the aim is to perform a maximal safe resection of the tumor leaving as little contrast enhancing tumor as possible. Extent-of-resection (EOR) is a well-known predictor for outcome where a gross total or even supratotal resection of the tumor implies better survival (Karschnia et al., 2021). Grabowski et al. furthermore demonstrated residual tumor volume (RTV) to be a superior predictor for outcome compared to EOR (Grabowski et al., 2014). Finally, molecular characteristics of the tumor have prognostic relevance. Epigenetic methylation of the MGMT (O6-methylguanine-DNA methyltransferase) gene promoter is associated with improved efficacy of alkylating chemotherapy in high-grade glioma and therefore results in superior outcome (Hegi et al., 2005).

Sarcopenia is defined as a progressive and generalized skeletal muscle disorder associated with adverse outcome in the general population (Cruz-Jentoft et al., 2019). The disorder is primarily characterized by low muscle strength, quantity or quality. In cancer patients,

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sarcopenia at diagnosis has been associated with adverse clinical outcome due to increased chemotherapy toxicity and reduced therapy response, ultimately leading to inferior survival (Davis and Panikkar, 2019). Various biomarkers for clinical and scientific use have been proposed (Cruz-Jentoft et al., 2019). Grip strength is an easy to use and strong predictor for sarcopenia (Cruz-Jentoft et al., 2019; Steindl et al., 2020). It is however difficult to assess in retrospective cohort studies when not routinely performed and registered. Muscle quantity can be assessed alternatively by X-ray absorptiometry or using more routinely performed imaging modalities such as CT- or MR-imaging (Cruz-Jentoft et al., 2019). Many modalities have been tested for their reliability and accuracy (Cruz-Jentoft et al., 2019).

Temporalis muscle thickness (TMT) for example correlates well with the cross-sectional area of lumbar vertebral muscles (Leitner et al., 2018). TMT might therefore be used as a surrogate biomarker for skeletal muscle mass in glioblastoma patients to identify frail patients “at risk for sarcopenia” (Ten Cate et al., 2022). Furtner et al. were the first to show reduced TMT as an independent negative prognostic parameter in patients with recurrent glioblastoma (Furtner et al., 2019). More recently, a meta-analysis of various cohort studies seemed to confirm TMT as a predictive parameter for clinical outcome in glioblastoma patients (Sadhwan et al., 2022). Nevertheless, various other studies could not find a negative prognostic value of TMT measurements (Huq et al., 2021; Wende et al., 2021). The value of TMT as a clinically relevant prognostic factor therefore remains uncertain.

This study aims to advance the literature concerning the prognostic value of temporal muscle measurements in glioblastoma patients. It focusses not only on temporal muscle thickness but explores if temporal muscle volume (TMV) could provide a stronger correlation with outcome in molecularly defined glioblastoma patients. Finally, the results are confronted with a critical review of the literature.

## 2. Material and methods

### 2.1. Patient selection and characteristics

A retrospective patient cohort study was performed. Patients newly diagnosed with an IDH-wildtype glioblastoma between 2005 and 2023 were included. All cases were histologically confirmed after obtaining surgical specimen. Patients were treated afterwards in accordance with the Stupp protocol (Stupp et al., 2005). Hypofractionated adjuvant radiotherapy, as proposed for older and/or frail patients, was allowed for inclusion (Perry et al., 2017; Malmstrom et al., 2012). Relevant clinical parameters were retrieved from the patient files: age at diagnosis, functional status at baseline (Karnofsky Performance Scale), molecular parameters of the tumor (IDH-mutation using NGS and MGMT promoter methylation status using MSP), residual tumor volume (RTV), completion of concomitant radiotherapy (45 Gy or 60 Gy) and number of adjuvant temozolomide cycles. Patients were excluded if: (1) not all clinical or radiological parameters were available for review; (2) they received experimental treatment within a clinical trial.

This study was approved by the ethics committee of Ghent University Hospital (reference: THE-2022-0069). The study was conducted in accordance with the Declaration of Helsinki.

### 2.2. Tumor and temporal muscle measurements

Residual tumor volume (RTV) was determined on postoperative Gd-enhanced T1 magnetization-prepared rapid acquisition gradient echo (MPRAGE) images obtained within 72h after surgery using semi-automated segmentation software available on the Medtronic Stealth-station S7 (Medtronic, Louisville, CO, US).

