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Original Research Article

Estimating survival in patients with gastrointestinal cancers and brain metastases: An update of the graded prognostic assessment for gastrointestinal cancers (GI-GPA)

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ABSTRACT

Background: Patients with gastrointestinal cancers and brain metastases (BM) represent a unique and heterogeneous population. Our group previously published the Diagnosis-Specific Graded Prognostic Assessment (DS-GPA) for patients with GI cancers (GI-GPA) (1985–2007, n = 209). The purpose of this study is to update the GI-GPA based on a larger contemporary database.

Methods: An IRB-approved consortium database analysis was performed using a multi-institutional (18), multi-national (3) cohort of 792 patients with gastrointestinal (GI) cancers, with newly-diagnosed BM diagnosed between 1/1/2006 and 12/31/2017. Survival was measured from date of first treatment for BM. Multiple Cox regression was used to select and weight prognostic factors in proportion to their hazard ratios. These factors were incorporated into the updated GI-GPA.

Results: Median survival (MS) varied widely by primary site and other prognostic factors. Four significant factors (KPS, age, extracranial metastases and number of BM) were used to formulate the updated GI-GPA. Overall MS for this cohort remains poor; 8 months. MS by GPA was 3, 7, 11 and 17 months for GPA 0–1, 1.5–2, 2.5–3.0 and 3.5–4.0, respectively. >30% present in the worst prognostic group (GI-GPA of $\leq$1.0).

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Conclusions: Brain metastases are not uncommon in GI cancer patients and MS varies widely among them. This updated GI-GPA index improves our ability to estimate survival for these patients and will be useful for therapy selection, end-of-life decision-making and stratification for future clinical trials. A user-friendly, free, on-line app to calculate the GPA score and estimate survival for an individual patient is available at brainmetgpa.com.

1. Introduction

In 2018, there were an estimated 320,000 invasive gastrointestinal (GI) cancers diagnosed, with >160,000 attributable deaths [1]. An estimated 300,000 patients develop brain metastases (BM) every year [2]. The cancers most likely to cause BM are lung, breast, melanoma and renal cell carcinoma. GI cancers cause approximately 6% of all BM, and because of this relative "rarity", few robust reports have been published [3]. A computerized search of the medical literature revealed extremely limited published data regarding the overall survival, or prognostic variables for this patient population [4,5].

Patients with brain metastases are markedly heterogenous and it is well-known that outcomes vary widely by diagnosis and diagnosis-specific prognostic factors [6]. Our group has published a series of articles defining and updating a prognostic index, the Graded Prognostic Assessment (GPA) for patients with various primary diagnoses (lung, breast, melanoma, renal cell and GI cancers) and BM. Our original GI-GPA was based on 209 GI cancer patients with BM diagnosed from 1985 to 2005 [7–11]. We recently published a study of how prognostic factors have changed in this patient population in a larger contemporary cohort [12]. The purpose of this study is to update the GI-GPA prognostic index with these newly identified prognostic factors.

2. Methods

Investigators from a multi-national [3] multi-institutional (18) consortium created an IRB-approved retrospective database of 845 patients with gastrointestinal cancers and newly-diagnosed BM between January 1, 2006 and December 31, 2017 using the Research Electronic Data Capture (REDCap) interactive software. After exclusions for incomplete data, 792 remained eligible for analysis. Multiple Cox regression was used to initially select and weight variables to be included in the new GI-GPA. The initial variables included in the model were KPS, age, presence of extracranial metastases, number of brain metastases, gender, stage, primary GI site, HER2 status and hemoglobin. Multiple imputation using predictive mean matching [13] was used to impute missing values, so that the full sample could be used to estimate model parameters. Both effect magnitude (hazard ratio) and statistical significance were used to select variables. Weighting options were evaluated using metrics including the concordance index and R-squared, using 200 bootstrap replications to estimate out-of-sample performance. The final GPA was chosen as a balance of performance metrics and simplicity. Kaplan-Meier survival estimates were calculated for the new GPA categories. Analysis was performed using R software [14,15].

