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Residential Proximity to Major Roadways and Renal Function

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Abstract

Background—Living near major roadways has been associated with increased risk of cardiovascular events, but little is known about its impact on renal function.

Methods—We calculated estimated glomerular filtration rate (eGFR) for 1103 consecutive Boston-area patients hospitalized with acute ischemic stroke between 1999 and 2004. We used linear regression to evaluate the association between eGFR and categories of residential distance to major roadway (0 to ≤ 50, 50 to ≤ 100, 100 to ≤ 200, 200 to ≤ 400, 400 to ≤ 1000, and >1000 m) adjusting for age, sex, race, smoking, comorbid conditions, treatment with angiotensin-converting enzyme inhibitor, and neighborhood-level socioeconomic characteristics. In a second analysis, we considered the log of distance to major roadway as a continuous variable.

Results—Patients living closer to a major roadway had lower eGFR than patients living farther away (P_{trend}=0.01). Comparing patients living 50 m versus 1000 m from a major roadway was associated with a 3.9 mL/min/1.73 m2 lower eGFR (95% CI: 1.0, 6.7; p=0.007); a difference comparable in magnitude to the reduction in eGFR observed for a 4 year increase in age in population-based studies. The magnitude of this association did not differ significantly across categories of age, sex, race, history of hypertension, diabetes, or socioeconomic status.

Conclusions—Living near a major roadway is associated with lower eGFR in a cohort of patients presenting with acute ischemic stroke. If causal, these results imply that exposures associated with living near a major roadway contribute to reduced renal function, an important risk factor for cardiovascular events.

Keywords

Traffic pollution; renal function; air pollution; cardiovascular; epidemiology

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INTRODUCTION

Ambient air pollution is a recognized risk factor for cardiovascular disease.[1] There is evidence that living near a major roadway contributes to the incidence of vascular disease[1, 2] including increased cardiovascular mortality, [3–5] acute myocardial infarction, [6] adverse prognosis among early survivors of acute myocardial infarction, [7] atherosclerosis as indicated by increased coronary artery calcium[8] and peripheral arterial disease, [9] and deep vein thrombosis.[10]

The kidney is a highly vascularized organ susceptible to both large vessel artherosclerotic disease and small vessel dysfunction. Given the detrimental effects of residential proximity to major roadway in other vascular beds, living near a major roadway may also be associated with impaired renal function. Impaired renal function, as assessed by estimated glomerular filtration rate (eGFR), is associated with increased risk of acute cardiovascular events and death, [11, 12] and may potentially underlie, at least partly, the observed association between traffic pollution and cardiovascular risk. We hypothesized that living near a major roadway would be associated with impaired renal function as assessed by eGFR. We examined this hypothesis in a convenience sample of 1103 consecutive patients presenting with acute ischemic stroke in the Boston metropolitan region.

METHODS

Study population

This study was approved by the Committee on Clinical Investigations (Institutional Review Board) at the Beth Israel Deaconess Medical Center (BIDMC) in Boston, Massachusetts. The study population consisted of consecutive patients ≥ 21 years of age, residing in the Boston metropolitan region and admitted to the BIDMC between April 1, 1999, and December 31, 2004, with a confirmed acute ischemic stroke, as previously described.[13]

GFR estimation

Serum creatinine at the time of hospital presentation (and therefore, prior to any diagnostic imaging related to the index admission) was measured by the clinical chemistry laboratory photometrically using the Jaffe reaction, with a coefficient of variation of 6.4% at the level of 0.7 mg/dl and 2.2% at the level of 5.6 mg/dl. We calculated eGFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation as follows:[14]

$$eGFR = 141 \times \min(Scr/\kappa,\ 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018\ [\text{if female}] \times 1.159\ [\text{if black}],$$

where *eGFR* represents the estimated GFR in mL/min/1.73 m^2, *Scr* represents measured serum creatinine, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, *min* denotes the minimum of Scr/κ or 1, and *max* denotes the maximum of Scr/κ or 1. This equation was developed in a population consisting of patients with and without chronic kidney disease (CKD), using pooled data on 8254 patients from 10 research studies, and validated on an additional 3896 patients from 16 studies.[14] The CKD-EPI equation has been found to provide more accurate cardiovascular risk prediction than the Modification of Diet in Renal Disease (MDRD) Study equation.[15]

