One-Hour Postload Plasma Glucose in Middle Age and Medicare Expenditures in Older Age Among Nondiabetic Men and Women

The Chicago Heart Association Detection Project in Industry

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OBJECTIVE — To examine associations in nondiabetic individuals of 1-h postload plasma glucose measured in young adulthood and middle age with subsequent Medicare expenditures for cardiovascular disease (CVD), diabetes, cancer, and all health care at age 65 years or older using data from the Chicago Heart Association Detection Project in Industry (CHA).

RESEARCH DESIGN AND METHODS — Medicare data (1984–2000) were linked with CHA baseline records (1967–1973) for 8,580 men and 6,723 women ages 33–64 years who were free of coronary heart disease, diabetes, and major electrocardiogram (ECG) abnormalities and who were Medicare eligible (65+ years) for at least 2 years. Participants were classified based on 1-h postload plasma glucose levels <120, 120–199, or ≥200 mg/dl.

RESULTS — With adjustment for baseline age, cigarette smoking, serum cholesterol, systolic blood pressure, BMI, ethnicity, education, and minor ECG abnormalities, the average annual and cumulative Medicare, total, and diabetes- and CVD-related charges were significantly higher with higher baseline plasma glucose in women, while only diabetes-related charges were significantly higher in men. For example, in women, multivariate-adjusted CVD-related cumulative charges were, respectively, $14,260, $18,909, and $21,183 for the three postload plasma glucose categories (*P* value for trend = 0.035).

CONCLUSIONS — These findings suggest that maintaining low glucose levels early in life has the potential to reduce health care costs in older age.

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Diabetes is associated with increased risk for nonfatal and fatal coronary heart disease, cardiovascular diseases (CVDs), blindness, kidney failure, and other chronic conditions (1) and is a serious economic burden in the U.S. and other countries (1,2). Preventing diabetes and decreasing subsequent health care costs is therefore an important goal of both health care professionals and policy makers.

Several studies have examined associations of diabetes, diabetes-related diseases such as CVD and stroke, and CVD risk factors with medical expenditures. These studies have documented that individuals with diabetes or CVD incur much higher health care costs compared with those free from these diseases (1–3). Previous studies have also demonstrated that a high blood glucose level at younger age is related not only with a higher risk of developing diabetes (4) but also with CVD and other nonfatal and fatal diseases (5–7). These relations, which progress in a continuous manner, may prevail even with glucose levels that are below the diabetic range (6,7). However, among people without clinically diagnosed diabetes, the association of blood glucose level earlier in life and health care expenditures in older age has not been well examined.

This study used data from the Chicago Heart Association Detection Project in Industry (CHA) linked to data from the Centers for Medicare and Medicaid Services to examine the association between 1-h postload plasma glucose level in young adulthood and middle age with Medicare expenditures in older age.

RESEARCH DESIGN AND METHODS

Between November 1967 and January 1973, the CHA study screened 39,522 employed individuals aged 18 years and older at 84 Chicago-area organizations. A

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Abbreviations: CHA, Chicago Heart Association Detection Project in Industry; CVD, cardiovascular disease; ECG, electrocardiogram.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

self-administered questionnaire was used to collect demographic data and diabetes, smoking, and hypertension history. Height, weight, blood pressure, and serum total cholesterol were obtained with standardized methods by trained staff. Electrocardiograms (ECGs), recorded while the participants were at rest, were classified as showing major, minor, or no abnormalities on the basis of the criteria of the Hypertension Detection and Follow-up Program (8).

Individuals not currently receiving treatment for diabetes were given a 50-g glucose load (customary at that time) to test for hyperglycemia without regard to fasting status or time of day. Venous blood for plasma glucose measurement was drawn ~1 h after loading and measured with the auto-analyzer adaptation of Hoffman's method (9). The study has received periodic institutional review board approval, and a waiver as described by the Health Insurance Portability and Accountability Act (HIPAA) was granted by the institutional review board before commencement of the study. Further, appropriate administrative and physical safeguards were established to protect the confidentiality of the data and to prevent unauthorized use or access.

