Impact of frailty on surgery for glioblastoma: a critical evaluation of patient outcomes and caregivers' perceptions in a developing country

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OBJECTIVE The authors aimed to evaluate the impact of age and frailty on the surgical outcomes of patients with glioblastoma (GBM) and to assess caregivers' perceptions regarding postdischarge care and challenges faced in the developing country of India.

METHODS This was a retrospective study of patients with histopathologically proven GBM from 2009 to 2018. Data regarding the clinical and radiological characteristics as well as surgical outcomes were collected from the institute's electronic database. Taking Indian demographics into account, the authors used the cutoff age of 60 years to define patients as elderly. Frailty was estimated using the 11-point modified frailty index (mFI-11). Patients were divided into three groups: robust, with an mFI score of 0; moderately frail, with an mFI score of 1 or 2; and severely frail, with an mFI score ≥ 3 . A questionnaire-based survey was done to assess caregivers' perceptions about postdischarge care.

RESULTS Of the 276 patients, there were 93 (33.7%) elderly patients and 183 (66.3%) young or middle-aged patients. The proportion of severely frail patients was significantly more in the elderly group (38.7%) than in the young or middle-aged group (28.4%) ($p < 0.001$). The authors performed univariate and multivariate analysis of associations of different short-term outcomes with age, sex, frailty, and Charlson Comorbidity Index. On the multivariate analysis, only frailty was found to be a significant predictor for in-hospital mortality, postoperative complications, and length of hospital and ICU stay ($p < 0.001$). On Cox regression analysis, the severely frail group was found to have a significantly lower overall survival rate compared with the moderately frail ($p = 0.001$) and robust groups ($p < 0.001$). With the increase in frailty, there was a concomitant increase in the requirement for readmissions ($p = 0.003$), postdischarge specialist care ($p = 0.001$), and help from extrafamilial sources ($p < 0.001$). Greater dissatisfaction with psychosocial and financial support among the caregivers of severely frail patients was seen as they found themselves ill-equipped to provide postdischarge care at home ($p < 0.001$).

CONCLUSIONS Frailty is a better predictor of poorer surgical outcomes than chronological age in terms of duration of hospital and ICU stay, postoperative complications, and in-hospital mortality. It also adds to the psychosocial and financial burdens of the caregivers, making postdischarge care challenging.

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KEYWORDS elderly; frailty; glioblastoma; surgical outcomes; caregivers' perception; end-of-life care

FROM a surgeon's perspective, traditionally, the age of the patient has been an important variable in decision making as the rates of complications and adverse events following major surgeries are significantly higher in the geriatric population than in the younger population.^{1,2} However, there is a brewing debate regarding the roles of chronological age versus biological age in determining postoperative outcomes.^{3,4} Frailty has gained rec-

ognition as a tool to predict the biological age, and hence, an individual's vulnerability to adverse outcomes following surgery. The use of frailty as a preoperative risk assessment model in different surgical specialties, including spine surgery, has gained popularity. However, most of the literature regarding the impact of frailty on postoperative outcomes is from the developed nations.^{5,6}

There is a paucity of literature on the impact of frailty

ABBREVIATIONS CCI = Charlson Comorbidity Index; DVT = deep venous thrombosis; GBM = glioblastoma; GOS-E = Glasgow Outcome Scale–Extended; KPS = Karnofsky Performance Status; mFI-11 = 11-point modified frailty index; PE = pulmonary embolus; VAP = ventilator-associated pneumonia.

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in cranial neurosurgery even from the developed world.⁷ In developing nations, the already poor financial status of caregivers compounds the challenges of caring for patients whose condition is made more precarious by frailty. Glioblastoma (GBM), as the most common primary intracranial tumor in the geriatric population, has special relevance in this regard because treatment must be tailored for each patient.⁸ In view of the poor neurological status and continued need for medical attention in GBM patients, postdischarge care forms an important component in the management of this disease,⁹ but in many areas of developing nations there is an absence of any system similar to hospice care for the palliative treatment of terminally ill patients. In this study, which is to our knowledge the first of its kind from a developing nation, we attempted to assess the role of preoperative frailty to predict the risk of morbidity and mortality following surgery in patients with GBM. We also attempted to study the impact of preoperative frailty on postdischarge care, with special emphasis on challenges faced in the developing countries.