Exposure assessment

We used ArcGIS (version 9.2; ESRI Inc., Redlands, CA) to geocode patients' addresses. We calculated distance from residence to the nearest major roadway with major roadways defined as those roads having US Census Feature Class Code A1 (primary highway with limited access) or A2 (primary road without limited access), as in previous studies.[16]

Covariate assessment

For each patient, trained abstractors recorded data on patient demographics and medical history from patient charts or electronic medical records using standardized forms, as previously described.[13] Race was categorized as white, black, or other. We used area-based measures of income and educational attainment available from the 2000 US Census as measures of neighborhood-level socioeconomic status. Both the median household income in 1999 and the percentage of people ≥ 25 years of age whose highest completed educational degree was below high school were determined at the census block group level, and we assigned these values to each patient according to their location of residence.

Statistical analysis

We used linear regression to evaluate the cross-sectional association between residential distance to major roadway and eGFR. As in previous studies, [8] we first considered categories of distance to major roadway (0 to ≤ 50, 50 to ≤ 100, 100 to ≤ 200, 200 to ≤ 400, 400 to ≤ 1000, and >1000 m) and estimated the adjusted mean eGFR for each category. These categories, with narrower bounds for more proximal distances, were chosen to reflect the approximately exponential decay function relating traffic pollution and noise as distance from roadway increases.[17–19] Tests for linear trends were performed by assigning each exposure category the natural log of the median distance within each category and including the term as a continuous variable in the regression model. The P value obtained represents the linear component of trend. To verify that our results were not sensitive to the choice of categories, we repeated this analysis considering fewer categories of distance to major roadway (≤100, 100– ≤300, >300). Additionally, we modeled the association between eGFR and the natural logarithm of residential distance to major roadway as a continuous variable. We present the results from this model by contrasting patients living 50 m to the nearest major roadway to those living 1000 m from the nearest major roadway, calculated as: $\ln(1000) * \beta - \ln(50) * \beta$, where β denotes the beta coefficient from the linear regression model treating log of distance to roadway as a linear continuous variable. This contrast reflects the mean adjusted difference in eGFR between subjects likely to have high levels of exposure to traffic-related pollution versus those exposed to levels indistinguishable from background.

To further characterize the functional form of the relationship between residential distance to nearest major roadway and eGFR we also modeled the natural logarithm of distance to nearest major roadway as a continuous variable using penalized splines (Greenland 1995). *A priori*, we selected 2 degrees of freedom based on biological plausibility; in these data this was also consistent with the number of degrees of freedom that minimized the Akaike Information Critierion (AIC) for the fitted model.

In all models, we controlled for potential confounding by age (continuous), sex, race (white, black, other), smoking status (current, former, never), history of diabetes, hypertension, heart failure, or coronary artery disease, current treatment with angiotensin converting enzyme inhibitor (ACEI), and census block level estimates of median household income (continuous) and percentage of residents ≥ 25 years of age without a high school diploma (continuous). We chose to adjust for current treatment with ACEI since in some patients ACEI use is associated with lower levels of GFR. These confounders were selected *a priori*. As a sensitivity analysis, we repeated these analyses excluding 30 (2.7%) patients with eGFR < 15 mL/min/1.73 m^2, the clinical cutoff for stage 5 CKD. Adjusted mean levels of eGFR were computed using the LSMEANS option in PROC GLM in SAS.

We examined whether the association between distance to major roadway and eGFR varied across subgroups defined by age (<70 vs. ≥ 70 years), sex, race (white vs. other), history of diabetes, history of hypertension, and neighborhood median household income (≤ $50000 vs. >$50000) by adding interaction terms into separate regression models. Statistical significance of interaction was assessed using the Wald test for the interaction terms.

A p-value of <0.05 (2-sided) was considered statistically significant. Statistical analyses were performed using SAS (version 9.2; SAS Institute Inc., Cary, NC) and R 2.13.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Between 1999 and 2004, 1120 patients were hospitalized at the Beth Israel Deaconess Medical Center with a confirmed acute ischemic stroke. Data on residential address and serum creatinine at the time of hospital presentation were available in 98.5% (n=1103) of these patients. Patients were elderly and predominantly female and white (Table 1). Patients living closer to major roadways tended to be older, were more likely to be male, and were less likely to be white compared to patients living further from major roadways. Consistent with the urban location of this study, just over half of the patients lived within 1 km of a major roadway with the remainder living between 1 and 10 km from a major roadway (Fig. 1). Mean eGFR levels were 66.4 (SD: 24.8, 25^{th} percentile: 48.9, 75^{th} percentile: 83.8) ml/min/1.73 m^2 with the lowest levels observed among participants living closest to major roadways (Table 1).