3. Results

The patient characteristics are shown in Table 1. Noteworthy observations include: 1) 83% (575/693) presented with stage III or IV disease; 2) 81% (622/772) had extracranial metastases (ECM) and 42% (322/772) had liver metastases at the time of diagnosis of the BM; 3) In this cohort, the most common primary sites were: rectum (24%), esophagus (23%), right colon (13%), rectosigmoid (11%) and GE junction (9%); 4) HER2 was reported in 148/274 (54%) and was present in 59/148 (40%) of patients with gastric, esophageal and gastro-esophageal cancers. In HER2-positive patients, 63% received Trastuzumab; 5) the time from primary diagnosis to brain metastases (TPDBM) was longer in patients with lung metastases ($p < 0.01$), females ($p < 0.001$), colorectal cancers ($p < 0.001$) and early stage (I-II) disease ($p < 0.001$).

3.1. Treatment

Table 2 shows a comparison of survival by treatment for the current cohort and our prior cohort [6,7]. Notably, treatment patterns have changed from the prior cohort (1989–2007, n = 209) to the current cohort (2006–2017, n = 792). The use of whole brain radiation therapy (WBRT) alone has decreased from 45% to 21% and the use of stereotactic radiosurgery alone has increased from 17% to 39%. Detailed data on systemic therapy before and after the diagnosis of brain metastases was of interest but was not available in this retrospective study.

3.2. Multivariable model

The multivariable model used to select and weight factors for the GI-GPA is shown in Table 3. Although 6 factors [Karnofsky Performance Status (KPS), age, extracranial metastases (ECM), number of BM, hemoglobin and primary GI site] were found to be significant, the predictive model was not further enhanced by adding hemoglobin or primary GI site to the index, and therefore, a simplified 4-factor model was generated.

3.3. Updated GI-GPA

Table 4 shows the definition of the updated GI-GPA and a scoring worksheet to calculate the GI-GPA for any individual patient. To compare predictive discrimination of the revised and original GI GPAs, we calculated the concordance probability (c-index) of two randomly chosen observations. If the patient predicted to live longer by the GPA actually did live longer, that pair is considered concordant. Since we have four GPA classes, about 32% of randomly chosen pairs will have the same predicted survival, thus our theoretical maximum achievable c-index is approximately 0.84. The c-index for the original GI-GPA was 0.610, which improved to 0.633 using the revised GPA.

Fig. 1 shows a Kaplan-Meier curve for survival by GI-GPA group showing clear separation between adjacent classes ($p < 0.001$). The overall MS for this cohort was 8 months. MS by GPA group (0–1.0, 1.5–2.0, 2.5–3.0 and 3.5–4.0) was 3, 7, 11 and 17 months, respectively ($p < 0.001$). MS (mo) by primary site were: anus (14 mo), left colon (10 mo), rectosigmoid (10 mo), esophagus (10 mo), small bowel (8 mo), right colon (7 mo), rectum (7 mo), GE junction (7 mo), gallbladder (5 mo), pancreas (4 mo), transverse colon (3 mo) and stomach (2 mo). Table 3 shows a comparison of survival by treatment and treatment era. Notably, use of WBRT decreased from 82% in the prior cohort to 34% in the contemporary era.

Table 1
Patient Characteristics, Survival and Time from Primary Diagnosis to Brain Metastases.

