Hispanic Ethnicity is Associated with Early Presentation and Advanced Stage of Gastric Adenocarcinoma

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Abstract

Introduction: Gastric adenocarcinoma (GA) is a heterogeneous disease with variable presentation and progression between ethnic groups. We aimed to assess factors related to the early age of GA presentation (< 45 years) between racial and ethnic groups.

Methods: Using the National Cancer Database, patients with GA and upfront surgery were selected. Those receiving neoadjuvant therapy were excluded to ensure accurate pathologic stage. Clinicopathologic data was correlated to factors associated with age at diagnosis. Ethnicity was classified into Non-Hispanic White (NHW), Hispanic (HS), African American (AA) and Asian (AS). Univariate and multivariate linear regression models were used to determine factors associated with age of presentation. Overall survival was estimated using the Kaplan–Meier method and compared using log-rank tests.

Results: Between 2006 and 2013, 13392 patients with GA and upfront surgery were identified. Median age was 67 years (IQR: 57-76) and 61% were male. Mean age at diagnosis was variable between ethnicity (NHW: 7609, 57%, 68 years, HS: 1720, 13%, 61 years, AA: 2727, 20%, 64 years and AS: 1336, 10%, 64 years; p<0.01). HS and AA presented with more advanced stage (Stage 4: HS 20.8%, AA 19.2%, NHW 17.8%, AS 16.2%; p<0.05). On univariate analysis, female gender, HS race, uninsured status, Medicaid, advanced pathologic stage, and poorly differentiated tumor grade were associated with young presentation (p<0.01). On multivariate analysis, factors associated with young presentation included female gender (1.52, 95%CI: 1.31-1.76), minority race compared to NHW (HS: 2.30 95%CI: 1.92-2.86; AA: 1.37 95%CI: 1.24-1.67), and poorly (2.40, 95%CI: 1.34-4.29) or undifferentiated grade (3.56, 95%CI: 1.84-6.99). Median survival was significantly different between races (NHW 23 months, HS 41 months, AA 26 months, AS 50 months, p<0.001).

Conclusion: Young presentation of GA is associated with HS race, female gender, and advanced tumors. Despite HS presenting at a young age with more advanced disease, median survival was prolonged compared to AA/NHW. Further research is necessary to determine underlying biologic basis of ethnic variation observed in GA.
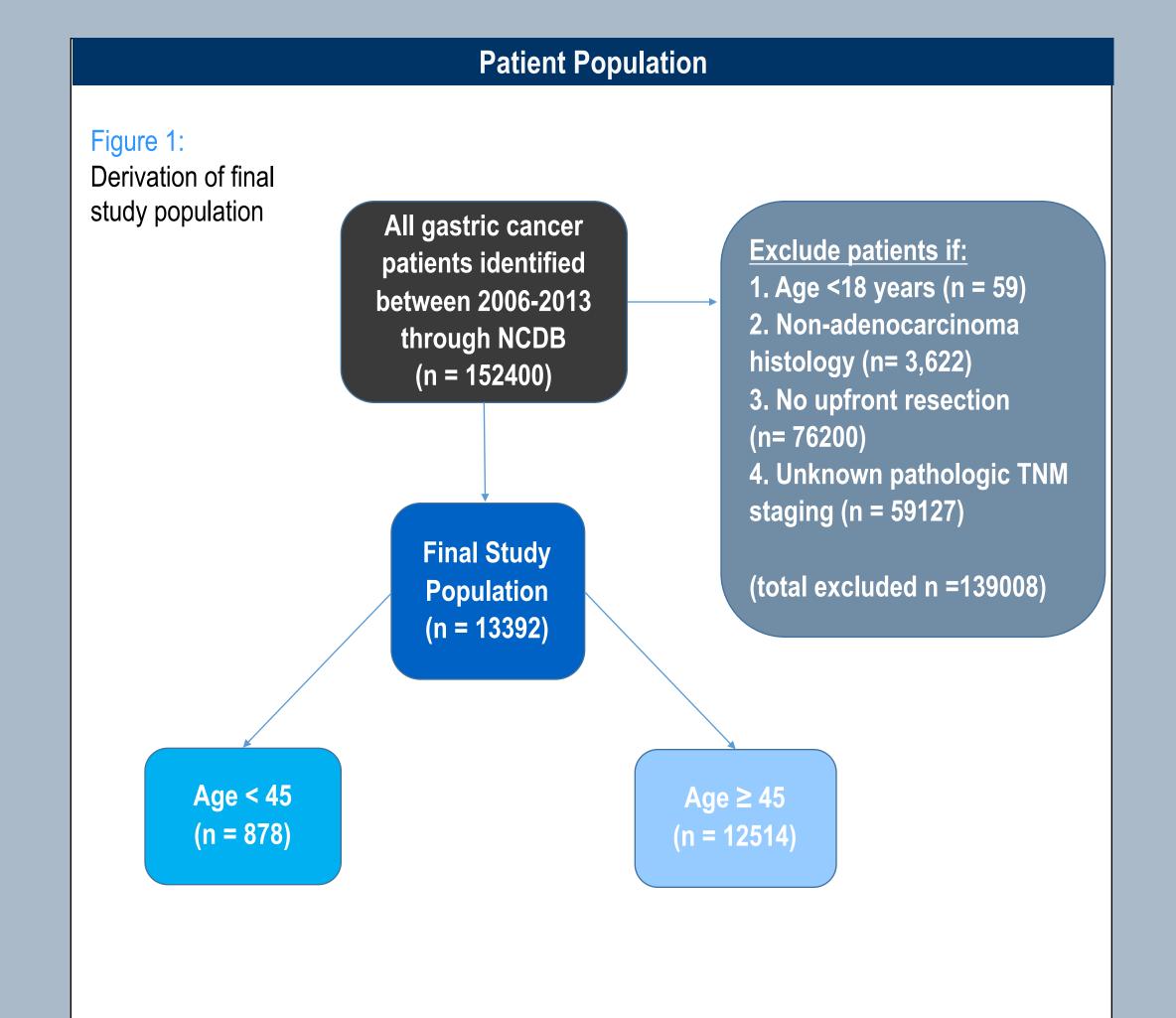
Background