In models adjusting for patient demographics, past medical history, and neighborhood-level measures of socioeconomic position, mean eGFR was lower among patients living closer to a major roadway as compared to patients living further away (Fig. 2; P_{trend}=0.01). Results were similar in a sensitivity analysis where we modeled residential distance to nearest major roadway in 3 categories (P_{trend}=0.03; Supplemental Figure 1) and when we modeled the natural logarithm of distance to roadway as a continuous variable (Table 2). In fully adjusted models, eGFR levels among patients living 50 m from the nearest major roadway were an average of 3.9 mL/min/1.73 m^2 (95% CI: 1.0, 6.7) lower than the eGFR levels of patients living 1000 m from the nearest major roadway. The results were not materially different in sensitivity analyses excluding patients with stage 5 chronic kidney disease (eGFR < 15 mL/min/1.73 m^2; Supplemental Figure 2 and Supplemental Table 1).

To further characterize the functional form of the relationship between residential distance to nearest major roadway and eGFR we additionally modeled residential distance to nearest major roadway as a continuous variable using penalized splines (Fig. 3). This analysis confirmed that the functional form of this relationship was approximately log-linear.

Our definition of major roadways includes those roads having US Census Feature Class Code A1 (primary highway with limited access) or A2 (primary road without limited access). Since A1 and A2 roads may represent different exposures, we estimated the association between eGFR and the natural logarithm of residential distance to nearest A1 or A2 roadway, separately and jointly. eGFR was most strongly associated with residential distance to nearest A2 roadway, even after adjustment for residential distance to nearest A1 roadway (Supplemental Table 2).

The association between distance to major roadway and eGFR did not vary by age, sex, race, diabetes, hypertension, or median income in the neighborhood (all p-values ≥ 0.20 in testing for interaction) (Supplemental Table 3).

DISCUSSION

In this cohort of patients hospitalized with acute ischemic stroke, we observed a statistically significant association between residential proximity to major roadway and lower renal function adjusting for patient demographics, past medical history, and neighborhood-level indicators of socioeconomic position. Specifically, renal function decreased approximately exponentially with increasing residential proximity to the nearest major roadway. In a model including the natural log of residential distance to major roadways as a continuous variable, mean eGFR levels among patients living 50 m from a major roadway were 3.9 mL/min/1.73 m^2 (95% CI: 1.0, 6.7) lower than mean levels in patients living 1000 m from a major roadway. To put this result into context, this difference in eGFR is comparable in magnitude to the reduction in eGFR observed for a 4 year increase in age in this cohort or among NHANES III participants.[20] The magnitude of this association did not differ significantly across categories of age, sex, race, history of hypertension, diabetes, or socioeconomic status.

There is growing evidence that living near major roadways contributes to the incidence of vascular disease, [3–6, 8–10] and adverse prognosis among patients with prevalent cardiovascular disease.[7] Living close to a major roadway is associated with higher levels of exposure to air pollution from traffic [17, 18] and an increased risk of stroke and other major adverse cardiovascular events including myocardial infarction.[5, 6] Long-term exposure to traffic pollution leads to vascular endothelial injury, systemic inflammation, atherosclerosis and microvascular changes.[1, 2, 21] Evidence from apo-E knockout mice and hyperlipidemic rabbits indicates that long-term exposure to urban air pollution causes increased atherosclerosis with inflammatory characteristics.[22, 23] Moreover, in community dwelling adults, traffic-related pollution is positively associated with carotid intima-media thickness (CIMT).[24–27] In the Multi Ethnic Study of Atherosclerosis (MESA), living closer to a major roadway was associated with smaller diameter retinal arteriolar vessels suggesting an impact on the microvasculature.[28] On the other hand, long-term exposure to ambient air pollution was not associated with urinary albumin/creatinine ratio in MESA, although there was an elevated but not statistically significant increase in the risk of microalbuminuria.[29]

