

# Relationship of Balance and Mobility Status to Quality of Life in Patients with Primary Brain Tumors: A Pilot Study

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Received date: 09 Feb 2014; Accepted date: 20 May 2014; Published date: 23 May 2014

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#### Abstract

**Objective:** Most research regarding the effectiveness of brain tumor treatments measure survival time, recurrence rate, and extent of surgical resection. Objective measurements of functional abilities and self-perceived quality of life (QoL) are important aspects of treatment response, yet these are not commonly assessed. This study was designed to determine the relationship between balance and mobility status and self-perceived QoL for patients before and after surgical excision of primary brain tumors.

**Methods:** Nine adults who underwent surgical excision of presumed primary brain tumor were assessed prior to, immediately following, and 3 months post-surgery utilizing the Timed Up-and-Go (TUG), Tinetti Performance-Oriented Mobility Assessment (Tinetti) and Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). ANOVA with repeated measures over time was performed on the data across the three time points. Outcome measures were correlated using Spearman's correlations. Statistical significance for all tests was accepted at p < 0.05.

**Results:** Balance, mobility and QoL measures changed significantly from pre-surgery to immediately postsurgery and from immediately post-surgery to 3 months later. However, neither QoL nor balance or mobility demonstrated significant change from pre-surgery to 3 months post-surgery. These results reflect clinically-noted changes in physical abilities the 3 time points. All measures significantly correlated at the two post-surgery measurements, indicating a close link between balance and mobility and QoL.

**Conclusion:** The TUG and Tinetti can be used in brain tumor patients to quantify clinical changes in balance and mobility. These changes correlate with QoL over time.

Keywords: TUG; Tinetti; SF-36; Brain Tumor; Quality of life

#### Introduction

Impairments standing balance and limitations with ambulation and transfers are common in patients with brain tumors [1]. Deficits in performing ambulation and balance skills reduce overall functional abilities and independence with daily activities. One goal of surgical excision of brain tumor is to improve brain function, including motor skills, mobility, balance, and overall quality of life [1].

Multiple studies have assessed the effectiveness of surgery in minimizing tumor volume, reducing recurrence rates, or increasing survival time following diagnosis [2-7]. However, very few studies specifically measure functional outcomes using reliable and valid instruments despite clinical tools to quantify this domain [8-10]. These studies refer to neurological deficits or physical function deficits, but fail to quantify these deficits or to objectively measure change over time [11].

The degree of physical dysfunction varies depending on tumor location, size and its invasive properties [12-13]. Clinical signs may be similar to those seen following stroke or traumatic brain injury

[1,11,14-16. While not every person with a brain tumor presents with physical deficits, impairments such as altered strength, muscle tone, coordination, and sensation often occur [13,17,18]. The common impairment of hemiparesis frequently results in decreased functional mobility limitations.

Researchers have examined physical impairments in patients with brain tumors, but the data is sporadic and not well quantified. Many of these studies fail to measure physical impairments or functional status objectively [2-5,7,19-21]. For instance, Qureshi et al. [6] incorporated two functional outcome scales – Rankin score and Barthel Index (BI)into a study assessing the physical effects of supratentorial mass lesions. However, these measures were determined by phone interview with the patient's caregivers and did not involve direct patient examination [6]. The 6 Minute Walk Test has also been used to assess physical functioning in gliomas, but its value in neurologically impaired patients is unknown [22].

Gait and balance are important components of physical functioning. The Timed-Up-and-Go (TUG) and Tinetti Performance-Oriented Mobility Assessment (Tinetti) are excellent assessments of balance and mobility for several reasons. Both tests are easy to

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administer. Both tests have a history of use in patients with neurological disorders.

