

Chemotherapy Toxicities and Geriatric Syndromes in Older Patients with Malignant Gliomas

Andrea Wasilewski MD, Ahmar Alam, Nimish Mohile MD

University of Rochester



BACKGROUND

Malignant gliomas (MG) are aggressive brain tumors including glioblastoma, anaplastic astrocytoma and anaplastic oligodendroglioma. Over 40% of MG occur in patients older than age 65, although few older adults are included in therapeutic clinical trials and the standard of care for these patients is not well defined. Typical treatment includes maximal safe resection followed by focal radiotherapy and concurrent and adjuvant chemotherapy with temozolomide.

Currently, there are no widely used or validated assessment and prognostication tools for older patients with MG. Median overall survival (OS) is 10-11 months for older patients with MG who are at risk for toxicities and geriatric syndromes which are poorly described.

OBJECTIVE

To describe treatment toxicities, polypharmacy and geriatric syndromes in older patients with malignant gliomas

METHODS

- IRB approved retrospective study of patients with MG at the University of Rochester, Wilmot Cancer Center from January 2012- December 2018
- The electronic medical record was used to assess:
 - Patient and tumor characteristics
 - Cancer therapies
 - Treatment delays and toxicities
 - Polypharmacy
 - Geriatric syndromes
 - Acute care utilization

PATIENT CHARACTERISTICS

	Patients (n=125)		
Gender	No.	%	
	Female	53	42.4
	Male	72	57.6
Median Age at Diagnosis	71 (65-89)		
Age at Diagnosis	No.	%	
	65-70	49	39.2
	71-75	35	28.0
	76-80	24	19.2
	81-85	12	9.6
	86+	5	4.0
Median Karnofsky Performance Status at Diagnosis	80 (40-100)		
% of Patients with KPS > 70	53.6 %		
Tumor Characteristics	No.	%	
	GBM, IDH wildtype	94	75.2
	GBM, IDH mutant	3	2.4
	GBM, IDH indeterminate/unknown	18	14.4
AA, IDH	No.	%	
	AA, IDH wildtype	8	6.4
	AA, IDH mutant	1	0.8
	AA, IDH indeterminate/unknown	1	0.8
MGMT status	No.	%	
	MGMT methylated	38	30.4
	MGMT unmethylated	57	45.6
	MGMT indeterminate/unknown	30	24.0
Degree of Surgical Resection	No.	%	
	Biopsy	36	28.8
	Subtotal	54	43.2
	Gross total	35	28.0
Median survival (months)	10.3		
	GBM		
	10.2		
	AA		
	10.8		
Death	No.	%	
	120	96.0	

GBM= Glioblastoma; AA= Anaplastic Astrocytoma; MGMT= O⁶-methylguanine-methyltransferase

RESULTS

- 125 patients with MG (115 GBM, 10 AA)
- Median OS= 10.3 months, Median PFS= 5.7 months
- 96% experienced at least one hospital admission (Range: 1-3), most commonly for seizures
- 64% reported at least one fall
- 83% of patients enrolled on hospice at time of death