Using published estimates of the association between eGFR and mortality in the general population, [30] we estimate that in this cohort of patients, a reduction in residential distance to major roadway from 1000 m to 50 m may be associated with a 3.6% higher rate of cardiovascular mortality and a 1.2% higher rate of all-cause mortality (i.e.: relative risks of 1.036 and 1.012, respectively). By comparison, an ecological study in England and Wales found that stroke mortality rates were 7% higher in census regions <200 m versus >1000 m away from a major road, [5] and in a previous study of early survivors of acute myocardial infarction, we found a 27% and 19% increase in all-cause and cardiovascular mortality, respectively, comparing patients living ≤ 100 versus >1000 m from a major roadway.[7]

This study has some limitations. First, although we were able to account for several potential individual and neighborhood-level confounders, we cannot exclude the possibility of residual confounding by socioeconomic status or unhealthy behaviors. Second, we do not have data on how much time patients spent away from home, nor do we have data on residential history or on the duration of residence at the address documented at the time of hospital admission. These sources of exposure misclassification may have biased our results towards the null hypothesis of no association. However, the utility of exposure measures based on home address is supported by national surveys showing that Americans spend an average of 68% of their time at home.[31] Third, most major roadways in the Boston area carry a combination of truck (diesel) and car (predominantly gasoline) traffic. Diesel and gasoline engine emissions may have different effects on cardiovascular endpoints, including renal function, but we are not able to assess this possibility. Interestingly, eGFR was most strongly associated with residential proximity to A2 roadways (primary road without limited access), which in the Boston area tend to favor local traffic with fewer trucks and moving at lower speeds. Fourth, living closer to a major roadway is associated with higher exposure to noise pollution, [19, 32] which may also be associated with higher cardiovascular risk.[33, 34] We do not have data on noise pollution in the study area and therefore cannot evaluate whether the observed associations are due to air pollution, noise, or other stressors related to living close to a major roadway. Fifth, all subjects resided in the same metropolitan area, potentially limiting the generalizability of these findings to other geographic areas or patient populations. In particular, our results are not necessarily generalizable to cities with a very different vehicle fleet, fuels, or topography. Lastly, we evaluated our hypothesis in a convenient sample of patients presenting to hospital with acute ischemic stroke. If residential proximity to a major roadway and impaired renal function are both causally associated with stroke incidence, eGFR and roadway proximity may appear conditionally associated among stroke patients even if eGFR and roadway proximity are marginally independent in the whole population (ie: a form of Berkson’s bias). However, under assumptions of no effect modification, this source of bias would be expected to lead us to underestimate the association between eGFR and residential distance to roadway.[35]

Despite these limitations, our study has several strengths including a novel hypothesis, the use of the CKD-EPI equation to more accurately estimate GFR over a wide range of values, a large sample size, and high-quality clinical data allowing for adjustment for potential confounding by clinical characteristics.

In summary, the current study suggests that living near a major roadway is associated with lower eGFR in a cohort of patients presenting with acute ischemic stroke. If causal, these results imply that exposures associated with living near a major roadway contribute to reduced renal function, an important risk factor for cardiovascular events. This novel hypothesis needs to be confirmed or refuted within the context of a prospective cohort study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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THUMBNAIL SKETCH

What is already known about the subject

Living near major roadways has been associated with vascular injury and increased risk of cardiovascular events. The kidney is a highly vascularized organ susceptible to both large vessel artherosclerotic disease and small vessel dysfunction. Living near a major roadway may also be associated with impaired renal function, but this hypothesis has not been previously evaluated.

What this study adds

We evaluated this hypothesis in a cohort of patients hospitalized with acute ischemic stroke and found that living near a major roadway was associated with lower renal function as assessed by estimated glomerular filtration rate. The magnitude of this association was similar in magnitude to the reduction in renal function observed for a 4 year increase in age in population-based studies. If causal, these results imply that exposures associated with living near a major roadway contribute to reduced renal function, an important risk factor for cardiovascular events.