The TUG correlates well with the Berg Balance Scale (BBS) (often used to assess patients with stroke), which in turn correlates well with the Tinetti [23-28]. Because neurological and mobility deficits and pattern of recovery of brain tumor patients is similar to that observed after stroke [14-16,29-31], and the TUG and Tinetti have been reliably validated for use in the stroke population [32,33], both the TUG and Tinetti are appropriate for use in brain tumor patients, too. The TUG and Tinetti have been shown to be valid in monitoring change in performance over time [23,34-36]. Finally, because "mobility, ambulation, and balance are not mutually exclusive constructs," [26] use of the TUG and Tinetti together a more complete picture of physical functioning in patients.

Physical functioning is a component of patient self-perceived quality of life (QoL). In patients with brain tumors, correlation between physical functioning and QoL has been mixed. In one study, functional measures did not correlate well with a QoL measure during rehabilitation of 10 patients with brain tumor [8], but another study of brain tumor subjects found functional status correlated well with QoL [37]. The TUG and Tinetti were not used in those studies.

The primary objective of this pilot study is to determine whether the (TUG) [23] and (Tinetti) [24] would be sensitive and appropriate outcome measures of balance and mobility status pre-operatively and post-operatively in patient with primary brain tumors. The secondary aim of this project was to determine if balance and mobility as measured by these tools would correlate with QoL. We hypothesize that the TUG and Tinetti would be sensitive and appropriate measures of balance and mobility in patient with primary brain tumors and would correlate with QoL measured by SF-36.

# Methods

Patients pre-operatively diagnosed with primary brain tumor were selected as part of a convenience sample and assessed by a single tester. Patients were evaluated the day before surgery, 3 days after surgery, and 3 months after surgical resection to determine 1) balance and mobility using TUG and the Tinetti instruments and 2) self-perceived QoL using the Medical Outcome Study (MOS) 36-Item Short Form Health Survey (SF-36).

Patients were included if they had surgical resection of presumed primary brain tumor and intact lower body structures. Exclusion criteria included age < 18 years old, preexisting neurological disorders, history of dementia or cognitive impairment with inability follow directions on standardized measures, or preexisting balance conditions. The study was approved by the Health Sciences Institutional Review Board at University of Missouri-Columbia (IRB #1091137).

In the TUG, test subjects are started in a comfortable seated position in a standard arm chair (seat height 46 cm, arm height 65 cm). On command, subjects arose from the chair, walked 3 meters to a marker on the floor, turned around, walked back to the chair, and sat down again. The test is scored by the time required to accomplish the sequence. Community-dwelling elderly should perform the test in < 12 seconds. Subjects taking less than 10 seconds function independently; those requiring > 15 seconds had fall risk, and those requiring > 30 seconds need assistance with transfers and stair ambulation [23].

The Tinetti is a standardized test which measures a person's ability to balance while performing activities, including walking, in two components: a 9-item balance portion and a 7-item gait section. The nine balance maneuvers include the following: sitting, arising, attempting to arise, immediate standing (first 5 seconds), standing, sternal nudge, eyes closed standing, turning 3600 while standing, and sitting.

Each item is scored as 0 (abnormal response), 1 (adaptive response), or 2 (normal response) with the exception of sitting balance and eyesclosed standing balance, in which abnormal scores 0 and normal scores 1; therefore, the maximum score for the balance component is 16. The gait portion includes 7 items: gait initiation, step symmetry, step continuity, path, trunk, walking time, and step length and height (right swing foot and left swing foot scored separately for both length and height). Each portion is scores as 0 for abnormal and 1 for normal, with the exception of path, which is scored 2 for normal; maximum score on the gait portion is 12, for a total maximum score of 28. Patients who score < 19 have a high fall risk.

The SF-36 contains 36 questions which cover 8 functional domains: physical functioning (10 items), role limitations due to physical health problems (4 items), bodily pain (2 items), role limitations due to emotional problems (3 items), vitality (4 items), social functioning (2 items), mental health (5 items), and general health perceptions (5 items). Each item has 5 levels of response. Scores for each domain range from 0 to 100 once scaled to the test manual. Higher scores indicate better health status for the domain. Two component summary scores – physical health component and mental health component – are also derived from the SF-36 manual. Scores can be compared to age-appropriate United States norms.