Temporal muscle thickness (TMT) and volume (TMV) were measured on preoperative T1-MPRAGE images using the same software. In short, muscle thickness was measured perpendicular to the skull on an axial slice parallel to the AC-PC plane. The orbital roof and Sylvian

fissure were used as landmarks (Furtner et al., 2017). Muscle thickness was measured bilaterally in each patient and the mean value was used for statistical analysis. If the patient was operated on one side before, this side was not measured to reduce the impact of postsurgical muscle atrophy. TMV was measured on the side with the thickest muscle.

To identify patients “at risk for sarcopenia” sex-specific cut-off values for TMT were used. These values were introduced before by Steindl et al. who examined TMT values in a healthy Caucasian population (Steindl et al., 2020). Cut-off points to identify patients “at risk for sarcopenia” were determined 6.3 mm for male and 5.2 mm for female persons.

### 2.2.1. Statistical analysis

The Pearson correlation coefficient was used to determine linear correlation between the various continuous variables. Multivariate Cox regression analysis was performed to investigate the prognostic relevance of the different temporal muscle measurements. Means were statistically compared using the independent-samples student t-test. For all statistical tests, a two-sided p-value of 0.05 was used to determine significance. Statistical analysis was performed using the SPSS software v29 (IBM, New York, US).

### 2.2.2. Literature review

In order to compare the results of this study with the current literature a review of the literature was performed. The Medline database was searched using the following Mesh terms: glioblastoma, temporal muscle, sarcopenia, survival rate, prognosis, survival analysis and treatment outcome. The precise search query is illustrated in supplementary material 1. Only manuscripts using a similar methodology were included. Furthermore, temporal muscle measurements should have been performed on preoperative MR-imaging in a glioblastoma only patient cohort. The quality of evidence for each included article was reviewed using the GRADE scale (Balshem et al., 2011).

## 3. Results

### 3.1. Epidemiology

In total, 137 patients were included for statistical analysis (Table 1). Mean age at diagnosis was 61.9 years; 36.5 % were female. Median overall survival time for the study population was 12 months. Diagnosis was pathologically confirmed after surgery in all cases; 38.7 % underwent surgical biopsy without resection. Mean tumor volume (in mL) at the start of radiochemotherapy was 19.4 in biopsy-only patients and 1.7 in surgically treated patients. Molecular review confirmed IDH-wildtype status in all patients and MGMT promoter hypermethylation status in 34.3 % of cases. After surgery, 94.9 % of patients completed their concomitant radiotherapy. The mean number of cycles of adjuvant temozolomide was 4. Patients identified at risk for sarcopenia using sex-specific cut-off values for TMT showed a significantly lower KPS at baseline (Table 1). There were no relevant differences in other epidemiological or treatment related parameters between both groups.

### 3.2. Correlation of temporal muscle thickness and volume

The mean thickness of the temporal muscle in the study cohort was 7.6 mm; the mean volume 21.5 cm<sup>3</sup>. Using sex-specific cut-off values for temporalis muscle thickness, 11 female patients (22.9 %) and 16 male patients (19 %) were identified “at risk for sarcopenia”. There was no correlation between age at diagnosis and temporal muscle thickness ( $r = -0.023$ ), nor muscle volume ( $r = 0.04$ ). On the other hand, there seemed moderate to strong positive correlation between muscle thickness and volume ( $r = 0.6$ ;  $P < 0.001$ ; Fig. 1).