- Gastric Adenocarcinoma (GA) is a heterogeneous disease with variable presentation between ethnic groups

- It is unknown how patients and tumor factors are associated with age at presentation

- Through a national database, we aimed to assess factors related to the early age of GA presentation (< 45 years)

Methods

- Retrospective review of National Cancer Database (NCDB) of patients with GA and upfront surgery were selected between 2006 and 2013. Patients receiving neoadjuvant therapy were excluded to ensure accurate pathologic stage

- Clinicopathologic data were correlated to factors associated with age at diagnosis

- Univariate and multivariate linear regression models were used to determine factors associated with age of presentation

- Overall survival was estimated using the Kaplan-Meier method and compared using log-rank tests

National Cancer Database (NCDB) Variable Definitions

NCDB term	Definition
Median Income Quartiles [a]	Median household income for each person's area of residence estimated by matching the zip code of the patient at the time of diagnosis against files derived from 2012 American Community Survey data, adjusted for inflation
Education Level [b]	Estimated by matching the zip code of the patient recorded at time of diagnosis against files derived from 2012 American Community Survey data. The item provides a measure of the number of adults who did not graduate from high school. (1: ≥ 29%, 2: 20-28.9%, 3: 14-19.9%, 4: <14%)

Patient Population

All gastric cancer patients identified between 2006-2013 through NCDB (n = 152400)

Exclude patients if:
1. Age <18 years (n = 59)
2. Non-adenocarcinoma histology (n= 3,622)
3. No upfront resection (n= 76200)
4. Unknown pathologic TNM staging (n = 59127)

(total excluded n =139008)

Final Study Population (n = 13392)