Prior to surgery, patients were assessed by the tester. Each patient completed 2 trials of the TUG; scores were averaged and recorded. Each patient then completed the SF-36 independently; on occasionally a caregiver or the tester who read the questions and indicated the answers provided by the patient. Finally, the patient completed the Tinetti balance and gait assessments, which were scored. Following surgery, once the patient was determined to be medically stable and often on the day prior to discharge from the hospital, the testing procedure was repeated. The measures were completed a third time as part of the patient's 3 month physician follow-up appointment; the tests were administered in the same sequence by the original tester; again, a caregiver or the tester could assist the patient in completing the SF-36 form by marking the patient's answers to the questions. For the TUG and the Tinetti, participants were allowed to use assistive devices or wear orthotics but no physical assistance was provided.

TUG, Tinetti, and SF-36 scores analyzed statistically with ANOVA with repeated measures over time across the three time points. Outcome measures were correlated with Spearman's correlations. Statistical significance for all tests was accepted at p < 0.05.

# Results

# Demographics

Nine patients were studied, 3 men and 6 women, aged 40 to 71 (mean 49.2 + /1 10.1 years). Three patients had a diagnosis of meningioma and five had a glial neoplasm, and 1, presumed to have a hemorrhagic glial neoplasm prior to surgery had no evidence on tumor on final pathology. Table 1 describes each patient's clinical findings at presentation and at follow-up.

Citation: Krug J, Litofsky NS (2014) Relationship of Balance and Mobility Status to Quality of Life in Patients with Primary Brain Tumors: A Pilot Study. Int J Phys Med Rehabil 2: 196. doi:10.4172/2329-9096.1000196

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Patient #	Age	Diagnosis	Tumor Location	Pre-Op Neurological Symptoms/Deficts	3 Month Post-Op Neurological Deficits	Post-Op Treatment	Survival
1	54	Hemorrhage (no evidence of tumor)	Temporal, right	Seizure; dysdiadokinesis, left	Anxiety, depression	none	84 months
2	64	Glioblastoma (Grade IV)	Front-parietal, left	Hemiparesis, right	Hemiparesis, right	XRT, chemotherapy	11 months (died)
3	51	Glioblastoma (Grade IV)	Parietal, right	Hemiparesis, left	No deficits	XRT, chemotherapy	(died)
4	71	Meningioma (atypical)	Frontal	Seizure; monoparesis,,left leg	No deficits	None	72 months
5	70	Meningioma	Temporal, left	None	No deficits	None	74 months
6	56	Anaplastic astrocytoma (Grade III)	Parietal, left	Seizure	Unsteady gait	XRT, chemotherapy	9 months (died)
7	43	Oligodendroglio ma (Grade II)	Fronto-parietal, right	Seizure; pronator drift, left	Dysdiadokinesis, left	none	74 months
8	40	Anaplastic astrocytoma (Grade III)	Frontal (posterior), right	Seizure; hemiparesis, left	Hemiparesis, left	XRT, chemotherapy	19 months (LTF)
9	45	Meningioma	Foramen magnum, right	Neck pain; no deficits	CN X1 paresis, right	Radiosurgery	85 months

Table 1: Patient's clinical findings.

#### **Outcome Measures over time**

**SF-36:** Mean SF-36 pre-surgery score was 57.3 +/16.9. Immediately following surgery, mean SF-36 score was 48.9+/-17.4. Three months following surgery, mean SF-36 score was 69.2+/-21.2. Changes in SF-36 score were significantly different between the pre-surgery and immediately after surgery time periods (p < 0.05), and between the immediately after surgery and 3 months after surgery time periods (p < 0.01). Pre-surgery to 3 months following surgery, SF-36 scores were not significantly different (p = 0.11). Like the TUG and Tinetti, SF-36 scores worsened immediately following surgery, and subsequently improved to near pre-surgery levels by 3 months following surgery. SF-36 scores are shown in Figure 1.