Variable	Category	N (%)	Median Survival (IQR)	P	TPDBM (IQR)	P
Overall		792 (100)	8 (3, 18)	.	23 (9, 51)	.
Original GI-GPA				<0.001		0.751
	0–1	267 (34)	4 (2, 12)	.	24 (7, 48)	.
	1.5–2	207 (26)	7 (3, 18)	.	24 (10, 53)	.
	2.5–3	187 (24)	12 (6, 21)	.	21 (10, 45)	.
	3.5–4	55 (7)	16 (7, 26)	.	23 (11, 61)	.
	Not Reported	76 (10)	10 (4, 19)	.	21 (9, 47)	.
KPS				<0.001		0.866
	<70	113 (14)	3 (1, 8)	.	28 (7, 54)	.
	70	154 (19)	6 (3, 13)	.	23 (8, 48)	.
	80	207 (26)	7 (3, 18)	.	24 (10, 53)	.
	90	187 (24)	12 (6, 21)	.	21 (10, 45)	.
	100	55 (7)	16 (7, 26)	.	23 (11, 61)	.
	Not Reported	76 (10)	10 (4, 19)	.	21 (9, 47)	.
Number BM				<0.001		0.610
	1	379 (48)	10 (4, 22)	.	23 (10, 47)	.
	2–3	237 (30)	8 (3, 17)	.	26 (10, 56)	.
	> 3	159 (20)	3 (2, 11)	.	23 (8, 49)	.
	Not Reported	17 (2)	12 (8, 18)	.	12 (0, 42)	.
Extracranial Mets				<0.001		<0.001
	Absent	150 (19)	14 (6, 26)	.	13 (5, 21)	.
	Present	622 (79)	7 (3, 15)	.	29 (10, 58)	.
	Not Reported	20 (3)	9 (3, 18)	.	14 (8, 41)	.
ECM Liver				<0.001		0.870
	Absent	450 (57)	10 (3, 19)	.	22 (10, 52)	.
	Present	322 (41)	6 (2, 15)	.	25 (8, 51)	.
	Not Reported	20 (3)	9 (3, 18)	.	14 (8, 41)	.
ECM Bone				<0.001		0.041
	Absent	604 (76)	9 (3, 18)	.	22 (9, 46)	.
	Present	168 (21)	5 (2, 14)	.	30 (9, 60)	.
	Not Reported	20 (3)	9 (3, 18)	.	14 (8, 41)	.
ECM Lung				0.004		<0.001
	Absent	335 (42)	9 (3, 20)	.	13 (5, 28)	.
	Present	437 (55)	7 (3, 16)	.	37 (16, 62)	.
	Not Reported	20 (3)	9 (3, 18)	.	14 (8, 41)	.
ECM Other				<0.001		0.499
	Absent	542 (68)	9 (4, 20)	.	24 (10, 51)	.
	Present	230 (29)	5 (2, 14)	.	22 (8, 52)	.
	Not Reported	20 (3)	9 (3, 18)	.	14 (8, 41)	.
Age				0.002		0.150
	25–52	195 (25)	10 (4, 20)	.	26 (12, 46)	.
	53–61	186 (23)	9 (3, 18)	.	24 (9, 57)	.
	62–68	214 (27)	7 (3, 19)	.	19 (7, 40)	.
	69–92	197 (25)	5 (2, 13)	.	25 (9, 59)	.
Sex				0.576		<0.001
	Male	500 (63)	8 (3, 18)	.	20 (8, 46)	.
	Female	287 (36)	7 (3, 16)	.	31 (12, 57)	.
	Not Reported	5 (1)	9 (8, 12)	.	24 (8, 62)	.
Race				0.481		0.940
	Asian	45 (6)	7 (2, 14)	.	23 (9, 55)	.
	African American	37 (5)	7 (3, 18)	.	23 (16, 38)	.
	White	635 (80)	8 (3, 18)	.	23 (9, 52)	.
	Unknown/Not Reported	75 (9)	7 (3, 18)	.	25 (5, 44)	.
Ethnicity				0.611		0.956
	Not Hispanic or Latino	658 (83)	9 (3, 18)	.	23 (9, 51)	.
	Hispanic or Latino	62 (8)	7 (3, 14)	.	24 (9, 56)	.
	Unknown/Not Reported	72 (9)	5 (2, 12)	.	26 (10, 46)	.
Primary Tumor Site				0.009		<0.001
	Esophagus	181 (23)	10 (3, 21)	.	12 (6, 22)	.
	GE junction	73 (9)	7 (2, 18)	.	10 (4, 20)	.
	Stomach	20 (3)	2 (1, 6)	.	14 (7, 23)	.
	Small Intestine (ie jejunum, d	27 (3)	8 (2, 14)	.	17 (2, 53)	.
	Colon-Right	100 (13)	7 (3, 20)	.	31 (12, 57)	.
	Colon-Transverse	15 (2)	3 (2, 5)	.	36 (23, 57)	.
	Colon-Left	35 (4)	10 (4, 14)	.	41 (22, 70)	.
	Rectosigmoid	90 (11)	10 (4, 20)	.	41 (24, 67)	.
	Rectum	189 (24)	7 (3, 17)	.	42 (17, 66)	.
	Anus	6 (1)	14 (5, 15)	.	35 (21, 46)	.
	Gallbladder	16 (2)	5 (1, 17)	.	13 (2, 27)	.