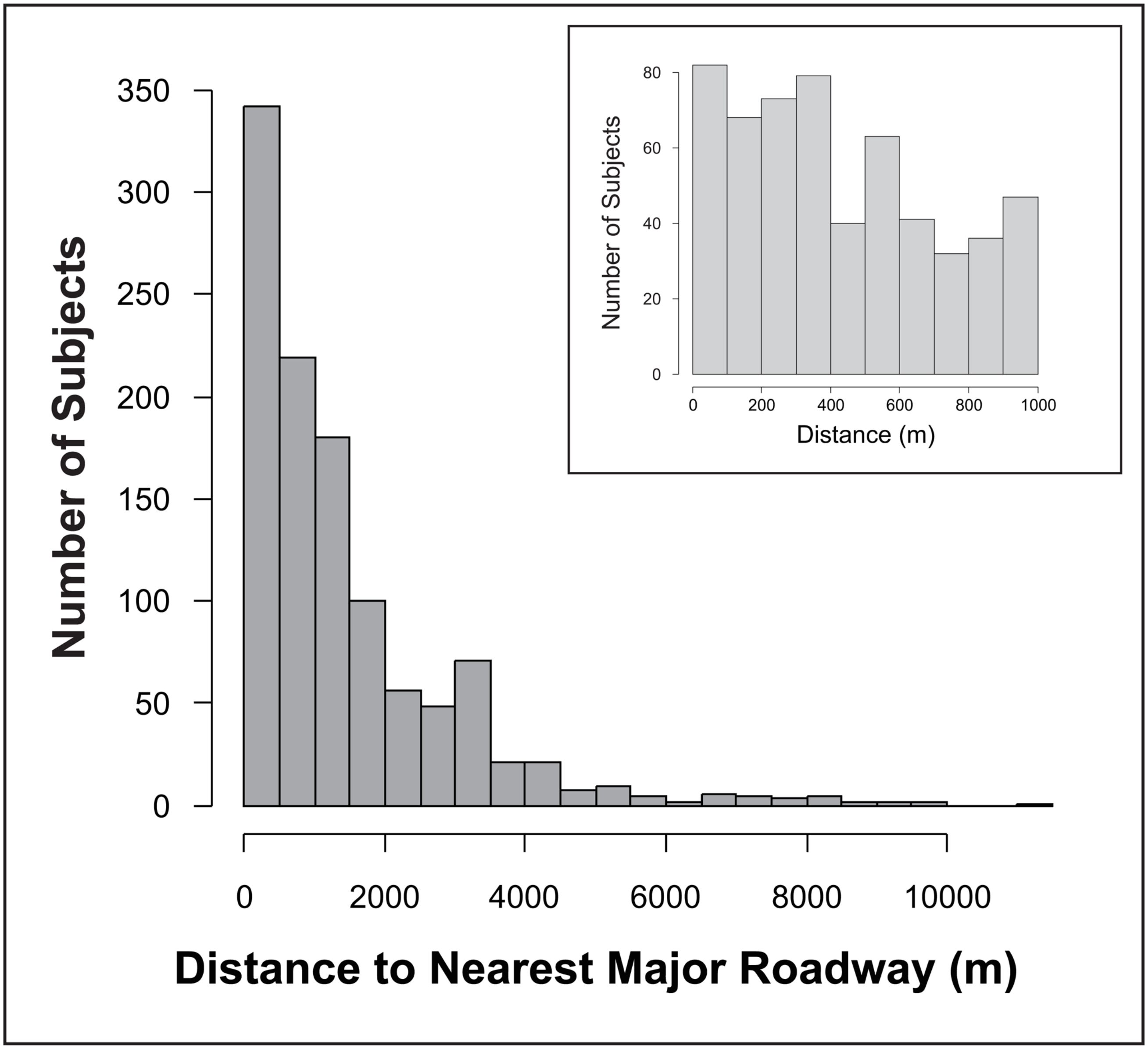

Figure 1.

Distribution of residential distance to major roadway among 1103 Boston-area patients admitted to a large tertiary-care medical center with confirmed acute ischemic stroke between April 1, 1999, and December 31, 2004. The inset shows the distribution among patients living ≤ 1 km from the nearest major roadway.