Follow-up data

Medicare fee-for-service claims data were obtained from the Centers for Medicare and Medicaid Services for participants ages 65 years or older who were thus eligible for Medicare benefits from 1984 (the 1st year Medicare data were available for research use) through 2000. Medicare files for each participant were cross-referenced by social security number, sex, and birth date. For each medical service billed to Medicare, records include date of service, total charges, principal diagnosis, and up to nine other diagnoses coded according to the ICD-9-CM (10). Charges for health care services with primary ICD-9-CM discharge diagnosis codes 390–459 were selected for CVD-related charges, codes 250.x were selected for diabetes-related charges, and codes 140–209 were selected for cancer-related charges.

Medicare claims data for acute inpatient (including skilled nursing facility) and outpatient hospital-related care were available from 1984 to 2000; these data were used in the main analyses of the study. In addition, the analyses based on the annualized Medicare charges were repeated for the period from 1992 to 2000 with the inclusion of physician visits, durable medical equipment claims, home health agency, and hospice claims. Outpatient charges encompass emergency room visits, clinic and ambulatory surgery, laboratory tests, radiography, rehabilitation therapy, radiation therapy, and renal dialysis. Physician-visit claims include charges for physician fees, visits to doctors' offices, and other non–hospital-related ambulatory care services.

All health care charges were totaled and then annualized by dividing the total by the number of years of Medicare coverage for all participants 65 years or older. For the subgroup of individuals with data from age 65 years to death or to the attainment of age 80 years, cumulative charges were summed across all years.

To account for inflation, all charges were adjusted to year 2000 dollars with use of the hospital and related services component of the consumer price index (11).

Glycemic status

Glycemic status at baseline was classified into three categories: <120, 120–199, and ≥200 mg/dl. These categories were used to maintain consistency with previous reports from the CHA study (5,12). In addition, because some people with 1-h postload glucose levels ≥200 mg/dl may have undiagnosed diabetes or impaired glucose tolerance, glycemic status was also classified into two categories: <200 and ≥200 mg/dl.

Eligibility

Of the 39,522 CHA participants, 20,950 men and women (baseline ages 33–64 years) were eligible for Medicare benefits between 1984 and 2000 (i.e., were not deceased before 1984 and were ≥65 years of age during 1984–2000). To increase the likelihood that participants would have incurred Medicare charges, participants with <2 years of eligibility for Medicare coverage (n = 2,096) were excluded. Of the remaining participants, 2,314 were excluded due to the following baseline criteria: diagnosed diabetes (n = 409), CHD (n = 225), major ECG abnormality (n = 1,635), and missing data on covariates (n = 45). We also excluded people whose blood was drawn before 30 min or after 65 min after the 50-g glucose load and those with missing or implausible times (n = 1,237) (12). Thus, this report is based on 15,303 participants (8,580 men and 6,723 women).

For the subcohort with available data for cumulative charges from age 65 to death or to the attainment of age 80 years (n = 2,540), we excluded the top 0.5% of individuals with the highest total charges to reduce overall skewness of charges. In sum, 1,479 men and 1,048 women, representing 99.5% of the study population, were included in the analyses on cumulative charges.

Statistical analyses

Analyses were undertaken for men and women separately. Baseline characteristics were compared across the three glucose strata. χ^2 (for categorical variables) or F (for continuous variables) tests were used to assess statistical significance of differences across strata.

Medicare charges (CVD, diabetes, cancer related, and total) were compared across glycemic strata using two general linear models. We performed comparisons for the three glucose categories (<120, 120–199 and ≥200 mg/dl) as well as for the two categories (<200 and ≥200 mg/dl). Model I included adjustment for baseline age, race (black versus nonblack), and years of education. Model II included adjustment for all variables in model I plus multiple baseline CVD risk factors (smoking, BMI, serum total cholesterol, systolic blood pressure, and minor ECG abnormalities) to examine the potential impact of adjustment for these variables on associations of glucose level with Medicare charges.

Given the skewed nature of charge data, a modified Cox regression technique was used to test for statistical significance of associations between baseline glucose levels and Medicare charges. In essence, this approach involves the inversion of the data (i.e., people with no charges were considered to have the longest survival time). Each person's average annual/cumulative charge was subtracted from the maximal average annual/cumulative charge. This inverted value of charges was treated as "survival time." Data on individuals with no charges were censored at the maximal charge. The method was used previously to analyze the cost data (3).