(*continued on next page*)

Table 1 (*continued*)

Variable	Category	N (%)	Median Survival (IQR)	P	TPDBM (IQR)	P
	Pancreas – adenocarcinoma	30 (4)	4 (3, 14)	.	18 (1, 45)	.
	Not Reported	10 (1)	15 (12, 23)	.	66 (29, 87)	.
Surgical Resection of Primary Tumor				0.004		<0.001
	0 = No	276 (35)	6 (2, 15)	.	10 (1, 20)	.
	1 = Yes	447 (56)	9 (3, 18)	.	40 (20, 65)	.
	Unknown	69 (9)	10 (4, 23)	.	20 (3, 34)	.
Stage				0.026		<0.001
	1 = I	28 (4)	8 (3, 17)	.	65 (28, 102)	.
	2 = II	90 (11)	11 (3, 26)	.	47 (23, 70)	.
	3 = III	245 (31)	9 (3, 18)	.	34 (16, 60)	.
	4 = IV	330 (42)	6 (2, 16)	.	12 (2, 28)	.
	Unknown	99 (13)	9 (3, 18)	.	29 (9, 63)	.
*HER2				0.066		0.570
	0 = Absent	89 (32)	6 (2, 16)	.	12 (7, 22)	.
	1 = Present	59 (22)	13 (6, 23)	.	10 (4, 21)	.
	Not Reported	126 (46)	7 (2, 18)	.	12 (5, 22)	.
*KRAS				0.111		0.047
	0 = Absent	111 (26)	6 (3, 14)	.	45 (23, 72)	.
	1 = Present	130 (30)	10 (4, 19)	.	36 (16, 61)	.
	Not Reported	188 (44)	7 (3, 16)	.	36 (15, 59)	.
*KRAS Exon				0.369		0.785
	1 = G12D	27 (20)	8 (4, 18)	.	29 (17, 61)	.
	2 = G12V	11 (8)	7 (4, 15)	.	48 (33, 68)	.
	3 = G13D	24 (18)	9 (3, 20)	.	50 (11, 77)	.
	9 = Other	32 (24)	14 (6, 26)	.	36 (12, 72)	.
	Unknown	39 (29)	10 (3, 19)	.	37 (15, 56)	.
*BRAF				0.917		0.938
	0 = Absent	130 (30)	9 (4, 17)	.	44 (21, 65)	.
	1 = Present	13 (3)	12 (2, 19)	.	49 (17, 68)	.
	Not Reported	286 (67)	7 (3, 17)	.	36 (16, 62)	.
EGFR				0.118		0.608
	0 = Absent	166 (21)	10 (4, 19)	.	33 (14, 57)	.
	1 = Present	16 (2)	5 (2, 14)	.	44 (13, 61)	.
	Not Reported	610 (77)	7 (3, 18)	.	21 (8, 46)	.
PIK3CA/P13K				0.398		0.377
	0 = Absent	92 (12)	9 (3, 18)	.	45 (21, 70)	.
	1 = Present	15 (2)	14 (6, 21)	.	28 (16, 59)	.
	Not Reported	685 (86)	7 (3, 18)	.	21 (8, 46)	.
*Hx of Crohns				0.315		0.513
	0 = No	353 (82)	7 (3, 17)	.	39 (19, 66)	.
	1 = Yes	2 (0)	6 (1, 11)	.	28 (24, 31)	.
	Unknown	74 (17)	10 (4, 20)	.	37 (19, 57)	.
*Hx of Ulcerative Col				0.514		0.192
	0 = No	350 (82)	7 (3, 16)	.	39 (19, 65)	.
	1 = Yes	5 (1)	4 (4, 20)	.	89 (37, 91)	.
	Unknown	74 (17)	10 (4, 20)	.	37 (19, 57)	.
Microsatellite status				0.380		0.803
	0 = Unstable	8 (1)	14 (6, 25)	.	24 (16, 56)	.
	1 = Stable	97 (12)	8 (3, 19)	.	30 (9, 58)	.
	Unknown	687 (87)	8 (3, 17)	.	23 (9, 49)	.
Hemoglobin				<0.001		0.473
	[5, 11)	121 (15)	3 (1, 6)	.	27 (9, 58)	.
	[11, 12.5)	123 (16)	6 (2, 18)	.	26 (12, 53)	.
	[12.5, 14.1)	122 (15)	7 (3, 19)	.	23 (10, 47)	.
	[14.1, 164]	124 (16)	11 (5, 19)	.	21 (7, 51)	.
	Not Reported	302 (38)	12 (4, 21)	.	21 (8, 47)	.
Neutrophil-to-lymphoc				0.569		0.498
	[0.07, 3.30)	76 (10)	6 (3, 16)	.	19 (11, 35)	.
	[3.30, 6.86)	80 (10)	4 (3, 12)	.	21 (5, 43)	.
	[6.86, 12.50)	76 (10)	5 (2, 12)	.	23 (10, 56)	.
	[12.50, 112]	78 (10)	4 (1, 18)	.	22 (8, 61)	.
	Not Reported	482 (61)	10 (4, 19)	.	24 (10, 52)	.
LDH				0.170		0.939
	[1, 196)	36 (5)	7 (3, 18)	.	22 (10, 51)	.
	[196, 347)	33 (4)	4 (3, 9)	.	25 (11, 60)	.
	[347, 517)	33 (4)	7 (3, 18)	.	17 (13, 40)	.
	[517, 4369]	33 (4)	5 (2, 14)	.	25 (5, 60)	.
	Not Reported	657 (83)	9 (3, 18)	.	24 (9, 49)	.