Methods

This was a retrospective study of patients ≥ 18 years of age with histopathologically proven GBM who underwent biopsy or resection as the primary intervention during the period from 2009 to 2018 at the Department of Neurosurgery, All India Institute of Medical Sciences, New Delhi, India. Due clearance was provided by the Institute Ethics Committee. Patients with nonlobar GBM, multicentric GBM, or recurrent disease at presentation were excluded. Patients with incomplete clinical or radiological follow-up were also excluded. Data regarding patient characteristics, clinical features, comorbidities, radiology, postoperative course, and long-term outcomes were collected from the electronic database. All patients received postoperative adjuvant therapy depending on age, performance status, comorbidities, and extent of resection, as was determined by a multidisciplinary neuro-oncology team. Information regarding postdischarge care, psychosocial support, and financial challenges faced by the caregivers was sought by means of outpatient and/or telephone interviews using a structured questionnaire after due consent was obtained (Supplementary Material).

Usually, the age of 65 years is used as a cutoff for defining the elderly population in developed countries like the United States, where the average life expectancy is > 75 years. However, developing countries like India have a lower life expectancy (69.73 years per 2019 statistics).¹⁰ Hence, the cutoff for the geriatric age group in India is 60 years. Considering these factors, we divided our study population into two groups (elderly and young or middle-aged patients) using the cutoff age of 60 years rather than 65 years.

Frailty was estimated using the 11-point modified frailty index (mFI-11)^{11,12} as detailed in Table 1. The mFI-11 is a validated abridged version of the 70-point frailty index developed by Rockwood et al.¹³ Patients were divided into three groups (robust, moderately frail, and severely frail) according to their preoperative mFI-11 scores as follows: 0, robust; 1 or 2, moderately frail; and ≥ 3 , severely frail. These cutoffs were decided based on a previous study

TABLE 1. Summary of mFI-11 components^{11,12}

mFI-11 Components
History of diabetes mellitus
Not independent in functional status
History of COPD or pneumonia
History of congestive heart failure
Myocardial infarction
History of percutaneous coronary intervention, cardiac surgery, or angina
Hypertensive medication
Peripheral vascular disease or rest pain
Impaired sensorium
Transient ischemic attack or cerebrovascular accident
Cerebrovascular accident with deficit

COPD = chronic obstructive pulmonary disease.

One point is given for each of the above and a cumulative point score is calculated.

evaluating the impact of frailty on GBM patients.¹⁴ The comorbidity burden was quantified using the age-adjusted Charlson Comorbidity Index (CCI).¹⁵

The patients were assessed for short-term outcomes, including postoperative complications, in-hospital mortality, Glasgow Outcome Scale–Extended (GOS-E) score at discharge, and lengths of hospital and ICU stays. Postoperative complications were classified based on the Glioma Outcome Project System by Chang et al.¹⁶ into neurological: transient or permanent motor deficit, speech deficits; regional: wound infection, meningitis, seizures, intracerebral hemorrhage; and systemic: deep venous thrombosis (DVT) or pulmonary embolus (PE), sepsis, and ventilator-associated pneumonia (VAP). These complications were analyzed in relation to frailty groups. The long-term outcome was assessed in terms of overall survival.

Statistical Analysis

The data were entered using Microsoft Excel 2011 and statistical analysis was done using IBM SPSS Statistics package version 20 (IBM Corp.). Kaplan-Meier plots were made using RStudio with additional packages like ggplot2, survival, survminer, dplyr, and tidyr. Chi-square test, Fischer exact test, independent-samples Kruskal-Wallis test, Student t-test, and simple and multiple logistic regression were used as appropriate. For survival data, a multivariate-adjusted Cox proportional hazards model was constructed. For all statistical tests, a p value < 0.05 was considered to be statistically significant.