Linear trends across the three glucose strata were tested using the significance level for coefficients for glucose as a con-

Table 1—*Baseline characteristics and Medicare information of the study participants by baseline postload glucose (1967–1973)*

Variable	Postload glucose (mg/dl)*			*P* value†
	<120	120–199	≥200	
Men				
n	2,755	4,967	858	
Glucose level	101.1 ± 13.0	151.6 ± 21.9	234.1 ± 46.6	—
BMI (kg/m^2)	26.5 ± 3.2	27.2 ± 3.4	27.9 ± 3.8	<0.001
Age (years)	45.2 ± 7.0	47.9 ± 7.5	50.0 ± 7.4	<0.001
White (%)	94.5	95.4	96.4	0.042
Education (years)	13.3 ± 2.9	13.0 ± 2.8	12.8 ± 2.8	<0.001
Minor ECG abnormalities (%)	6.8	7.5	7.9	0.401
Smoking (% smoker)	38.3	36.5	39.4	0.133
Cigarettes/day (smokers)	8.6 ± 13.1	8.3 ± 12.8	9.5 ± 14.0	0.029
Systolic blood pressure (mmHg)	134.8 ± 16.4	140.2 ± 18.3	147.4 ± 21.0	<0.001
Diastolic blood pressure (mmHg)	80.3 ± 10.2	83.5 ± 11.1	86.6 ± 11.8	<0.001
Cholesterol (mg/dl)	206.2 ± 36.1	211.3 ± 35.1	214.4 ± 36.2	<0.001
Medicare eligibility‡	8.9 ± 4.8	9.8 ± 4.8	9.8 ± 4.9	<0.001
Vital status (death, %)	23.8	33.1	48.8	<0.001
Women				
n	2,502	3,659	562	
Glucose level	100.1 ± 13.8	149.7 ± 21.5	231.7 ± 47.1	—
BMI (kg/m^2)	24.5 ± 4.0	25.3 ± 4.4	25.4 ± 4.5	<0.001
Age (years)	47.5 ± 6.9	49.9 ± 7.1	51.3 ± 6.5	<0.001
White (%)	91.3	94.9	95.9	<0.001
Education (years)	12.0 ± 2.1	11.9 ± 2.2	11.9 ± 2.2	0.030
Minor ECG abnormalities (%)	4.6	5.2	5.7	0.426
Smoking (% smoker)	35.6	34.0	39.2	0.043
Cigarettes/day (smokers)	6.1 ± 10.0	6.1 ± 9.9	7.2 ± 10.8	0.049
Systolic blood pressure (mmHg)	130.4 ± 17.6	136.5 ± 19.5	141.2 ± 20.7	<0.001
Diastolic blood pressure (mmHg)	77.5 ± 10.6	80.0 ± 11.4	83.4 ± 11.8	<0.001
Cholesterol (mg/dl)	212.4 ± 41.2	218.7 ± 39.4	227.1 ± 41.4	<0.001
Medicare eligibility‡	10.7 ± 4.8	11.5 ± 4.8	11.6 ± 4.7	<0.001
Vital status (death, %)	21.0	29.1	40.9	<0.001

Data are means ± SD unless otherwise indicated. *Divide by 18 to convert mg/dl to mmol/l. †*P* values for overall group comparison based on *F* or χ^2 tests. ‡Number of years eligible for Medicare coverage during 1984 through 2000.

tinuous variable in age-, race-, and education-adjusted and multivariate-adjusted Cox regressions.

All analyses were conducted using SAS statistical software (v. 8.02; SAS Institute, Cary, NC).

RESULTS — The follow-up period after the baseline survey averaged ~28 years. The study cohort had a mean baseline age of 47.3 years for men and 49.2 years for women. The majority of the study population was white (94.5%) with an average of 12.5 years of education (data not shown). In general, mean age, systolic and diastolic blood pressure, BMI, and total cholesterol were higher with higher glucose levels in both men and women, while mean education was lower (Table 1). In addition, the percentage of participants who died between 1984 and 2000 was also higher with higher baseline glucose levels in both men and women.