Table 1 (*continued*)

Variable	Category	N (%)	Median Survival (IQR)	P	TPDBM (IQR)	P
BMI				0.396		0.044
	[11.8, 22.1)	82 (10)	4 (2, 17)	.	23 (15, 54)	.
	[22.1, 26.0)	86 (11)	6 (3, 16)	.	17 (6, 38)	.
	[26.0, 30.1)	87 (11)	7 (3, 22)	.	17 (6, 44)	.
	[30.1, 80.8]	86 (11)	9 (3, 14)	.	22 (10, 41)	.
	Not Reported	451 (57)	10 (3, 18)	.	27 (10, 56)	.

* Only applies to a subset of primary tumor types. PT: Primary Tumor. Median survival is in months from start of BM treatment (Kaplan-Meier estimate). IQR = Interquartile Range. TPDBM = time from primary diagnosis to start of BM treatment, in months. Variables were measured at time of BM diagnosis. P-values are from log-rank (survival) or Kruskal-Wallis (TPDBM) test of equivalence among categories, excluding unknown/not reported.

Table 2
Survival by Treatment and Treatment Era.

	Overall	WBRT	SRS	WBRT+SRS	S+SRS	S+WBRT	S+WBRT+SRS
Historical Cohort							
N (%)	209	95 (45%)	35 (17%)	35 (17%)	2 (1%)	34 (16%)	8 (4%)
Mean GPA	2.0	1.8	2.4	2.1	3.5	2.4	1.8
Median Survival	5	3	7	7	9	10	8
Risk of Death (HR)		1.0	0.72	0.69	2.30	0.33	0.39
95% CI			0.40, 1.28	0.39, 1.22	0.43, 12.4	0.19, 0.56	0.17, 0.90
P-value			0.26	0.21	0.33	<0.01	0.03
Current Study							
N (%)	792	166 (21%)	309 (39%)	31 (4%)	121 (15%)	67 (8%)	5 (1%)
Mean GPA	2.0	1.7	2.1	2.0	2.1	2.1	1.6
Median Survival	8	3	6	12	11	14	4
Risk of Death (HR)		1.0	0.87	0.67	0.45	0.49	0.70
95% CI			0.69, 1.10	0.43, 1.04	0.33, 0.60	0.35, 0.68	0.24, 2.07
P-value			0.25	0.08	<0.01	<0.01	0.52

Abbreviations: WBRT: whole brain radiation therapy; SRS: stereotactic radiosurgery; S: surgery (craniotomy).
Hazard ratio (HR), 95% CI, and p (each treatment vs. WBRT alone within each cohort) adjusted for GPA. Median survival is unadjusted, in months. 11 patients in the current study did not have an initial treatment reported. 70 had surgery alone and 12 had fractionated partial brain radiation alone.