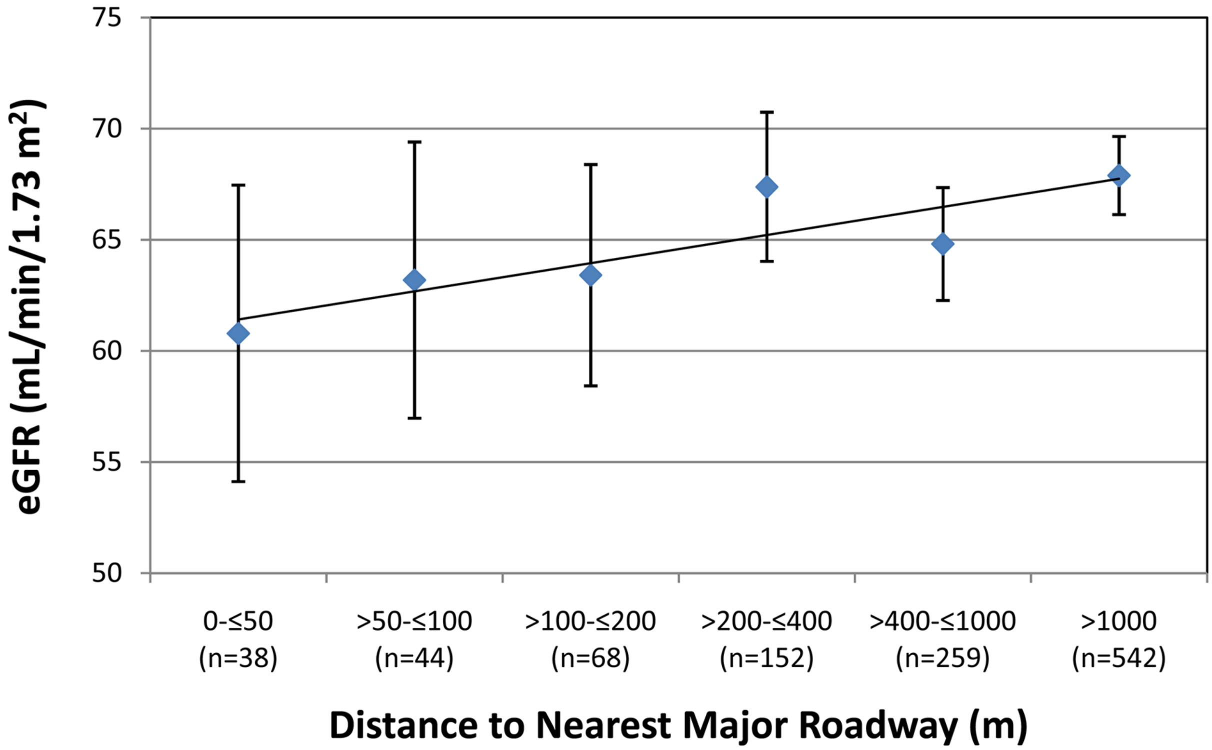

Figure 2.

Adjusted mean eGFR (and 95% confidence intervals) by distance to major roadway. Adjusted for age, sex, race, smoking status, diabetes, hypertension, heart failure, coronary artery disease, treatment with angiotensin-converting enzyme inhibitor, median household income, and percentage of residents without high school diploma.

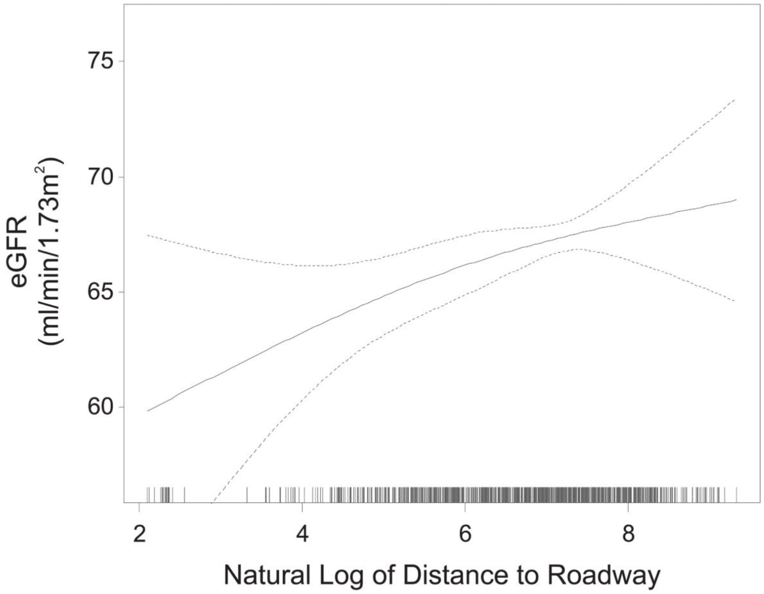

Figure 3.

Penalized spline fit showing eGFR as a function of residential distance to nearest major roadway among 1103 patients hospitalized with ischemic stroke. Data were fitted using a penalized spline with 3 degrees of freedom and adjusted for age, sex, race, smoking status, diabetes, hypertension, heart failure, coronary artery disease, treatment with angiotensin-converting enzyme inhibitor, median household income, and percentage of residents without high school diploma. The solid line represents adjusted mean eGFR and the dashed lines 95% confidence interval bands. The distribution of distance to roadway is displayed by the rug plot along the x-axis.