Results

A total of 276 patients met the eligibility criteria and were included in the study. The study population was divided according to chronological age into two groups, elderly and young or middle-aged, with a cutoff age of 60 years. Of the 276 patients, there were 93 (33.7%) elderly and 183 (66.3%) young or middle-aged patients. Comparisons of various clinical characteristics between elderly

TABLE 2. Comparison of clinical characteristics of elderly and young or middle-aged GBM patients

Characteristic	Total	Elderly (n = 93)	Young or Middle-Aged (n = 183)	p Value
Sex				0.039
Male	191 (69.2%)	72 (77.4%)	119 (65%)	
Female	85 (30.8%)	21 (22.6%)	64 (35%)	
Mean BMI $\pm$ SD, kg/m ²	23.69 $\pm$ 3.58	23.62 $\pm$ 3.90	23.73 $\pm$ 3.41	0.806
Admission GCS score	15 [12–15]	15 [13–15]	15 [12–15]	0.546
mFI-11 score				0.008
Overall	2 [0–3]	2 [1–4]	1 [0–3]	
Robust (score 0)	80 (29%)	16 (17.2%)	64 (35%)	
Moderately frail (score 1–2)	108 (39.1%)	41 (44.1%)	67 (36.6%)	
Severely frail (score >2)	88 (31.9%)	36 (38.7%)	52 (28.4%)	
Diabetes mellitus	51 (18.5%)	24 (25.8%)	27 (14.8%)	0.033
Hypertension	88 (31.9%)	43 (46.2%)	45 (24.6%)	<0.001
Preop KPS score	50 [30–80]	50 [30–65]	50 [30–80]	0.102
CCI score	2 [1–4]	4 [3–5]	2 [0–2]	<0.001
Postop GCS score	15 [11–15]	15 [13–15]	15 [11–15]	0.434
Tracheostomy due to prolonged ventilation	50 (18.1%)	16 (17.2%)	34 (18.6%)	0.779
Complications				
Overall	142 (51.4%)	53 (57%)	89 (48.6%)	0.204
Neurological	119 (43.1%)	44 (47.3%)	75 (41%)	0.368
Regional				
Seizures	36 (13.1%)	13 (14.1%)	23 (12.6%)	0.709
Wound infection	31 (11.3%)	12 (13%)	19 (10.4%)	0.547
Meningitis	38 (13.8%)	12 (13%)	26 (14.2%)	0.855
Intracranial bleed	68 (24.7%)	22 (23.9%)	46 (25.1%)	0.883
Systemic				
DVT/PE	5 (1.8%)	4 (4.3%)	1 (0.5%)	0.04
VAP	54 (19.6%)	22 (23.9%)	32 (17.5%)	0.26
Sepsis	89 (32.4%)	33 (35.9%)	56 (30.6%)	0.413
Duration of ICU stay, days	2 [1–7]	3 [1–7]	2 [1–7]	0.74
Duration of hospital stay, days	5 [4–11]	6 [3–11]	5 [4–11]	0.94
In-hospital mortality	21 (7.6%)	7 (7.5%)	14 (7.7%)	1.00
GCS score at discharge	15 [13–15]	15 [14–15]	15 [12–15]	0.712
GOS-E score at discharge	5 [4–7]	4 [4–6]	5 [4–7]	<0.001
Surgery for recurrent disease	49 (17.8%)	9 (9.7%)	40 (21.9%)	<0.001
Overall survival	11 [5–17]	10 [4–14]	13 [6–18]	0.035

Elderly = age $\geq$ 60 years; GCS = Glasgow Coma Scale; young or middle-aged = age < 60 years.
 Values are presented as the number (%) of patients or median [IQR] unless otherwise indicated.

and young or middle-aged GBM patients are summarized in Table 2.

Using the mFI-11 score, we also divided the patients based on their frailty into robust (mFI = 0), moderately frail ($0 < \text{mFI} < 3$), and severely frail (mFI ≥ 3) groups. There were 80 robust (29.0%), 108 moderately frail (39.1%), and 88 severely frail (31.9%) patients in our cohort.

