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Original Article

Do HbA1C Levels Correlate With Delayed Gastric Emptying in Diabetic Patients?

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Background/Aims
Gastroparesis is characterized by delayed gastric emptying without obstruction. Diabetes is frequently associated with poor glycemic control and delayed gastric emptying. Gastric emptying scintigraphy (GES) is the standard for measuring gastric emptying. Serum hemoglobin A1C (HbA1C) measures prolonged glycemic control with normal as < 7% glycated. To date, no correlation of serum HbA1C level with gastric emptying, demonstrated by GES, in diabetics has been performed. The aim of the present investigation is to determine if a relationship exists between serum HbA1C levels and gastric emptying, assessed by GES, in diabetics.

Methods
All diabetics, having both GES and serum HbA1C level within 3 months from July 1, 2003 - June 30, 2008 were eligible for study. Demographic data collected included gender, age and ethnicity. Abnormal gastric emptying was defined as T½ > 120 minutes and serum HbA1C as percent glycated.

Results
Nuclear Medicine GES database review revealed 431 examinations performed during the study interval. A total of 181 were not eligible due to the following: 29 duplicates, 22 diabetes not documented and 130 without HbA1C levels, resulting a study group of 250 cases. No significant correlation was observed between gastric emptying time, HbA1C or age. Among patients with HbA1C ≥ 7%, HbA1C was inversely related to age with a coefficient of correlation of $r = -0.175$ ($p = 0.038$).

Conclusions
There is no correlation observed between gastric emptying time, using GES, and serum HbA1C levels. In diabetics, serum HbA1C is not as important as daily glycemic control regarding gastric emptying.
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Key Words
Diabetes Mellitus; Gastric emptying; Gastroparesis; HbA1C; Scintigraphy

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Introduction

Gastroparesis is characterized by evidence of delayed gastric emptying without obstruction. It is estimated to affect 4% of the population.[1] Diabetes is frequently associated with gastroparesis; in one study of 146 patients with gastroparesis, 29% had diabetes.[2] Conversely, gastroparesis is present in 25%-55% of patients with type 1 diabetes and in 30% of those with type 2 diabetes.[3-6] There is poor correlation between symptoms and delayed gastric emptying. Indeed, gastric emptying scintigraphy (GES) is the standard for the measurement of gastric motility in clinical practice.[7] Many theories have been suggested regarding the pathogenesis of gastroparesis in diabetics including impaired phasic antral contractions, defects in tone, pylorospasm, autonomic neuropathy, impaired smooth muscle contractile responses in type 1 diabetes secondary to circulating antibodies to L-type calcium channels and genetic defects such as mitochondrial DNA mutation 3243 in type 2 diabetics.[8-13] Poor glycemic control has been associated with delayed gastric emptying.[11,12] Modest hyperglycemia (> 250 mg/dL) corresponds with near absent gastric emptying.[14] Barnett and Owyang[14] demonstrated that serum glucose levels of 140-175 mg/dL may cause gastric emptying delays in diabetic patients when compared to euglycemic patients. They suggested this may be due to hyperglycemia which leads to disruption of normal antral motor complexes. Also, it is regarded that diabetes can worsen gastroparesis severity.[15] Gastroparesis may complicate diabetic control by altering the pharmacokinetics of orally administered hypoglycemic agents through delayed gastric emptying resulting in erratic medication levels, influencing postprandial insulin, in addition to altering carbohydrate absorption. Hemoglobin A1C (HbA1C) is used to identify the average plasma glucose concentration over the previous four weeks to 3 months in diabetic patients. The goal HbA1C level for a diabetic patient is < 7%.[16] To date, no correlation of serum HbA1C level with delayed gastric emptying (by GES), in patients with diabetes has been performed. The aim of this study sought to determine the relationship of serum HbA1C and gastric emptying time in diabetics.