Table 2 shows adjusted average annual Medicare charges for inpatient and outpatient care (1984–2000) across glycemic strata by sex. For men, except for charges for cancer, there was a significant positive association between glucose level and age-, race-, and education-adjusted Medicare charges (model I). For instance, the average annual total Medicare charges were $6,952, $7,349, and $9,124 for men with plasma glucose levels <120, 120–199, and ≥200 mg/dl, respectively.

With additional adjustment for multiple baseline CVD risk factors (model II), glucose was no longer significantly associated with CVD-related or total charges (*P* values for trend 0.315 and 0.258, respectively). This suggests that for men the associations of glucose level with CVD and total charges are due in part to associations of glucose with other CVD risk factors. As expected, the association of glucose with diabetes-related charges remained significant with adjustment for other CVD risk factors (*P* value for trend <0.001). In contrast, glucose was not associated with cancer-related charges. Similar findings were also obtained for comparisons between plasma glucose levels <200 and ≥200 mg/dl.

Women generally had lower CVD-related, cancer-related, and total charges but higher diabetes charges than men. For example, among individuals with glucose ≥200 mg/dl, average annual CVD-related and diabetes-related charges with adjust-

Table 2—*Adjusted* average annual Medicare charges† for inpatient and outpatient care from 1984 through 2000 by baseline postload glucose (1967–1973) and sex*

	Men					Women				
Postload glucose‡	*n*	CVD	Diabetes	Cancer	Total	*n*	CVD	Diabetes	Cancer	Total
Model 1										
<120 mg/dl	2,755	2,259	15	990	6,952	2,502	1,261	13	685	5,276
120–199 mg/dl	4,967	2,421§	56¶	1,034	7,349	3,659	1,584‖	74¶	684	6,253
≥200 mg/dl	858	3,259‖	138¶	1,449	9,124‖	562	2,409‖	453¶	967	8,913§
P trend#		0.001	<0.001	0.552	0.018		<0.001	<0.001	0.473	0.002
<200 mg/dl	7,722	2,364§	42	1,018	7,208	6,161	1,453	49	685	5,859
≥200 mg/dl	858	3,255	137	1,448	9,113	562	2,401	452	967	8,889
P value##		0.049	<0.001	0.939	0.008		0.042	<0.001	0.790	0.053
Model 2										
<120 mg/dl		2,412	20	1,009	7,211		1,354	33	699	5,516
120–199 mg/dl		2,388	55¶	1,034	7,307		1,548	62¶	679	6,151
≥200 mg/dl		2,960	130¶	1,385	8,536§		2,228	443¶	941	8,508§
P trend#		0.315	<0.001	0.531	0.258		0.030	<0.001	0.468	0.002
<200 mg/dl		2,396	43	1,025	7,273		1,470	50	687	5,896
≥200 mg/dl		2,961	129	1,383	8,531		2,220	442	941	8,481
P value##		0.549	<0.001	0.874	0.055		0.205	<0.001	0.856	0.051

*Model I included baseline age, race (indicator for black), and education (years); model II included all variables in model I in addition to smoking (cigarettes/day), serum cholesterol (mg/dl), systolic blood pressure (mmHg), minor electrocardiographic abnormalities, and BMI (kg/m^2). †Charges were adjusted to year 2000 U.S. dollars. ‡Divide by 18 to convert mg/dl to mmol/l. #*P* values for trend in charges by glucose level as a continuous variable based on modified Cox models; §$P < 0.05$, ‖$P < 0.01$, ¶$P < 0.001$ for comparisons with the first group (<120 mg/dl) based on modified Cox models. ##*P* value for comparisons between groups <200 mg/dl and ≥200 mg/dl based on modified Cox models.

ment for CVD risk factors were $2,228 and $443, respectively, for women and $2,960 and $130, respectively, for men (model II).

Patterns of associations of glucose and Medicare charges for women were similar to those for men. However, associations of glucose with CVD-related and total charges remained significant with adjustment for other CVD risk factors (model II) in women only (*P* values for trend 0.030 and 0.002, respectively).