TABLE 1

Characteristics of 1103 patients residing in the greater Boston area admitted to the Beth Israel Deaconess Medical Center with confirmed acute ischemic stroke between April 1, 1999, and December 31, 2004

	Total	Distance of residence to nearest major roadway (m)					
		0 to ≤50	50 to ≤ 100	100 to ≤ 200	200 to ≤ 400	400 to ≤ 1000	>1000
	(n=1103)	(n=38)	(n=44)	(n=68)	(n=152)	(n=259)	(n=542)
Age, y, mean ±SD	72.9 ±14.3	74.8±12.4	78.6±12.2	70.7±13.8	73.3±14.8	73.3±14.3	72.3±14.5
Male, n (%)	500 (45.3)	20 (52.6)	20 (45.5)	32 (47.1)	76 (50.0)	111 (42.9)	241 (44.5)
Race, n (%)							
White	696 (63.1)	21 (55.3)	27 (61.4)	44 (64.7)	92 (60.5)	166 (64.1)	346 (63.8)
Black	107 (9.7)	2 (5.3)	3 (6.8)	13 (19.1)	22 (14.5)	24 (9.3)	43 (7.9)
Other	300 (27.2)	15 (39.5)	14 (31.8)	11 (16.2)	38 (25.0)	69 (26.6)	153 (28.2)
Current Smoker, n (%)	161 (14.6)	5 (13.2)	1 (2.3)	10 (14.7)	20 (13.2)	44 (17.0)	81 (14.9)
Medical History, n (%)							
Diabetes	325 (29.5)	7 (18.4)	16 (36.4)	25 (36.8)	42 (27.6)	65 (25.1)	170 (31.4)
Hypertension	768 (69.6)	25 (65.8)	26 (59.1)	51 (75.0)	117 (77.0)	178 (68.7)	371 (68.5)
Coronary artery disease	292 (26.5)	7 (18.4)	9 (20.5)	20 (29.4)	44 (29.0)	65 (25.1)	147 (27.1)
Heart failure	137 (12.4)	6 (15.8)	3 (6.8)	6 (8.8)	13 (8.6)	30 (11.6)	79 (14.6)
Medication use, n (%)							
ACEI	407 (36.9)	14 (36.8)	11 (25.0)	25 (36.8)	53 (34.9)	105 (40.5)	199 (36.7)
Aspirin	466 (42.3)	18 (47.4)	18 (40.9)	35 (51.5)	62 (40.8)	112 (43.2)	221 (40.8)
Statins	327 (29.7)	10 (26.3)	14 (31.8)	24 (35.3)	45 (29.6)	68 (26.3)	166 (30.6)
Census variables							
Median household income, $1000, median (IQR)	56.1 (33.3)	61.1 (42.5)	56.4 (37.3)	52.8 (42.1)	47.5 (37.2)	49.9 (32.1)	59.2 (27.8)
Percent of people ≥ 25 years of age without high school diploma, %, median (IQR)	10.5 (15.9)	6.4 (11.7)	5.8 (9.4)	10.3 (19.0)	14.8 (19.0)	10.6 (16.1)	10.5 (14.8)
eGFR, ml/min/1.73 m^2, mean ± SD	66.4 ± 24.8	60.7 ± 24.7	59.3 ± 24.1	64.2 ± 27.1	66.8 ± 24.8	64.9 ± 23.7	68.2 ± 24.9

eGFR: estimated glomerular filtration rate; SD: standard deviation; ACEI: angiotensin-converting enzyme inhibitor;

TABLE 2

Mean adjusted change in eGFR (95% CI) levels comparing patients living 50 m to patients living 1000 m from the nearest major roadway.*

Model	eGFR difference† (mL/min/1.73 m^2)	95% CI	p-value
Unadjusted	−5.7	−9.0, −2.3	<0.001
Adjusted for age and sex	−3.8	−6.7, −0.9	0.01
Fully adjusted‡	−3.9	−6.7, −1.0	0.007

*From a model where the natural logarithm of residential distance to major roadway was entered as a continuous variable.

†A negative value indicates that adjusted mean eGFR is lower among patients living 50 m than patients living 1000 m from a major roadway.

‡Adjusted for age, sex, race, smoking status, diabetes, hypertension, heart failure, coronary artery disease, treatment with angiotensin-converting enzyme inhibitor, median household income, and percentage of residents without high school diploma.