Materials and Methods

1. Study population

A retrospective review of the Nuclear Medicine procedure database was performed for all patients having GES using an egg meal between June 1, 2003 and June 30, 2008 at the University of Florida College of Medicine-Jacksonville. Patients were considered eligible for the study if GES was performed and serum HbA1C drawn within 3 months of the index study. Demographics (age, race and sex), GES times and HbA1C levels were recorded for each patient. The research protocol was approved by the Institutional Board Review of the University of Florida College of Medicine-Jacksonville. Exclusion criteria were duplicate studies, absence of diabetes, serum HbA1C outside of 3-month period or none available, medications known to affect gastric function and previous gastric surgery. GES studies with values in minutes or showing normal vs abnormal gastric emptying were included for analysis.

2. Gastric emptying scintigraphy

All patients reported to the nuclear medicine imaging department after an 8 hour overnight fast. GES was performed after ingestion of a standard technetium 99-sulfur colloid radiolabeled liquid egg white (Eggbeaters, ConAgra Foods, Inc, Omaha, NE, USA) sandwich with jam and 300 mL of water. The meal specifically consisted of 4 oz (120 g, equal to 2 large eggs) liquid egg white (99% real eggs, cholesterol and fat free, low calorie); 2 slices of white bread (120 kcal), strawberry jam (30 g, 74 kcal) and water. The total caloric value of the meal was 255 kcal (72% carbohydrates, 24% protein, 2% fat and 2% fiber).[17,18] After consumption of the meal, scintigraphic images were obtained at 0, 30, 60, 120, 180 and 240 minutes after ingestion. The geometric center of the decay-corrected anterior and posterior counts was calculated for each time point. Gastric emptying was analyzed as the percent radioactivity retained in the stomach over time.[17,19] Abnormalities in gastric emptying were defined as using the imaging data from the 1, 2 and 4 hour imaging intervals.[17,18] Delayed gastric emptying was defined as a T½ > 90 minutes (mean ± 2 SD). Patients with a T½ > 90 minutes but < 180 were classified as having mild gastroparesis and those with T½ > 180 minutes were designated as severe.

3. Statistical methods

Baseline data are expressed as the mean ± SD and/or percentages. Comparisons between groups were made using Chi-square analysis for categorical data, as well as *t* testing and ANOVA for continuous data. Pearson's correlation analysis was done to assess the relationship between continuous variables. Differences between groups were considered significant at a p-

value < 0.05. Data analysis was performed using SPSS 17 (SPSS Inc, Chicago, IL, USA).

Results

Review of the Nuclear Medicine GES database revealed 431 studies performed during the study period. A total of 181 studies were not eligible for the following reasons: 29 duplicate procedures, 22 in which diabetes was not documented and 130 without HbA1C levels. This resulted in 250 cases for inclusion and analysis. Table 1 demonstrates the baseline characteristics of the patients, including ethnicity, gender, age, mean HbA1C and gastric emptying time from GES. Table 2 describes the study population with regard to gender, ethnicity, serum HbA1C and gastric emptying time. No statistically significant difference was observed in gastric emptying time, HbA1C and age according to gender or ethnicity. No statistically significant correlation was observed overall between gastric emptying time, HbA1C and age. Table 3 shows that among patients with HbA1C ≥ 7%, HbA1C was inversely related to age with a coefficient of correlation of r = -0.175 (p = 0.038). This was not observed in patients with HbA1C < 7. Categorical analysis of patients with abnormal HbA1C and gastric emptying times (table not shown) showed no statistically significant association (Chi-square = 0.525).

Table 1. Baseline Characteristics in 250 Patients

Ethnicity	
African american (n = 142)	57.6%
Non hispanic white (n = 91)	36.4%
Hispanic (n = 12)	4.8%
Other (n = 5)	2.0%
Gender (%)	
Male (n = 56)	22.4 %
Female (n = 194)	77.6 %
Age in years (mean ± SD, yr)	58.9 ± 13.9
HbA1C (mean ± SD, %)	7.9 ± 2.2
Gastric emptying time (mean ± SD, min)	102 ± 91.8

HbA1C, hemoglobin A1C.