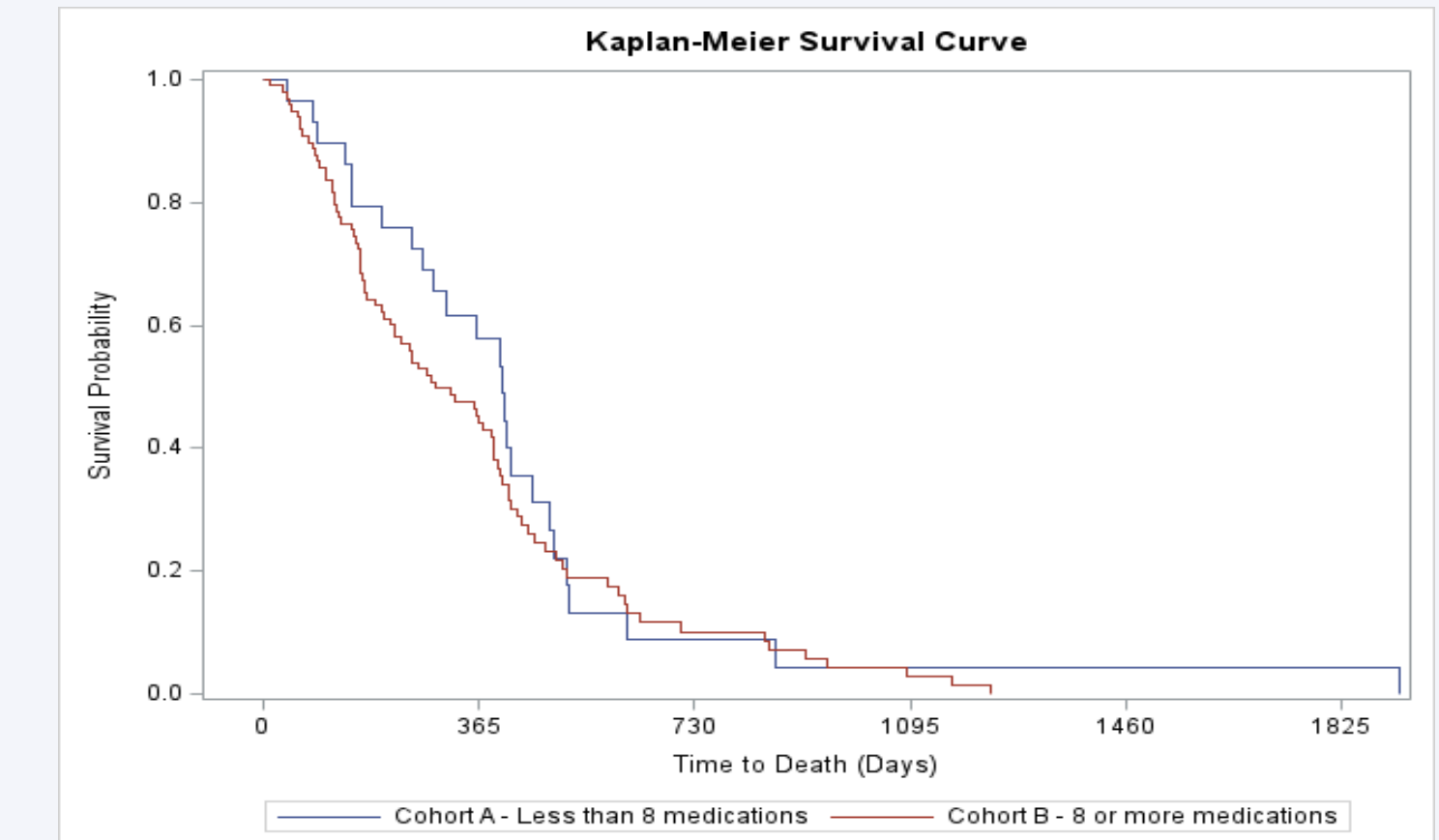
TREATMENT CHARACTERISTICS & TOXICITIES

	Patients Treated	
No Treatment Received	20/125	16%
Radiation (n=105)	105/125	
	84%	
60 Gy/30 fractions		
Completed	69/75	92%
Not completed	6/75	8%
40 Gy/15 fractions		
Completed	30/30	100%
Concurrent Chemotherapy (n=98)	74/98	
	76%	
Completed concurrent TMZ	24/98	24%
Concurrent TMZ not completed		
Adjuvant Chemotherapy (n=76)	4 cycles	
	60%	
Median # of cycles of TMZ completed	46/76	60%
# of patients completing at least 6 cycles of TMZ	41/76	54%
# of patients with treatment delays		
Chemotherapeutic toxicities (n=98)*	11	
	4	
Polypharmacy (n=125)	14 months	
	8.6 months	
Median # prescription medications at diagnosis		
Median # medications prescribed during treatment		
Overall survival with <8 prescribed medications		
Overall survival with >= 8 prescribed medications		
Supportive Care Medications		
	Antidepressant	
	Corticosteroid	68/125 (54%)
	Proton pump inhibitor	124/125 (99%)
	Anti-emetic	124/125 (99%)
	Anti-epileptic	100/125 (80%)
Patients with medications on Beer's List at diagnosis**	51/125 (41%)	
	38/125 (30%)	

TMZ= temozolomide; *Toxicities resulting in dose reductions or delays in treatment

POLYPHARMACY

- Patients prescribed Median of 11 medications at diagnosis
- Median OS was 8.6 months vs. 14 months for those taking < 8 vs. 8 or more medications
- 30% were prescribed a medication on Beer's List
- Median of 5 medications added during cancer treatment
- 54% were started on an antidepressant after diagnosis



DISCUSSION

- Treatment toxicities are common, likely due to comorbidities, decreased performance status and older age
- Consideration should be given to omission of TMZ for patients with tumors with MGMT-unmethylated promoters
- Use of validated assessments such as the Comprehensive Geriatric Assessment and Geriatric-8 survey should be considered in all older patients with MG
- Polypharmacy is common, associated with decreased survival and should be mitigate when possible (eg. de-prescribing protocols)
- Education and appropriate treatment of seizures and venous thromboembolism may reduce hospitalizations

CONCLUSION

- Treatment toxicities and geriatric syndromes are common in older patients with MG and are likely underrecognized
- Tools for evaluation, longitudinal assessment and screening are needed to better identify and treat these conditions
- Clinical trials should be more inclusive of older patients or designed to specifically address the needs of this population