With exclusion of individuals with diabetes diagnoses in 1984–2000 (data not shown), Medicare charges were still the highest for participants with the highest glucose levels, particularly among women, but differences in charges between individuals with the highest (≥200 mg/dl) and those with the lowest (<120 mg/dl) glucose levels were smaller than those with inclusion of individuals with diabetes (e.g., $768 vs. $2,992, respectively, for multivariate-adjusted average annual total charges in women; corresponding total charges with the inclusion of individuals with diabetes for the two groups are $5,516 vs. $8,508 [Table 2]).

Subgroups with Medicare data from age 65 years to death or to attainment of age 80 years

Patterns of associations between glycemic status and cumulative Medicare charges for both men and women were similar to those observed for annual charges, except for cumulative total charges in men (Table 3). Women in general had lower cumulative charges than men. With multiple

Table 3—*Adjusted* cumulative Medicare charges† for inpatient and outpatient care from age 65 years to death or to age 80 years (1984–2000) by baseline postload glucose (1967–1973) and sex*

	Men					Women				
Postload glucose‡	*n*	CVD	Diabetes	Cancer	Total	*n*	CVD	Diabetes	Cancer	Total
<120 (mg/dl)	452	25,741	152	12,572	79,181	403	14,260	309	10,587	62,808
120–199 (mg/dl)	865	26,467	621¶	13,928	85,560	533	18,909§	700¶	9,686	73,823
≥200 (mg/dl)	162	30,174	1,699¶	18,186	91,602	112	21,183‖	1,079¶	10,808	87,246§
P trend#		0.565	<0.001	0.638	0.949		0.035	<0.001	0.419	0.039
<200 (mg/dl)	1,317	26,220	461	13,466	83,391	936	16,917	531	10,072	69,104
≥200 (mg/dl)	162	30,156	1,686	18,152	91,442	112	21,102	1,075	10,824	87,054
P value##		0.816	<0.001	0.193	0.308		0.041	0.002	0.173	0.054

*Adjusted for baseline age, race (indicator for black), education (years), smoking (cigarettes/day), serum cholesterol (mg/dl), systolic blood pressure (mmHg), minor electrocardiographic abnormalities, and BMI (kg/m^2). †Charges were adjusted to year 2000 U.S. dollars. ‡Divide by 18 to convert mg/dl to mmol/l; #*P* values for trend in charges by glucose level as a continuous variable based on modified Cox models. §$P < 0.05$, ‖$P < 0.01$, ¶$P < 001$ for comparisons with the first group (<120 mg/dl) based on modified Cox models. ##*P* value for comparisons between groups <200 mg/dl and ≥200 mg/dl based on modified Cox models.

baseline risk-factor adjustment, there was a strong positive association between glucose and cumulative diabetes charges in both men and women (both *P* values for trend <0.001). Glucose was also significantly related to cumulative CVD-related and total charges with adjustment for CVD risk factors in women (*P* values for trend 0.035 and 0.039, respectively) but not in men. Similar findings were also observed for comparisons between plasma glucose levels of <200 and ≥200 mg/dl. Glucose was not significantly related to cumulative cancer charges in men or women.

CONCLUSIONS — Our main finding is that postload plasma glucose in middle age is positively associated with age-, race-, and education-adjusted CVD-related, diabetes-related, and total Medicare charges in older age for both women and men. In general, charges were the highest for individuals with the highest glucose levels (≥200 mg/dl) and the lowest for individuals with the lowest glucose values (<120 mg/dl). With adjustment for CVD risk factors, the association between glucose level and diabetes charges remained significant for both men and women. Associations of glucose with CVD and total charges remained significant with adjustment for multiple CVD risk factors in women but not in men. There was no association between glucose and cancer charges in either men or women.

To date, there has been little research on the association of long-term economic consequences (e.g., effects on Medicare expenditures) with blood glucose levels. While a few studies have focused on the combined effects of multiple risk factors, including blood glucose concentration, on health care costs (13–15), to our knowledge, only two studies (13,14) have shown that high blood glucose levels are associated with higher health care costs. For example, Goetzel et al. (14) found that employees who reported having a high glucose level had 35% higher health care expenditures than those who did not. However, these studies examined glucose level only as a dichotomous variable and had short-term follow-up (up to 3 years). To our knowledge, the impact of midlife glucose levels on health care costs incurred in older age among nondiabetic individuals has not previously been examined.