**TUG:** Mean TUG pre-surgery was 13.9 +/- 4.2 seconds. Immediately following surgery, TUG mean time deteriorated to 18.8 +/-7.1 seconds. At three months following surgery, mean TUG improved to 13.0+/-5.7 seconds. Changes in TUG time were significantly different between pre-surgery and immediately after surgery time periods (p < 0.05), and between immediately after surgery and 3 months after surgery time periods (p < 0.05). Pre-surgery to 3 months following surgery TUG times were not significantly different (p = 0.86). Figure 2 illustrates TUG times for each patient at each time point.



**TINETTI:** Mean Tinetti pre-surgery score was  $20.4 \pm -5.7$ . Immediately following surgery, mean Tinetti score was  $14.4 \pm -8.2$ . Three months following surgery, mean Tinetti score was  $23.6 \pm -4.6$ .

Changes in Tinetti score were also significantly different between the pre-surgery and immediately after surgery time periods (p < 0.05), and between the immediately after surgery and 3 months after surgery time periods (p < 0.001). Comparing pre-surgery to 3 months following surgery, Tinetti scores were not significantly different (p = 0.11). Like the TUG, Tinetti scores worsened immediately following surgery, and subsequently improved to near pre-surgery levels by 3 months following surgery. Tinetti results are depicted in Figure 3.



Due to small sample size, no covariates were included in any ANOVA models.

### **Correlation of Outcome Measures**

Pre-surgery, the TUG and Tinetti significantly correlated with each other. (r=0.992, p<0.05). SF-36 did not correlate with either balance and gait test prior to surgery. However, all scores significantly correlated with each other at the two time points following surgery. TUG and Tinetti correlated immediately post-surgery (r=-0.833, p<0.01) and 3 months post-surgery (r=-0.966, p<0.05. SF-36 and TUG (r=-0.762, p<0.05) and SF-36 and Tinetti (r=0.883, p<0.005) correlated immediately post-surgery. Lastly, balance and gait measures and QoL correlated at 3 months post-surgery (SF-36 and TUG: r=-0.845, p<0.005; SF-36 and Tinetti: r=0.849, p<0.005) (Figure 4).





# Discussion

While survival remains an important endpoint, other endpoints warrant assessment in patients with cancer or other neoplasms [25]. Two domains not routinely measured in patients with brain tumors include physical function and QoL. Therefore, the goals of this study were to examine the utility of the TUG and Tinetti assessments of gait and balance in patients with primary brain tumors to determine whether such measures of physical function would also correlate with QoL We found that the TUG and Tinetti were appropriate and sensitive measures in patients with primary brain tumors. Furthermore, and the tests correlated well with each other and with SF-36 QoL tool.

The TUG data in this study is comparable to values calculated by Mayo et al. [38] in recovery of 111 patients in first three months following stroke. At three months, the TUG scores between Mayo et al. and our patients were virtually the same (post-stroke TUG was 15.2+/-11.2 seconds and brain tumor patients were 13.0+/-5.7 seconds), reinforcing similarities between stroke and brain tumor populations with regard to gait and balance.

In patients with brain tumors, the greatest impairment and loss of function typically occurs immediately after surgery [1]. Patients then improve over time. Therefore, physical functioning and QoL should not only be assessed shortly after surgery, but also after a period of time during which recovery can occur. Such trends were noted in this study, in which TUG, Tinetti, and SF-36 measures worsened initially after surgery, but improved to near pre-surgery levels at 3 months following surgery. As such, these tests results appropriately reflect patients' status.