Association of Biological Age (Frailty) With Chronological Age

The frailty scores were found to be positively corre-

lated with increasing age ($p = 0.008$) (Fig. 1A). Similarly, the proportion of severely frail patients was significantly greater in the elderly group (38.7%) than in the young or middle-aged group (28.4%, $p < 0.001$) (Fig. 1B).

Surgical Decision Making

Association of Frailty With Decision to Perform Biopsy

The total number of patients who underwent biopsy was 7, all of whom were severely frail ($p < 0.001$), while all of the patients in the moderately frail and robust groups

FIG. 1. Distribution of mFI-11 scores (A) and frailty categories (B) according to chronological age.

were planned for resection. However, even among the severely frail patients an attempt at resection (81 patients, 92.1%) was preferred over biopsy (7 patients, 7.9%).

Association of Frailty With Decision to Perform Resection for Recurrent/Residual Disease

Of the 108 patients who were diagnosed with recurrent/residual disease, the severely frail patients were less likely to undergo resection (8 of 23 patients, 34.7%) than the patients in the moderately frail (21 of 47 patients, 44.6%) and robust (20 of 38 patients, 52.6%) groups; however, the difference failed to reach statistical significance ($p = 0.39$).

Postoperative Adjuvant Therapy

Of the 276 patients who underwent surgery, 21 died during the hospital stay. The postoperative adjuvant therapy was individualized for each of the surviving 255 patients by a combined neuro-oncology team taking into consideration the age, postoperative Karnofsky Performance Status (KPS) score, MGMT methylation status, comorbidities, and willingness of the patient or their caregivers. Twenty-six patients (10.2%) received only best supportive care. Of the remaining 229 patients, 47 patients received adjuvant therapy at peripheral medical centers due to the long waiting list at our center. Details regarding the nature of adjuvant therapy of these patients was not available owing to the retrospective nature of study. In total, 182 patients received adjuvant therapy at our center. Of these, 141 patients (77.5%) received concurrent chemoradiation (temozolomide [TMZ] + 60 Gy radiation therapy [RT] in 30 fractions) followed by TMZ. Fifteen patients (8.2%) received TMZ alone while 22 patients (12.1%) received hypofractionated RT alone (30–45 Gy in 10–15 fractions). Four patients (2.2%) received both TMZ and hypofractionated RT. The type of adjuvant therapy administered showed a trend toward greater likelihood of concurrent chemoradiotherapy among the robust and moderately frail compared to the severely frail group; however, the difference failed to reach statistical significance ($p = 0.06$).

Predictors of Short-Term Outcomes

We performed univariate analysis of possible associations of different surgical outcomes with age, sex, frailty,

and CCI score. On univariate analysis, frailty was found to be a significant predictor for in-hospital mortality, postoperative complications, and length of hospital and ICU stay ($p < 0.001$). CCI score correlated significantly only with the rate of postoperative complications ($p < 0.001$). On multivariate analysis, only frailty was found to be a significant predictor across all of the above outcomes, while CCI score lost its significance for predicting postoperative complications ($p = 0.758$).

Correlation of Frailty With Postoperative Complications

Patients in the severely frail group were found to be more predisposed to postoperative regional and systemic complications ($p < 0.001$). In this group, approximately 80 of 88 patients (90.9%) suffered from some type of postoperative complications, 64 patients (72.7%) suffered regional complications, and 76 patients (86.4%) suffered systemic complications (Fig. 2A). On evaluating the in-hospital mortality associated with the primary admission among the patients with different levels of frailty, we found similar results. Of 88 severely frail patients, 16 patients (18.2%) succumbed in the postoperative period compared to 3.7% of the moderately frail and 1.3% of the robust patients, as shown in Fig. 2B. Of the 255 surviving patients at discharge, the median GOS-E score was significantly lower in the severely frail patients (4, IQR 4–4.5) compared to the moderately frail (5, IQR 4–6) and robust (7, IQR 7–7) patients ($p < 0.001$).

The proportion of patients who underwent tracheostomy was also significantly higher in the frailer groups. It was observed that 37 of 88 severely frail patients (42.1%) underwent tracheostomy, while the proportion of patients who needed tracheostomy was 13.9% in the moderately frail and just 1.25% in the robust patients ($p < 0.001$).