### 3.3. Correlation of temporal muscle measurements and clinical outcome

Survival analysis was performed using a multivariate Cox regression

**Table 1**  
Epidemiology of study cohort.

| Variables                        |                             | Reference cohort (n = 110) | Cohort "at risk for sarcopenia" (n = 27) | P-value            |
|----------------------------------|-----------------------------|----------------------------|--|--------------------|
| Sex                              | female                      | 39 (35,5 %)                | 11 (40,7 %)                              | 0,261 <sup>a</sup> |
|                                  | male                        | 71 (64,5 %)                | 16 (59,3 %)                              |                    |
| Age-at-diagnosis (years)         | mean                        | 62,0                       | 61,6                                     | 0,880 <sup>b</sup> |
| Karnofsky Performance Scale      | <70                         | 15 (13,6 %)                | 9 (33,3 %)                               | 0,016 <sup>a</sup> |
|                                  | ≥70                         | 95 (86,4 %)                | 18 (66,7 %)                              |                    |
| MGMT promoter methylation status | unmethylated                | 72 (65,5 %)                | 18 (66,7 %)                              | 0,905 <sup>a</sup> |
|                                  | methylated                  | 38 (34,6 %)                | 9 (33,3 %)                               |                    |
| Surgery                          | Biopsy only                 | 43 (39,1 %)                | 10 (37,0 %)                              | 0,844 <sup>a</sup> |
|                                  | Resection                   | 67 (60,9 %)                | 17 (63,0 %)                              |                    |
|                                  | Mean RTV (ml)               | 8,4                        | 9,2                                      | 0,789 <sup>b</sup> |
| Completion of radiotherapy       | 60 Gy                       | 97/102 (95,1 %)            | 21/23 (91,3 %)                           | 0,545 <sup>a</sup> |
|                                  | 45 Gy                       | 9/9 (100 %)                | 4/4 (100 %)                              |                    |
| Number of TMZ cycles             | mean                        | 3,6                        | 6  | 0,062 <sup>b</sup> |
| Overall survival time (months)   | median                      | 11,6                       | 11,0                                     | 0,323 <sup>c</sup> |
|                                  | mean                        | 15,2                       | 12,5                                     |                    |
| Temporal muscle measurements     | mean TMT (mm)               | 8,3                        | 5,2                                      | –                  |
|                                  | mean TMV (cm <sup>3</sup> ) | 22,9                       | 16,3                                     |                    |

<sup>a</sup> Pearson-Chi square test.

<sup>b</sup> Independent samples Student t-test.

<sup>c</sup> Log-rank test.

analysis using all known prognostic risk factors in glioblastoma as covariates (Table 2). Absolute temporal muscle thickness was not associated with inferior outcome after correction for age at diagnosis, clinical status of the patient (KPS), MGMT promoter methylation status, residual contrast-enhancing tumor volume on postoperative imaging (in ml), completion of concomitant radiotherapy (45 Gy or 60 Gy) and number of adjuvant cycles of Temozolomide (HR 0.982; P = 0.687). The same was true for temporal muscle volume after correction for the same covariates (HR 1.024; P = 0.054). Finally, the risk for sarcopenia was not associated with inferior outcome as determined by a multivariate Cox regression analysis (HR 0.873; P = 0.582) (see Fig. 2).

## 4. Discussion

### 4.1. Prognostic role of temporal muscle measurements

At the time of diagnosis in glioblastoma patients, several patient and tumor specific parameters determine patient outcome. The most important patient specific factors include age and overall performance grade, while IDH-mutation and MGMT-promoter methylation status are tumor-specific factors strongly correlated with outcome. Several studies have shown a correlation between temporal muscle thickness and overall survival of glioblastoma patients, which would render TMT an important prognostic parameter (Table 3). The assessment of temporal

muscle measurements furthermore seems appealing due to its easy and straightforward applicability on preoperative MR imaging. Question remains however, if these measurements really hold a true independent relationship with patient outcome, as they are likely influenced by a range of other biometric variables. Various earlier reports suggested for example a clear relationship of patient age and sex with temporal muscle thickness (Lin et al., 2023; Pesonen et al., 2025; Mohajerani et al., 2025). Medical comorbidities might influence muscle quality and quantity in patients as well. In this patient cohort, the patient group at risk for sarcopenia significantly showed lower KPS values at baseline (Table 1). This may explain the lack of correlation between temporal muscle measurements and outcome in this cohort of uniformly treated glioblastoma patients. Although intuitively quite attractive, this relationship is not clearly established in the current literature (Klingenschmid et al., 2023, 2024). Temporal muscle measurements therefore seem to act as a surrogate biomarker for treatment outcome and not necessarily as an independent predictor.