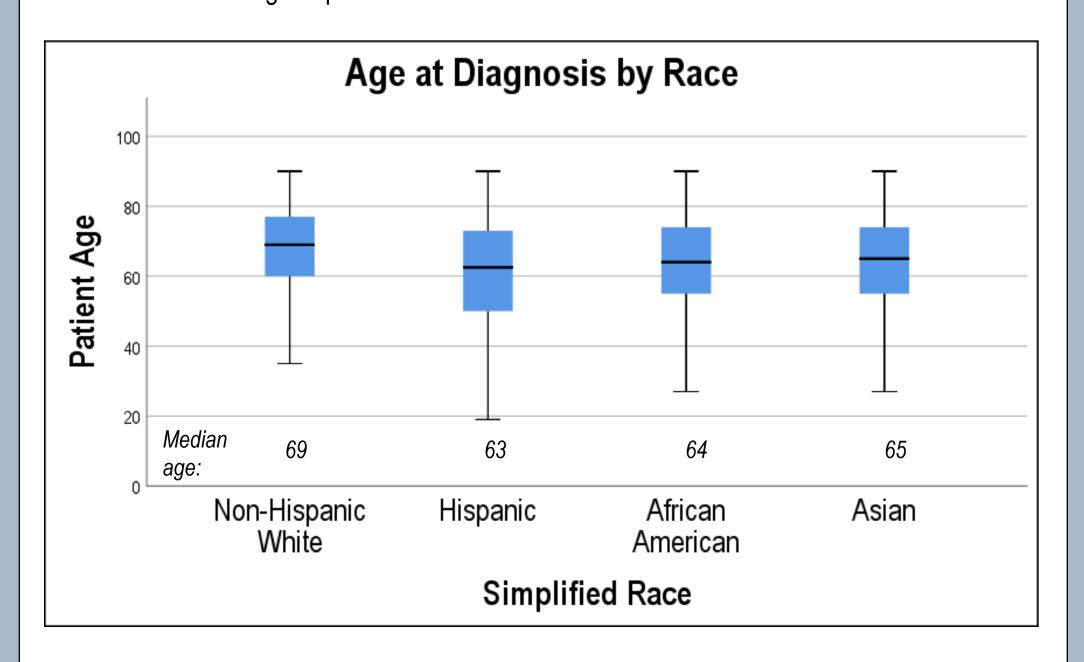Age < 45 (n = 878)

Age ≥ 45 (n = 12514)

Comparison of Patient Characteristics Between Groups

Table 1: Significant differences exist between patient groups. Younger patient group had comparatively more patients with female gender, minority race, uninsured status, private insurance, Medicaid, poorly/undifferentiated tumors and advanced pathologic stage compared to older patient group

		Age < 45 878 N (%)	Age ≥ 45 12514 N (%)	Total 13392 N (%)	P-value
Sex	Male	449 (51.1)	7699 (61.5)	8148 (60.8)	<0.01
	Female	429 (48.9)	4815 (38.5)	5244 (39.2)	
Race	Non-Hispanic White	325 (37.0)	7284 (58.2)	7609 (56.8)	<0.01
	Hispanic	251 (28.6)	1469 (11.7)	1720 (12.8)	
	African American	202 (23.0)	2525 (20.2)	2727 (20.4)	
	Asian	100 (11.4)	1236 (9.9)	1336 (10.0)	
Insurance Status	Not Insured	126 (14.4)	486 (3.9)	612 (4.6)	<0.01
	Private Insurance	530 (60.4)	4163 (3.3)	4693 (35.0)	
	Medicaid	181 (20.6)	968 (7.7)	1149 (8.6)	
	Medicare	31 (3.5)	6782 (54.2)	6813 (50.9)	
	Other Government	10 (1.1)	115 (0.9)	125 (0.9)	
Median Income Quartiles [a]	< $30,000	166 (18.9)	2199 (17.6)	2365 (17.7)	0.42
	$30,000 - $35,999	153 (17.4)	2269 (18.1)	2422 (18.1)	
	$36,000 - $45,999	249 (28.4)	3354 (26.8)	3603 (26.9)	
	$46,000 +	310 (35.3)	4692 (37.5)	5002 (37.4)	
Education Level [b]	1	233 (26.5)	2916 (23.3)	3149 (23.5)	<0.01
	2	242 (27.6)	3121 (24.9)	3363 (25.1)	
	3	165 (18.8)	2731 (21.8)	2896 (21.6)	
	4	238 (27.1)	3746 (29.9)	3984 (29.7)	
Grade	Well differentiated	13 (1.5)	496 (4.0)	509 (3.8)	<0.01
	Moderately differentiated	98 (11.2)	3207 (25.6)	3305 (24.7)	
	Poorly differentiated	723 (82.3)	8460 (67.6)	9183 (68.6)	
	Undifferentiated, anaplastic	44 (5.0)	351 (2.8)	395 (2.9)	
Pathologic Staging Group	Stage 0	1 (0.1)	41 (0.3)	42 (0.3)	<0.01
	Stage 1A	31 (3.5)	778 (6.2)	809 (6.0)	
	Stage 1B	73 (8.3)	1324 (10.6)	1397 (10.4)	
	Stage 2A	103 (11.7)	1982 (15.8)	2085 (15.6)	
	Stage 2B	124 (14.1)	1909 (15.3)	2033 (15.2)	
	Stage 3A	181 (20.6)	2485 (19.9)	2666 (19.9)	
	Stage 3B	148 (16.9)	1937 (15.5)	2085 (15.6)	
	Stage 3C	79 (9.0)	856 (6.8)	935 (7.0)	
	Stage 4	138 (15.7)	1202 (9.6)	1340 (10.0)	