It should be noted that >40% of individuals reported to have diabetes are older than 65 years (16) and that direct medical expenditures attributable to diabetes among the elderly were almost two-thirds of all direct medical expenditures attributable to diabetes (2). With the proportion of Americans ages 65 years and older increasing rapidly (from ~12% of the population currently to 20% by 2050 [17]), costs due to diabetes and related disease among the elderly have important implications for expenditures by Medicare. The predictive role of an early screening test for diabetes on subsequent Medicare charges therefore has important implications for Medicare expenditures.

Findings from our study are consistent with hypothesized mechanisms. People with high blood glucose levels are at higher risk of developing diabetes, CVD, and other diabetes complications and have higher mortality rates than those with normal glucose tolerance. We found Medicare charges to be highest for individuals with blood glucose levels ≥200 mg/dl. These levels were also associated with higher diabetes charges after adjustment for CVD risk factors. Our findings of multiple-adjusted relations of glucose levels and CVD-related and total charges in women (but not in men) are consistent with results from a previous study on associations of glucose levels and coronary heart disease mortality in the same cohort (5) and with other studies (18,19) showing that the relative impact of diabetes on CVD morbidity and mortality risk was more marked in women than in men.

These results suggest that even a casual assessment of blood glucose at younger ages can identify individuals at risk for diabetes and/or CVD later in life who are therefore likely to ultimately suffer from the ravages of diabetes and CVD as well as to incur increased health care costs at older ages. This further suggests that early screening may provide an opportunity for primary prevention before the development and diagnosis of frank disease, with the potential for reducing personal suffering, debility, and Medicare health care costs.

This study has several strengths, including the availability of blood glucose and other potential risk factors (including BMI) from a large sample of men and women with long-term follow-up (mean follow-up time 28 years). However, a single measurement of blood glucose instead of multiple measurements and the lack of information on fasting status and time of day when the blood was drawn are likely to bias results toward the null. Moreover, the use of 1-h glucose levels after a 50-g glucose dose (instead of the current recommended 2-h glucose levels with a 75-g glucose load [20]) may lead to lower glucose levels; therefore, many participants with levels ≥200 mg/dl may have had undiagnosed diabetes.

Other limitations of the study include the use of charges instead of costs. Charges may be higher than costs, but they are highly correlated (21). Nevertheless, using estimated costs (obtained by applying annual cost-to-charge ratios for hospital patient care services [22] to each year's Medicare charges), similar patterns of associations and levels of significance were observed.

In addition, there is no information on costs for long-term nursing home care and prescription drugs, which are not covered by Medicare. As a result, we are unable to estimate the health care costs for the use of those services. Furthermore, the use of only fee-for-service Medicare data may also lead to underestimation of actual total health care costs, since health care costs incurred outside the Medicare system, mainly HMO and Veterans Administration (VA) costs, are not included. However, exclusion of beneficiaries enrolled in managed care organizations during 1992–2000 did not have any significant impact on the associations of glucose with Medicare charges in both men and women. Moreover, only a very small proportion (<2%) of our cohort had VA health care utilization and billing records. Data on out-of-pocket payments are also not available, although these constitute only a small proportion of total expenditures. It is highly likely that income influences these and other health care expenditures not covered by Medicare. Nevertheless, all analyses were adjusted for education, which has been shown to be strongly correlated with income. In addition, Medicare is the largest single source of health care spending in the U.S., covering almost all of the elderly population (23). Therefore, it is a valuable source for studies of costs incurred by the elderly.

In conclusion, our findings demonstrate an important association between glucose level in middle age and future Medicare charges. Among individuals

with low levels of plasma glucose in middle age, the costs of health care in older age are markedly lower. Low plasma glucose levels in middle age may not only reduce the risk of diabetes, CVD, other diabetes-related chronic complications, and mortality, but could also potentially decrease subsequent Medicare expenditures. With the current trend of increasing diabetes prevalence, preventive measures are important not only to reduce the burden of disease and disability associated with diabetes, but also to decrease future health care costs in the aging population. Public health efforts need to include comprehensive national strategies and resources for primary prevention of diabetes including screening for high blood glucose levels from early life on, with the goal to end the diabetes epidemic and reduce health care costs among older individuals.

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