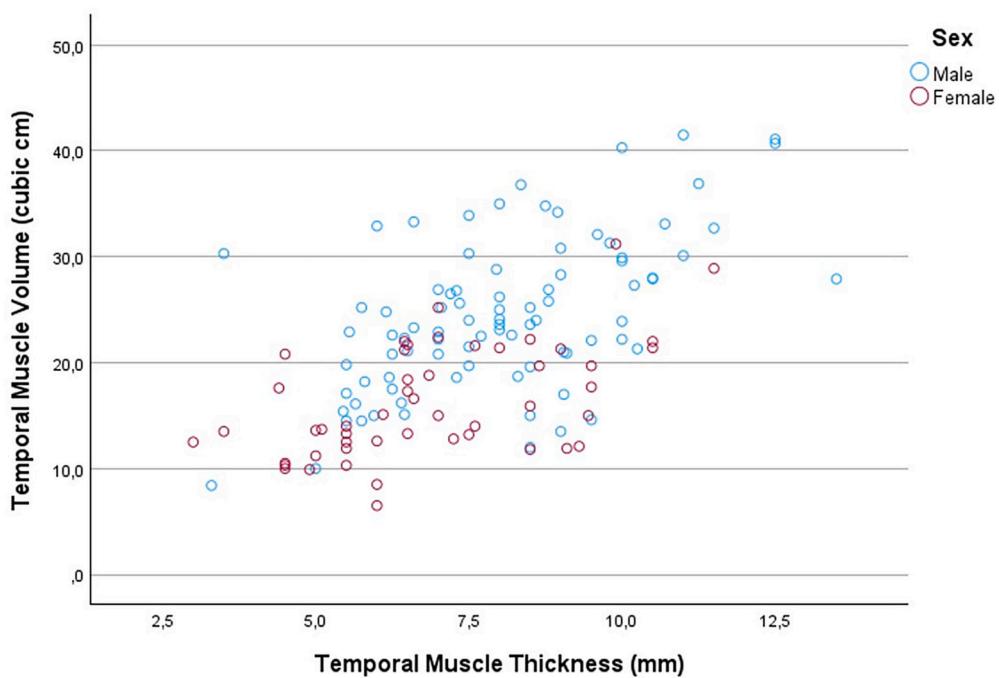
Given the relationship and possible interchangeability of TMT and KPS, a critical review of the literature was performed to assess and compare the used methodologies in the various reports published in the recent years.

### 4.2. Temporal muscle measurements and outcome in newly diagnosed glioblastoma patients: literature review

An overview of the relevant literature is presented in Table 3. The papers are listed chronologically and their statistical methodology is presented. The inclusion of known prognostic factors as covariates in the multivariate Cox regression model is reviewed for each paper: age at diagnosis, functional status at baseline (KPS or ECOG), molecular parameters of the tumor (IDH-mutation status and MGMT promoter methylation status), extent of resection or residual tumor volume and administration of adjuvant radio- and chemotherapy. The larger and/or statistically more robust studies are discussed hereafter.

Furtner et al. published a prospectively monitored cohort study analyzing the value of TMT in newly diagnosed molecularly-undefined glioblastoma patients (Furtner et al., 2022). In this first study on the topic, they used data from the CENTRIC EORTC and CORE trials in which the added value of Cilengitide to standard-of-care in MGMT promotor methylated (CENTRIC) and unmethylated patients (CORE) was examined. In both trials, only patients with ECOG 0/1 were eligible for inclusion. About half of the patients in both trials underwent gross total resection of their tumor. IDH-mutation analysis was not available. The authors used sex-specific TMT values to dichotomize their cohorts as proposed by Steindl et al. (2020).

In the subgroup with MGMT promotor methylated tumors, the authors found an inferior outcome in patients "at risk for sarcopenia" (TMT below sex-specific cut-off) when corrected for age at diagnosis, cognitive performance and EOR. Interestingly, no IDH-mutation analysis was performed within the CENTRIC-trial (Stupp et al., 2014). Given the somewhat younger mean age of the patient cohort (58 years), median overall survival time of 26.3 months and exclusive inclusion of patients with MGMT promoter methylated tumors, it should be assumed a significant number of grade 4 IDH-mutant astrocytoma patients were included in this trial. This is relevant given the likely influence of age on temporal muscle volumes and treatment outcome in glioblastoma patients. Finally, around 25 % of patients in the CENTRIC trial did not complete their course of radiation therapy and more than 10 % did not complete full adjuvant treatment with temozolomide due to early progression or treatment toxicity (Stupp et al., 2014). Adjuvant treatment and IDH-mutation status were, however, not included in the multivariate Cox regression model or at least not significant (Furtner et al., 2022). In the MGMT promoter unmethylated group, the authors found an inferior outcome in patients "at risk for sarcopenia" when corrected for age at diagnosis, steroid use at baseline, ECOG-status and RPA class (Furtner et al., 2022).