Discussion

The aim of the present investigation was to evaluate the relationship of serum HbA1C with gastric emptying time in diabetic patients. Although poor glycemic control and modest hyperglycemia (> 250 mg/dL) are associated with delayed gastric emptying, a relationship of serum HbA1C with this remains to be determined.[11,12,14] This study failed to find any such relationship, implying that HbA1C alone may have no correlation with gastric emptying time. This is not surprising since HbA1C values reflect glycemic control over a 3-month period. It is possible that patient's acute glycemic management improved during this time prior to GES evaluation. Additionally, normal HbA1C values may have no relationship to gastric emptying time in patients who have already suffered permanent neurologic damage from diabetes. In these patients, adequate glycemic control could mitigate further worsening but existing neural damage may not be reversible.

Several limitations of this investigation require recognition and discussion. The first was performance of a retrospective study, using only existing GES and HbA1C values within 3

Table 3. Correlation of Hemoglobin A1C With Age and Gastric Emptying Time in 141 Patients With Hemoglobin A1C ≥ 7

	Pearson's coefficient of correlation	p-value
Age	-0.175	0.038
Gastric emptying time	-0.055	0.516

Table 2. Serum Hemoglobin A1C and Gastric Emptying Time by Gender and Ethnicity in 250 Patients

		HbA1C (mean ± SD, %)	p-value	GET (mean ± SD, min)	p-value	Age (mean ± SD, yr)	p-value
Gender[a]	Male (n = 56)	7.9 ± 2.0	0.902	101 ± 67.5	0.893	57.9 ± 13.9	0.834
	Female (n = 194)	7.9 ± 2.2		103 ± 97.8		59.1 ± 13.9	
Ethnicity[b]	Non hispanic white (n = 91)	7.7 ± 2.1	0.286	97 ± 60.5	0.810	58.5 ± 14.0	0.672
	African american (n = 142)	8.1 ± 2.3		104 ± 109.3		59.9 ± 14.2	
	Hispanic (n = 12)	7.6 ± 1.9		122 ± 78.0		55.7 ± 13.3	
	Other (n = 5)	6.4 ± 1.5		102 ± 44.5		55.8 ± 9.0	

HbA1C, hemoglobin A1C; GET, gastric emptying time.
[a]*t* test, [b]ANOVA analysis.

months of each other. No information was available on individual day-to-day glucose control or the presence of diabetes diagnosis for each patient. Blood glucose measurements at the time of test meal consumption as well as patient medication profiles allowing for comparison of oral and injectable glycemic agents were not available for analysis. This database also did not distinguish between type 1 and type 2 diabetics. The average glycated hemoglobin of 7.9 suggests that this population of patients were not optimally controlled. Thus, this study does not allow direct analysis on the relationship of HbA1C and gastric emptying in the context of acute glycemic control, duration and type of diabetes or the proportion of patients who were insulin-requiring. Comorbidities were not assessed, thus a comparison between patients with coexisting anemia, hemoglobinopathy, neurological, cardiovascular or other disorders which might affect HbA1C or gastric emptying could not be conducted. Finally, we observed a weak but significant inverse correlation between HbA1C and age in this population of patients when HbA1C $\geq$ 7. This relationship may warrant further characterization as this observation has not been noted previously.

In summary, while HbA1C is a suitable measure of glycemic control over 3 months in the general diabetic population, HbA1C alone should not be considered a substitute for daily glucose logs in the management of gastroparesis. Day-to-day glycemic control may be a more relevant therapeutic target than serum HbA1C when managing this condition. Comorbid conditions, which may influence gastric emptying or HbA1C, were not evaluated in the present investigation and deserve analysis in future investigations of HbA1C and gastroparesis. The retrospective nature of this analysis is limited by potential confounders. In addition, a comparison of type 1 and type 2 diabetes along with analysis of body mass index, waist measurements and/or diabetic medications prescribed could further delineate relationships in glycemic control and gastric function in these patients.

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