HS Patients Present at Younger Age

Figure 2: Box plot of age at diagnosis of gastric cancer patients stratified by race. HS patients with earliest median age at presentation.

Age at Diagnosis by Race

Median age: Non-Hispanic White 69; Hispanic 63; African American 64; Asian 65

Factors Associated with Early Age at Presentation

Table 2: Univariate and Multivariate Analysis of factors associated with age at presentation. Female gender, HS race and advanced tumors are associated with younger age at presentation

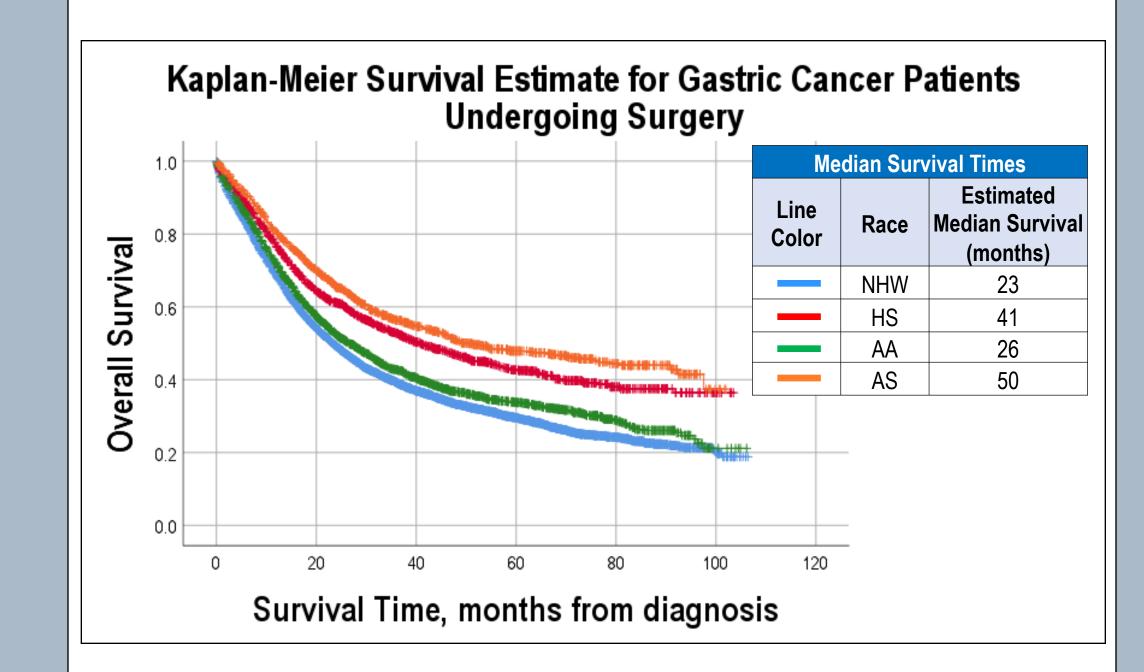|		Univariate Analysis OR	95% CI	P-value	Multivariate Analysis OR	95% CI	P-value
Sex	Male	ref	-	-	ref	-	-
	Female	1.53	1.33 - 1.75	<0.01	1.52	1.31 - 1.76	<0.01
Race	Non-Hispanic White	ref	-	-	ref	-	-
	Hispanic	3.83	3.22 - 4.56	<0.01	2.30	1.92 - 2.86	<0.01
	African American	1.80	1.50 - 2.15	<0.01	1.37	1.12 - 1.67	<0.01
	Asian	1.81	1.44 - 2.29	<0.01	1.23	0.96 - 1.57	0.10
Insurance status	Not insured	ref	-	-	ref	-	-
	Private Insurance	0.49	0.40 - 0.61	<0.01	0.59	0.47 - 0.74	<0.01
	Medicaid	0.72	0.56 - 0.93	0.01	0.73	0.56 - 0.95	0.02
	Medicare	0.01	0.01 - 0.03	<0.01	0.02	0.02 - 0.04	<0.01
	Other Government	0.34	0.17 - 0.66	<0.01	0.41	0.21 - 0.82	0.01
Median Income Quartiles [a]	< $30,000	ref	-	-	ref	-	-
	$30,000 - $35,999	0.89	0.71 - 1.12	0.33	1.02	0.79 - 1.32	0.87
	$36,000 - $45,999	0.98	0.80 - 1.21	0.87	1.02	0.80 - 1.32	0.87
	$46,000 +	0.88	0.72 - 1.06	0.18	0.91	0.68 - 1.22	0.53
Education Level [b]	1	ref	-	-	ref	-	-
	2	0.97	0.81 - 1.17	0.75	1.19	0.95 - 1.49	0.14
	3	0.76	0.62 - 0.93	0.02	1.06	0.81 - 1.38	0.67
	4	0.80	0.66 - 0.96	0.02	1.17	0.88 - 1.57	0.28
Grade	well-differentiated	ref	-	-	ref	-	-
	moderately-differentiated	1.17	0.65 - 2.10	0.61	1.14	0.62 - 2.09	0.68
	poorly differentiated	3.26	1.87 - 5.69	<0.01	2.40	1.34 - 4.30	<0.01
	undifferentiated, anaplastic	4.78	2.54 - 9.01	<0.01	3.56	1.84 – 7.00	<0.01
Pathologic Staging Group	Stage 0	ref	-	-	ref	-	-
	Stage 1A	1.63	1.11 - 1.25	0.63	1.57	0.19 - 12.42	0.67
	Stage 1B	2.26	0.31 - 16.67	0.42	1.54	0.20 - 11.98	0.68
	Stage 2A	2.13	0.29 - 15.64	0.46	1.37	0.18 - 10.61	0.76
	Stage 2B	2.66	0.36 - 19.52	0.34	1.57	0.20 - 12.22	0.66
	Stage 3A	2.99	0.41 - 21.84	0.28	1.79	0.23- 13.86	0.58
	Stage 3B	3.13	0.43 -22.93	0.26	1.63	0.21 - 12.65	0.64
	Stage 3C	3.78	0.51 - 27.88	0.19	1.72	0.22 - 13.41	0.61
	Stage 4	4.71	0.64 - 34.49	0.13	2.47	0.32 - 19.16	0.39