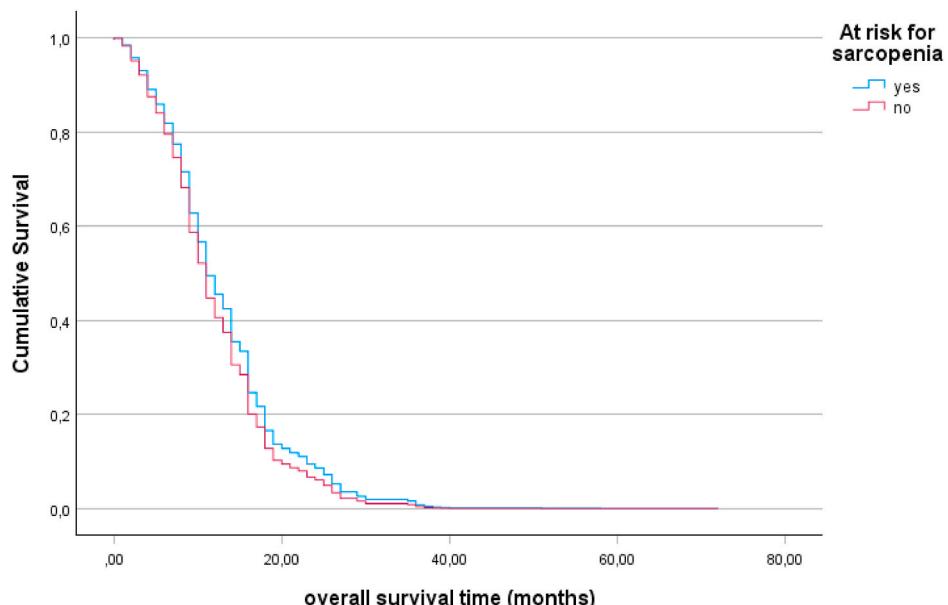
**Fig. 1.** Correlation of temporal muscle measurements according to sex.

**Table 2**

Multivariate Cox regression analysis for temporal muscle thickness as independent prognostic marker for overall survival in IDH-wildtype glioblastoma.

| Parameter                                 | Hazard Ratio for death | P-value |
|---|------------------------|---------|
| Age at diagnosis (year)                   | 1,02                   | 0,012   |
| Karnofsky Performance Scale (<70)         | 2,17                   | 0,006   |
| MGMT promoter methylation status (no)     | 2,26                   | <0,001  |
| Residual Tumor Volume (ml)                | 1,01                   | 0,063   |
| Completion of adjuvant radiotherapy (no)  | 4,70                   | <0,001  |
| Number of adjuvant cycles of Temozolomide | 0,83                   | <0,001  |
| Temporal muscle thickness (mm)            | 0,98                   | 0,687   |

Broen and colleagues published a large multicentric retrospective cohort study analyzing 328 IDH-wildtype glioblastoma patients (Broen et al., 2022). They used similar sex-specific cut-off values for TMT to identify patients “at risk for sarcopenia” (Steindl et al., 2020). A significant inferior survival in the patient cohort with lower TMT values was found using a multivariate Cox regression model including adjuvant treatment, ECOG at baseline, surgery and MGMT promoter methylation (Broen et al., 2022). Nevertheless some methodological remarks should be made. First of all, the mean age of the at-risk group was significantly higher at baseline (67.1 vs 62.3 years); age at diagnosis was nevertheless not included in the final Cox regression model. Furthermore, surgery was dichotomized into biopsy versus resection; nor extent of resection, nor residual tumor volume were evaluated. Finally, the completion of adjuvant treatment was not incorporated in the model although patients



**Fig. 2.** Kaplan-Meier curve for patients “at risk for sarcopenia”.

**Table 3**

Overview of the literature concerning temporal muscle measurements as predictor for clinical outcome in IDH-wildtype glioblastoma patients.