Other measures of functional status used in brain tumor studies include the Functional Independence Measure (FIM), the Karnofsky Performance Scale (KPS), the Berg Balance scale (BBS), DGI, gait speed, and the five time sit to stand test. The FIM is a rehabilitation measure and does not specifically measure gait, balance, or the specifics of ambulation [23,39,40]. The KPS measures activities of daily living [2]; gait and balance are not considered in scoring. As such, these measures were not appropriate for assessing patient mobility in terms of gait and balance. The BBS has proven reliable and valid for use in assessing and quantifying balance and fall risk in older community dwelling individuals or with stroke older stroke patients [41]. It also correlates well with the TUG [42]. The BBS is also sensitive to change in stroke patients over time [43-45]. However, the BBS does not include an analysis or measure of ambulation abilities and was therefore excluded. The Dynamic Gait Index (DGI) is another reliable and valid measure used to evaluate and document a patient's ability to modify gait in response to changing task demands in ambulatory patients with balance impairments, specifically older communitydwelling adults and patients with vestibular dysfunction [46]. The DGI has been shown to discriminate between people with balance disorders and those without [47]. The DGI mainly assesses ambulation skills but has a limited number of balance-specific tasks compared to the Tinetti, therefore the Tinetti can offer more specific information on balance impairments. The 10m Walk Test measures how quickly a person can ambulate a distance of ten meters. This time can be compared to norms for functional community ambulators and help determine a person's functional abilities [45]. However, the 10m Walk Test measures only one aspect of ambulation, gait speed, and does not assess balance or quality of movement and does not assess other functional movements. The Five-Times-Sit-to-Stand test (FTSST) has been shown to identify people with balance dysfunction [47] but not as

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well as the DGI. It also looks only at one domain-sit to stand-whereas the Tinetti assesses multiple aspects of functional balance. Despite the availability of other balance and gait measures shown reliable and valid for neurologically impaired subjects, we chose the Tinetti for its ability to assess both domains as well as for its inclusion of several specific items for balance assessment. The TUG was chosen for its ease of administration and its use of everyday functional mobility: sit to stand, walking short distance, turning around, and moving stand to sit.

To assess QoL in this study, the SF-36, a generic QoL measure, was used. The SF-36 is quick to administer and has been used in more than 4000 publications representing a variety of disease-related studies [48]. Its wide-spread use across populations indicates evidence for its validity [49]. While the FACT-Br has been used more frequently for patients with cancer (including those with brain metastases) [50], the SF-36 has been used reliably and appropriately in neurological and cancer populations [51-56], including those with high-grade glioma [57] and craniopharyngioma [58]."Evidence of content, concurrent, criterion, construct, and predictive validity" has also been documented [48, 59]. Finally, the SF-36 "can also be used in repeated measures of the same patients over time" [48], is sensitive to change and can be used as a pre- and post- test [60] as it was here. Since this study focused on gait and balance as components of physical function, and the SF-36 includes a physical functioning domain [61] use of the SF-36 allowed us to analyze the influence of physical status changes on a person's overall QoL.

In this study, the SF-36 did not correlate with either the TUG or Tinetti prior to surgery. This finding supports the differences between QoL and balance and gait measures: they are not measuring the same constructs. However, immediately after surgery and at 3 months postsurgery, the SF-36 significantly correlated with the TUG and Tinetti. As physical status changed, so did the patients' self-perception of their QoL. While mobility is not the equivalent to QoL as measured by SF-36, in this study change in mobility scores did correlate with QoL. The relationship TUG and Tinnetti score to each of the 8 domains of the SF-36 was not assessed in this study because of our small patient population, but physical functioning is an important component of self-perceived QoL. This study suggests that as balance and gait worsen or improve, QoL may follow. Correlation of changes in scores of the TUG, Tinetti, and SF-36 supports use of these measures for research in the brain tumor population.

Both TUG and Tinetti are measures of gait and balance. Despite the Tinetti being more comprehensive and providing specifics regarding gait, the TUG is more practical to administer. Where time is limited, use of the TUG is appropriate and would provide adequate information regarding functional constructs of balance and mobility. However, if time is available, the Tinetti provides more specifics regarding balance and gait especially regarding quality of movement. The Tinetti includes balance activities (sternal nudge, eyes closed standing, turning 360°o while standing) that the TUG does not assess. The Tinetti also assesses quality of gait through items such as gait initiation, step symmetry, step continuity, path, trunk, walking time, and step length and height (right swing foot and left swing foot scored separately for both length and height) whereas the TUG measures only how fast a person performs a specific task.