Table 3
Hazard Ratio Results of Multi-Variable Analyses of Significant Prognostic Factors.

Parameter	Categories	N (%)	HR (95% CI)
KPS	90–100	242 (31)	1.0 (Ref)
	80	207 (26)	1.6 (1.3, 2.0)
	<80	267 (34)	2.1 (1.6, 2.7)
Age	<60	340 (43)	1.0 (Ref)
	≥60	452 (57)	1.3 (1.1, 1.6)
ECM	Absent	150 (19)	1.0 (Ref)
	Present	622 (79)	1.8 (1.4, 2.2)
# BM	1	379 (48)	1.0 (Ref)
	2–3	237 (30)	1.4 (1.1, 1.7)
	>3	159 (20)	1.9 (1.6, 2.4)

Note: Two other factors (hemoglobin and primary GI site) were significant but incorporating those factors did not improve the model so were excluded for simplicity.

4. Discussion

Brain metastases in patients with GI cancers are not uncommon. Survival varies widely within this cohort based on the prognostic factors presented in this report. In contrast to the prior cohort in which only KPS status was prognostic, this study identifies multiple new prognostic factors and incorporates them into an updated user-friendly prognostic index, the Graded Prognostic Assessment for gastrointestinal cancer patients with brain metastases (GI-GPA). Patients with GI cancers and brain metastases also represent a unique patient population because they have a worse prognosis than any other primary diagnosis except small cell lung cancer. Our findings are consistent with prior reports [3–6] that performance status and number of metastases are important prognostic factors but further refine our ability to predict survival for these patients with the identification of additional factors.

Other smaller studies [3–5] have reported that brain metastases in GI cancer patients occur late in the course of disease.

Table 4
Definition of the Updated Prognostic Index, the Graded Prognostic Assessment for Patients with Gastrointestinal Cancers and Brain Metastases (GI-GPA) and Scoring Worksheet to Estimate Survival.

Prognostic Factor	GI-GPA Scoring Criteria					Patient Score
	0	0.5	1.0	1.5	2.0	
KPS	<80	n/a	80	n/a	90–100	–
Age	≥60	<60	n/a	n/a	n/a	–
ECM	Present	Absent	n/a	n/a	n/a	–
# of BM	>3	2–3	1	n/a	n/a	–
					Sum Total	–

Median Survival by GI-GPA Group: 0–1.0, 1.5–2.0, 2.5–3.0, 3.5–4.0 was 3, 9, 12 and 17 months, respectively. Abbreviations: KPS, Karnofsky Performance Score; ECM, extracranial metastases; # of BM, number of brain metastases; n/a, not applicable.

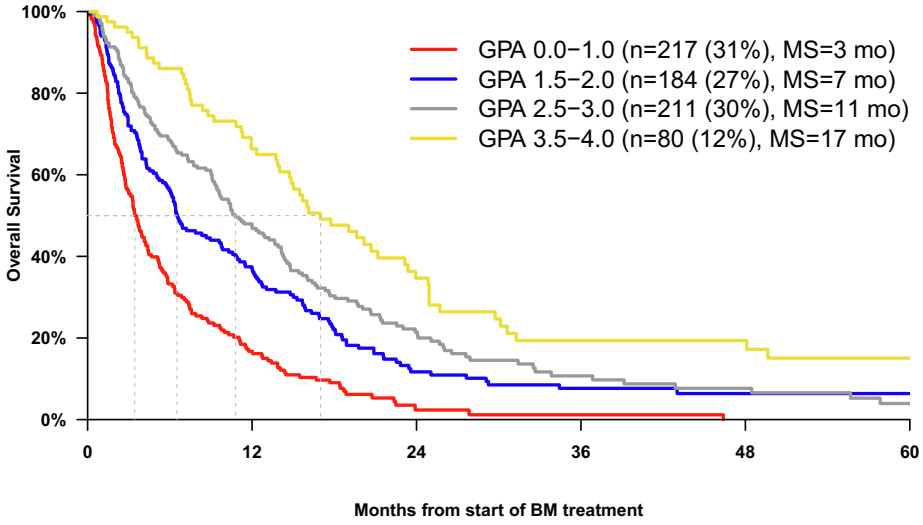

Fig. 1. Kaplan-Meier Curve for Survival by GI-GPA Group.