| study                                | date of publication | n   | GRADE    | predictor | age | KPS/ECOG | molecular parameters | EOR/RTV | adjuvant treatment | measurement |
|--------------------------------------|---------------------|-----|----------|-----------|-----|----------|----------------------|---------|--------------------|-------------|
| Furtner et al. (progressive disease) | 2019                | 308 | very low | +         | no  | no       | no                   | no      | yes                | TMT         |
| Cinkir et al.                        | 2019                | 47  | very low | —         | yes | no       | no                   | no      | no                 | TMT         |
| An et al.                            | 2020                | 177 | very low | +         | yes | yes      | no                   | yes     | no                 | TMT         |
| Liu et al.                           | 2020                | 130 | very low | +         | yes | no       | no                   | no      | yes                | TMT         |
| Furtner et al.                       | 2021                | 755 | very low | +         | yes | yes      | no                   | no      | no                 | TMT         |
| Huq et al. (newly diagnosed)         | 2021                | 378 | low      | —         | yes | yes      | yes                  | yes     | yes                | TMT         |
| Huq et al. (progressive disease)     | 2021                | 163 | low      | —         | yes | yes      | yes                  | yes     | yes                | TMT         |
| Muglia et al.                        | 2021                | 51  | very low | —         | yes | yes      | yes                  | yes     | no                 | TMT         |
| Wende et al.                         | 2021                | 335 | low      | —         | yes | yes      | yes                  | yes     | yes                | TMT         |
| Broen et al.                         | 2022                | 328 | very low | +         | no  | yes      | yes                  | no      | no                 | TMT         |
| Mi et al.                            | 2022                | 96  | very low | +         | yes | no       | no                   | no      | no                 | CSA         |
| Pasqualetti et al.                   | 2022                | 52  | very low | +         | yes | no       | no                   | yes     | yes                | TMT         |
| Sütçüoglu et al.                     | 2023                | 74  | very low | —         | yes | yes      | no                   | no      | no                 | TMT/CSA     |
| Tang et al.                          | 2024                | 102 | very low | +         | yes | yes      | no                   | no      | yes                | TMT         |
| this study                           | 2025                | 137 | low      | —         | yes | yes      | yes                  | yes     | yes                | TMT/TMV     |

KPS – Karnofsky Performance Scale; ECOG – Eastern Cognitive Oncology Group Performance Scale; EOR – extent-of-resection; RT V – residual tumor volume; TMT – temporal muscle thickness; CSA – cross sectional area; TMV – temporal muscle volume.

with lower TMT-values showed increased risk of early discontinuation of the adjuvant treatment (Broen et al., 2022).

Huq et al. performed a retrospective cohort study including 378 newly-diagnosed grade 4 glioma patients, including 42 cases of IDH-mutant grade 4 astrocytoma (Huq et al., 2021). Using a TMT cut-off value of 7.1 mm, they identified 9 % of cases as patients with low TMT at baseline. Using a well-built multivariate Cox regression analysis, including age at diagnosis, KPS, adjuvant treatment, extent of resection and molecular characteristics, the authors could not identify TMT as negative prognostic parameter for outcome. The authors identified their optimal TMT cut-off value using maximally selected rank statistics (Huq et al., 2021).

Finally, Wende et al. published a large retrospective cohort study with 335 IDH-wildtype glioblastoma patients (Wende et al., 2021). They could not show a negative prognostic significance of TMT thickness using an extensive multivariate Cox regression analysis including age at diagnosis, KPS, MGMT promoter methylation, extent of resection and adjuvant treatment. The authors did not use cut off points for TMT to identify patients at risk for sarcopenia but used TMT as a continuous variable instead (Wende et al., 2021).

Overall, the presented papers use a very similar methodology to measure TMT on preoperative MR-imaging, as was first proposed by Furtner and colleagues in 2017 (Furtner et al., 2017). Nevertheless, these values were applied differently in the subsequent statistical analysis in each paper. TMT values were used as a continuous variable or dichotomized using different cut-off points. These cut-off points were sex-specific as determined by Steindl et al. or based on the Youden index or log rank statistics. Furthermore, multivariate Cox regression analysis was used in all aforementioned papers to examine the prognostic significance of TMT. The covariates included in these analyses, or at least mentioned in the individual papers, are unfortunately very heterogeneous. It therefore seems rather difficult to directly compare the different papers or to process them in a meta-analysis. Nonetheless, the papers with a more robust methodology and thoroughly built multivariate Cox regression analysis tend to show no clear correlation of TMT and clinical outcome in newly diagnosed IDH-wildtype glioblastoma patients. The results of this current retrospective cohort study are in line with these findings.