Association of Frailty With Lengths of Hospital and ICU Stays

The lengths of hospital and ICU stays were found to be significantly correlated with the level of frailty. The median duration of hospital stay was significantly longer among the severely frail patients (12 days; IQR 7–16 days) than the moderately frail (5 days; IQR 3–7 days) and robust (4 days; IQR 3–5.5 days) patients ($p < 0.001$). Similarly, the median duration of ICU stay was also found to be significantly lon-

FIG. 2. Comparison of postoperative complications (A) and in-hospital mortality (B) among frailty categories.

ger in the severely frail (8.5 days; IQR 4–13 days) than in the moderately frail (2 days; IQR 1–2 days) and robust (2 days; IQR 1–2 days) patients ($p < 0.001$). The time trends of discharge from ICU to ward and further discharge to home have been summarized in Fig. 3A and B.

Predictors of Long-Term Outcome

Overall Survival

The overall survival was found to be independently associated with the level of frailty as well as chronological age. On multivariate Cox regression analysis, the severely frail group was found to have a significantly lower overall survival than the moderately frail (HR 1.75; 95% CI 1.23–2.5) and robust (HR 1.83; 95% CI 1.26–2.68) groups. Similarly, the elderly group had lower overall survival than the young or middle-aged group (HR 1.43; 95% CI 1.06–1.95). The Kaplan-Meier survival curves for the different levels of frailty are shown in Fig. 3C (log-rank test, $p = 0.037$).

Impact of Frailty on Caregiver's Perceptions of End-of-Life Care in GBM

Of the total study population, caregivers of 181 patients gave consent for participation in an end-of-life care survey. The frailty of the patients was also found to have an impact on the postdischarge care of the patients and the consequent impact on the caregivers. The moderately and severely frail patients were found to require care in local hospitals and sometimes the primary hospital during the last month of life more frequently than their robust counterparts ($p < 0.001$). The requirement for readmissions to the primary hospital after discharge showed a similar trend. Similarly, the need for postdischarge specialist care from a neurosurgeon or an oncologist was encountered more among the severely frail (63.6%) patients than the moderately frail (46.2%) and robust (30%) patients. The caregiver's need to seek help from extrafamilial sources like social acquaintances, maids, or medically accredited nurses was also found to be significantly greater with increasing level of patient frailty (Table 3).

The caregiver's satisfaction with the surgical treatment received by the patient during the primary admission remained high across all the groups of frailty (Fig. 4A). There was a trend toward greater dissatisfaction with psy-

chosocial support among the caregivers of severely frail patients; however, it failed to reach statistical significance ($p = 0.20$) (Fig. 4B). As the frailty increased, the caregivers found themselves unequipped to provide postdischarge care at home ($p < 0.001$) (Fig. 4C). Caregivers of severely frail and moderately frail patients also reported facing a greater financial burden imposed by the postdischarge care of the patient ($p < 0.001$) (Fig. 4D).

Discussion

GBM carries a poor prognosis, which can be attributed to the malignant nature of the disease, the frail nature of the predominantly elderly patient population, and the molecular patterns of the disease.^{17,18} Most of the studies in the literature have focused primarily on surgical factors like the extent of resection for understanding the prognosis and survival of patients with GBM. However, considering the advanced age and comorbidities of the patients, surgery as well as the postoperative course can be challenging. To evaluate the impact of these premonitory patient characteristics, the majority of the researchers have used variables such as age, functional status, presence of neurological deficits, etc., with mixed results.^{7,19,20} However, the concept of biological age, i.e., frailty, has gained popularity among different medical and surgical specialties as well as in spine surgery. Assessment of patient frailty has emerged as an important tool in predicting the mortality, morbidity, and length of the hospital stay in the elderly population.^{14,21–23}

Different studies have used different age cutoffs to define the elderly population and assess the impact of frailty on surgical outcomes.^{24,25} The rationale to use a cutoff age of 60 years to define the geriatric population in our study is based on a lower life expectancy in our country compared to developed nations.