HS and AA Patients Presented with Advanced Stage

Table 3: Gastric Cancer Staging (analytic stage group) stratified by race. HS (20.8%) and AA (19.2%) patients presented with more advanced stage compared to NHW and AS patients

Stage vs Race	NHW N (%)	HS N (%)	AA N (%)	AS N (%)	P value
Stage 0	29 (0.4)	6 (0.3)	12 (0.4)	4 (0.3)	<0.01
Stage I	1255 (16.5)	269 (15.6)	444 (16.3)	270 (20.2)	
Stage II	1887 (24.8)	425 (24.7)	721 (26.4)	318 (23.8)	
Stage III	3083 (40.5)	663 (38.5)	1027 (37.7)	527 (39.4)	
Stage IV	1355 (17.8)	357 (20.8)	523 (19.2)	217 (16.2)	

Median Survival Prolonged in HS Patients Compared to AA/NHW Patients

Figure 3: Kaplan-Meier survival analysis for gastric cancer patients undergoing surgery with median survival table stratified by race. Although HS patients presented at an earlier age and with more advanced disease, median survival was prolonged.

Kaplan-Meier Survival Estimate for Gastric Cancer Patients Undergoing Surgery

Line Color	Race	Estimated Median Survival (months)
	NHW	23
	HS	41
	AA	26
	AS	50

Conclusions

- **Young presentation of GA is associated with HS race, female gender, and advanced tumors.**

- **Despite HS patients presenting at a young age with more advanced disease, median survival was prolonged compared to AA/NHW.**

- **Further research is necessary to determine underlying biologic basis of ethnic variation observed in GA.**

Limitations

- Several factors limit the ability of this study to be generalized:
  - Retrospective analysis
  - Incomplete treatment data

Acknowledgement