In 2022, a systematic review and meta-analysis on TMT as predictor for outcome in glioblastoma was published by Sadhwani et al. (2022). They concluded TMT is associated with shorter overall and progression free survival in glioblastoma patients based on a pooled hazard ratio. These findings are nevertheless the result of inclusion of very diverse and difficult to compare retrospective cohort studies, as mentioned earlier. These studies do not only use inconsistent covariates in the Cox

regression analysis, they include different patient cohorts (including grade 3 astrocytomas) and use varying methods to measure TMT as well. Due to this heterogeneity, the results of the meta-analysis seem therefore weak and difficult to generalize.

#### 4.3. Temporal muscle measurements and outcome in glioblastoma patients with progressive disease

Some years before Furtner et al. published their results on the value of TMT in newly diagnosed glioblastoma patients, the authors analyzed a patient cohort with progressive glioblastoma first (Furtner et al., 2019). The study was based on prospectively gathered clinical data of the EORTC 26101 trial (Wick et al., 2017). In this phase 3 trial, patients with progressive but molecularly-undefined glioblastoma were randomized to receive second-line chemotherapy (Lomustine/CCNU) with or without anti-VEGF targeted therapy (Bevacizumab). Overall, 23 % of included patients showed MGMT promoter methylation, 28.6 % were unmethylated and 47.6 % had missing data. After further progression, more than half of the included patients received further treatment with various combinations of repeat surgery, repeat radiotherapy and/or rechallenge chemotherapy (Wick et al., 2017).

The authors used 308 patients of the phase III trial to investigate TMT as prognostic parameter for outcome. They determined 7.2 mm of thickness using the Youden index as an optimal cut-off value to dichotomize their patient cohort in a proof-of-concept test cohort (Furtner et al., 2019). Using this value in a multivariate Cox regression model with steroid use, MGMT promotor methylation status, tumor diameter and localization, the authors found a significant inferior outcome in patients with TMT below 7.2 mm (Furtner et al., 2019).

These findings are in line with a high-quality retrospective cohort study performed by Huq et al. (2021). They analyzed 149 patients with progressive glioblastoma. In a multivariable Cox regression analysis, they found a TMT value below 7.1 mm predictive for inferior outcome (Huq et al., 2021).

The literature concerning progressive glioblastoma is limited to these two reports. Both draw the same conclusion from their respective patient database which is probably even more heterogeneous compared to studies concerning newly diagnosed patients. Huq et al. however found, interestingly, no prognostic value of TMT in their cohort with only newly diagnosed patients. The validity of these results is difficult to appraise at this moment due to the limited number of studies and strong heterogeneity of the patient population after disease progression. However, TMT values seem to decline during treatment in a subgroup of patients (60 % in the study cohort of newly diagnosed glioblastoma patients of Furtner et al. (2022)). It remains uncertain if this subgroup

might experience systemic consequences of temozolomide treatment, rendering these patients less resilient to second-line treatment. Further analysis could shed more light on this topic.

#### 4.4. Limitations and strengths

The retrospective design of this cohort implies an increased risk for bias in the clinical information gathering. For example, a significant number of patients had to be excluded due to incompleteness of the medical files with missing radiographical or molecular data. Due to this smaller patient cohort, statistical power might be lacking to identify a statistically significant but small prognostic role of temporal muscle measurements in IDH-wildtype glioblastoma patients. On the other hand, all patients in this study were uniformly treated according to the Stupp protocol, IDHwt status was confirmed in all patients using NGS and tumor volumes before start of radiochemotherapy were determined in all cases. This allowed a trustworthy multivariable survival analysis, using internationally accepted prognosticators. Moreover, this is the first study to use temporal muscle volume, and not only thickness, as a covariate. Although muscle volume might seem more representative for the actual “muscle health” in patients, no clear prognostic role could be identified.

### 5. Conclusion

This retrospective cohort study could not find any prognostic value of temporal muscle measurements in newly diagnosed IDH-wildtype glioblastoma patients. These findings fall in line with some other well executed cohort studies. The literature concerning the prognostic value of temporal muscle measurements uses heterogenous statistical methods to analyze TMT as predictor for outcome making firm conclusions unconvincing. Overall, the evidence in favor for TMT as an individual prognostic factor in glioblastoma seems controversial at best.

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bas.2025.105914>.

### Data availability

Some statistical data are available for review upon request to the corresponding author.

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