In our study, the incidence of severe frailty was 38.7% of the elderly population, whereas in the studies by Cloney et al.¹⁴ and Giaccherini et al.²⁶ the incidence rates were 19.3% and 44.1%, respectively. The higher proportion of frailty in our study, despite the lower cutoff age used to define “elderly,” can be explained by considering the difference in the race and socioeconomic status of our population. In a study conducted by Asemota and Gallia,²¹ the authors' finding that frailty rates were higher in patients

FIG. 3. Kaplan-Meier survival curves comparing postoperative hospital stay (A), ICU stay (B), and overall survival (C) among the different categories of frailty (log-rank test).

of low- to medium-income groups lends support to this hypothesis. On the other hand, the higher rate of frailty reported by Giaccherini et al.²⁶ may be attributed to the different definitions of frailty used.

In the geriatric population, surgical decision making in cranial surgeries is complex and is influenced by the chronological age and comorbidities of the patient and often comes down to the surgeon's decision and the willingness of the patient, which are arrived at subjectively.^{1,2,27} A simple yet accurate objective tool is imperative to guide the treatment in such patients, because the use of only chronological age to determine frailty is fraught with error. In oncological neurosurgery, the most commonly used tools are standardized assessments such as the American Society of Anesthesiologists (ASA) score, Acute Physiology and Chronic Health Evaluation (APACHE-II), Physiological and Severity Score for the Enumeration of Mortality and Morbidity (POSSUM), and the prognostic nutritional index (PNI). While the KPS assessment does not consider any comorbidities, the ASA score is subjective, and

APACHE-II and POSSUM are cumbersome to calculate at the bedside and thus are not useful to guide treatment in the geriatric population.^{7,28} Thus, there has been a vacuum in terms of a simple yet effective tool for decision making. Frailty, widely considered to be an indicator of biological age, has been reported in the literature to perform well in this regard not only in other surgical specialties but in spine surgery as well.²⁹ One of the most commonly used frailty indices, the mFI-11, may prove to be an important bedside tool for this purpose by providing an objective alternative to the more subjective decision-making process being utilized currently in clinical practice.

We found that frailty is associated with increased hospital and ICU stay durations as well as with lower overall survival in GBM patients. Dasgupta et al.³⁰ and Makary et al.³¹ also concluded that frailty is an independent predictor of length of hospital stay following surgery, irrespective of chronological age.

In our study, we used the Glioma Outcome Project system proposed by Chang et al.¹⁶ to classify the postopera-

TABLE 3. Comparison of end-of-life care characteristics between robust, moderately frail, and severely frail GBM patients

End-of-Life Care Characteristics	Total (n = 181)	Robust (n = 50)	Moderately Frail (n = 65)	Severely Frail (n = 66)	p Value
Place					<0.001
Primary hospital	28 (15.4%)	3 (6%)	10 (15.38%)	15 (22.72%)	
Local hospital	83 (45.8%)	9 (18%)	33 (50.76%)	41 (62.12%)	
Home	70 (38.6%)	38 (76%)	22 (33.84%)	10 (15.15%)	
Need for specialist care	87 (48.06%)	15 (30%)	30 (46.15%)	42 (63.64%)	0.001
Rehospitalization	38 (21.0%)	5 (10%)	13 (20%)	20 (30.3%)	0.03
Primary extrafamilial help*	93 (51.38%)	18 (36%)	27 (41.54%)	48 (72.73%)	<0.001

Values are presented as the number (%) of patients unless otherwise indicated.

* Social acquaintance, maid, and medically accredited nurses.

tive complications into systemic, local, and neurological complication categories. The rates of complications were observed to be higher in the severely frail group than the robust population, a finding which is in consensus with the existing literature.¹⁴

Our study showed an overall median survival period following surgery of 11 months, which is slightly less than that reported elsewhere in the literature.^{32–35} Keeping the predominant socioeconomic strata of patients in mind, the lower overall survival may be attributable to the lack

FIG. 4. Caregiver satisfaction with surgical treatment (A) and psychosocial support (B); and caregiver perception regarding ability to provide postdischarge care at home (C) and financial burden imposed by postdischarge care (D).

of proper care of patients following discharge from the hospital, combined with the lack of any hospice system in developing countries compared with the availability of such a system in Western countries. In the absence of any established system, social acquaintances and maids form the support system for the caregivers in lower- to middle-income countries. The greater need for postdischarge care for GBM patients, compounded further by frailty, makes the dependence on such extrafamilial sources imperative.