Interestingly, the average time from primary diagnosis of a GI cancer to BM (TPDBM) is 23 months [12] which is longer than that of lung cancer (16 mo) and renal cell carcinoma (19 mo) but shorter than the TPDBM for melanoma (32 mo) and breast cancer (38 mo). However, MS of a GI cancer patient after the diagnosis of BM (8mo) is far worse than any other diagnoses listed above. (lung non-adenocarcinoma 9 mo, lung adenocarcinoma 15 mo, breast 14 mo, melanoma 10 mo, renal cell 12 mo) [6–11]. Certainly the proclivity of GI cancers to not just extracranial sites (80%) but particularly the liver (42%) is a likely explanation for the worse prognosis.

Given the fact that 83% of patients in this study presented with stage III or IV disease, physicians should be aware that such patients are at high risk for developing BM, and although a role for routine screening has not been established, any CNS symptoms deserve scrutiny.

Her2-positivity may become a prognostic factor in the future as more and more patients are being tested in the current era. In this study, HER2-positivity showed a trend ($p = 0.066$) toward improved survival in patients with gastric, esophageal and gastroesophageal cancers.

For patients with poor prognosis (GI-GPA $\leq$ 1.0), discussion of supportive care or hospice, as established by the QUARTZ trial for NSCLC BM patients [16] might be reasonable. Physicians should have frank conversations with their patients and their families regarding expected survival, quality-of-life, and end-of-life care.

4.1. Limitations

Limitations of this study include the retrospective nature of the database and the selection bias inherent in all retrospective studies. Accordingly, one cannot conclude one treatment is better than another (Table 2) based on these data. Secondly, although the sample size is large, the molecular profile was not frequently reported. Thirdly, detailed data on use of chemotherapy and immunotherapy before and after the diagnosis of brain metastases are lacking in these data. Fourthly, we grouped all primary GI sites in this analysis but each primary GI site may behave differently as suggested by the HER2 data discussed above.

5. Conclusions

Contrary to conventional wisdom, brain metastases are not uncommon in patients with GI cancers. Furthermore, median survival within this cohort varies widely (from 3 to 17 months) based on multiple recently identified prognostic factors. Compared to other diagnoses, patients with GI cancers and BM are a unique population associated with poor prognosis overall. The updated GI-GPA prognostic index improves our ability to estimate survival for these patients and will be useful for end-of-life decision-making and stratification for future clinical trials. In order to simplify calculation of individual patient's GPA, a free, user-friendly app, which can be easily downloaded to a smart phone or clinic computer is available at brainmetgpa.com.

Declaration of Competing Interest

None of the authors have a conflict of interest related to this work. The following authors have no relationships to report: PWS, PF, JL, WB, PDB, DC, JBY, VC, SJ, LEG, SM, SB, PS, BC, A Attia, JKM, CCW, JP, JMB, RS, DDT, DS, MC, HS, HA, LM. The following authors have relationships to report, but again none are related to this work: A Aizer (Astra Zeneca), AS (Elekta, Varian, Accuray), TJCW (Merck, Astra-Zeneca, Doximity, Novocure, Elekta, Wolters Kluwer), EL (Novocure, Nomocan Pharmaceuticals), JPK (Varian), HAS (Genentech), DR (Varian, Siemens, Accuray, BrainLab, Elekta, Pfizer, EMD Serono), MPM (Agenus, Insys, Remedy, IBA, Varian, Oncoceutics, Astra-Zeneca, Monteris.

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3. Paul Sperduto and Ryan Shanley had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctro.2019.06.007.

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