Clinically relevant observations can be made using the Minimal Detectable Change (MDC) when examining raw scores. MDC is the amount of change on the score of an instrument that indicates a clinically relevant improvement or decline; the MDC is a change that is observable and demonstrates a variation in function. For the TUG,

the MDC has not been clearly established; in patients with neurological diagnoses, values ranging from 2 to 11 seconds [49, 51, 52]. In a study of patients following stroke, Flansbjer et al determined MDC for TUG should be 23% times the average baseline score [27]; this translates to 3.1 seconds for our sample of patients with brain tumors. Using a conservative cut-off instead of 5 seconds as a value for MDC 3 of 9 subjects improved their TUG time and 2 subjects had a worse TUG time beyond the MDC comparing pre-surgery to 3 months post-surgery times. The 4 other subjects all improved their TUG scores but not beyond the 5 second MDC threshold.

The MDC for the Tinetti has been established as 5 points [62]. From pre-surgery to 3 months post-surgery, 5 subjects improved while 2 declined beyond this threshold; one subject improved 4 points, from 24 to the maximum possible score of 28 and one subject stayed the same, scoring the maximum of 28 both prior to and at 3 months postsurgery. Having a clinically relevant number upon which to gauge change in a particular patient can be used by health care professionals to proceed with therapeutic interventions.

Examining individual patients' TUG and Tinetti MDC's can yield additional insights. Mean values of the study group alone may obscure some observations. The limited number of patients in this study may have allowed extreme scores in one or two patients to skew group outcome data. Ceiling effects may exist, especially with the Tinetti, which limit the amount of improvement which can be demonstrated. For instance, a subject may score from 19 to24 on the Tinetti while demonstrating mild balance impairments. These impairments may resolve at 3 months, but the scores on the Tinetti can only improve several points due to the maximum possible score of 28. Also, several patients had minimal physical deficits. These patients would be completely functional both before and after surgery and therefore demonstrate little overall improvement.

Finally, mean group scores may have been influenced by tumor type. Some patients had aggressive tumors which recurred and progressed following surgery, resulting in decline in function, as evidenced in two subjects with gliobastoma. The scores of these two individuals may well have offset the improvement noted in the other patients, resulting in limited change in the patients as a group from pre- to 3 months post-surgery. This limitation is important to note for future research design.

Our study has a number of limitations. First and foremost, this report is only a pilot study involving a small number of patients. Additionally, the study involves a limited number of tumor types in different brain locations with variable degrees of aggressiveness and growth. Patients had different post-operative treatments. As such, the results may not be generalizable to the entire group of patients with brain tumors. Clearly, a larger follow-up study with a greater number of patients is necessary.

Data analysis should include comparison of age, postoperative complications, surgical management (technique and extent of resection), use of adjuvant therapies, patient participation in rehabilitation therapies, gender, recurrence, and tumor type, size, and location Pain can also affect mobility and QoL, and should be included. Balance and gait deficits present prior to surgery are important to assess. Patients without pre-operative deficits should be grouped separately from those with significant pre-surgery deficits to minimize ceiling effects. Such further evaluation and study should serve to validate our results presented here.

## Conclusions

This study illustrates that an evaluation of balance and gait, and their relationship to QoL is possible in patients with brain tumors. The TUG, Tinetti, and SF-36 are appropriate measures to use in future studies of patients with brain tumor. The strong correlation of the TUG and Tinetti suggest they may measure similar constructs, so the TUG may be favored as it can be carried out quickly in the clinical setting.

# Acknowledgements

This research was done in partial fulfillment of the requirements for Mr. Krug's Master of Science degree at the University of Missouri, Columbia, Missouri.

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This article was originally published in a special issue, entitled: "Cancer Rehabilitation", Edited by J Luo, Temple University School of Medicine, USA