According to our survey on caregivers' perceptions, the increasing level of frailty significantly added to the already taxed financial condition of the patients' families. Poor socioeconomic status often prevents the caregivers from providing adequate end-of-life care. Caregivers had also reported that patients require more rehospitalizations with increasing levels of frailty. These findings warrant the need for establishment of local nursing facilities or hospice centers for better care, providing financial assistance for caregivers, and developing appropriate infrastructure at the rural level for better end-of-life care of terminally ill patients.

The previously existing literature assessing the predictors of neurosurgical outcomes has primarily focused on patient chronological age. Frailty, which is widely accepted as a marker for biological age, has much more clinical significance in determining surgical outcomes than chronological age.³⁶ Our study adds to the growing body of evidence that chronological age may just be a number and frailty is a better predictor of surgical outcomes. Hence, robust patients should not be deprived of the benefit of aggressive surgical management, irrespective of their age.

Our study is unique as it is to our knowledge the first study conducted in the developing world to assess the impact of frailty on surgical outcomes of GBM patients. This report adds to the existing scarce literature dealing with the role of frailty in cranial neurosurgery. We have also described the impact of frailty on the caregiver's perceptions regarding end-of-life care. The special challenges faced by the patients and their caregivers in resource-constrained settings have been highlighted.

This study has some limitations owing to its retrospective design. As the apex tertiary care center of our country, our facility receives more patients than can be accommodated in existing healthcare facilities. Due to long waiting lists at our center, some of our patients underwent adjuvant therapy at peripheral medical centers. The data regarding the type of adjuvant therapy for these patients were thus incomplete. Although we found a trend in favor of less frail patients receiving concurrent chemoradiotherapy, currently the decision regarding the type of adjuvant therapy is usually based on chronological age and postoperative KPS score. We feel that postoperative frailty needs to be evaluated as a criterion to decide the form of adjuvant therapy in future studies.

In different studies of this topic, there is significant heterogeneity not only in the various scores assessing frailty but also in the categorization cutoffs used.³⁷ Also, all such scores have been validated in the developed world. To address these concerns, specifically with regard to developing countries, we are doing a prospective study to validate the mFI-11 scale for assessing frailty in the Indian popula-

tion. Since the current study is a single-center study conducted at a tertiary care center, it may not be representative of frailty trends and their impact across the entire country, a concern that highlights the need for a national database of preoperative risk assessment variables in our country. Thus, a large prospective multicenter study is warranted to evaluate the effects of preoperative frailty on surgical outcomes and postdischarge care, particularly in developing countries.

Conclusions

The biological age of the patient as manifested by frailty is a better predictor than chronological age of poorer surgical outcomes in terms of durations of hospital and ICU stays, postoperative complications, and in-hospital mortality in patients undergoing surgery for GBM. Frailty also adds to the psychosocial and financial burden of the caregivers. An attempt should be made to evaluate the frailty of GBM patients before surgical intervention for better surgical decision making and counseling regarding postdischarge care.

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Disclosures

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Author Contributions

Conception and design: Tandon, Katiyar, Sharma. Acquisition of data: Katiyar, Goda. Analysis and interpretation of data: Katiyar, Sharma. Drafting the article: Katiyar, Sharma, Goda, Ganeshkumar. Critically revising the article: Tandon, Katiyar, Sharma, Goda, Ganeshkumar. Reviewed submitted version of manuscript: Katiyar, Sharma. Statistical analysis: Katiyar. Administrative/technical/material support: Tandon, Sharma, Suri, Chandra, Kale. Study supervision: Sharma, Suri, Chandra, Kale.

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