



Green space and mortality following ischemic stroke



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ABSTRACT

Background: Residential proximity to green space has been associated with physical and mental health benefits, but whether green space is associated with post-stroke survival has not been studied.

Methods: Patients ≥ 21 years of age admitted to the Beth Israel Deaconess Medical Center (BIDMC) between 1999 and 2008 with acute ischemic stroke were identified. Demographics, presenting symptoms, medical history and imaging results were abstracted from medical records at the time of hospitalization for stroke onset. Addresses were linked to average Normalized Difference Vegetation Index, distance to roadways with more than 10,000 cars/day, and US census block group. Deaths were identified through June 2012 using the Social Security Death Index.

Results: There were 929 deaths among 1645 patients with complete data (median follow up: 5 years). In multivariable Cox models adjusted for indicators of medical history, demographic and socioeconomic factors, the hazard ratio for patients living in locations in the highest quartile of green space compared to the lowest quartile was 0.78 (95% Confidence Interval: 0.63–0.97) (p -trend=0.009). This association remained statistically significant after adjustment for residential proximity to a high traffic road.

Conclusions: Residential proximity to green space is associated with higher survival rates after ischemic stroke in multivariable adjusted models. Further work is necessary to elucidate the underlying mechanisms for this association, and to better understand the exposure–response relationships and susceptibility factors that may contribute to higher mortality in low green space areas.

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1. Introduction

Over half of the world's population live in urban areas, and the majority of population growth over the next four decades is expected to occur in cities (United Nations, 2012). Most but not all studies have reported that access to green space in urban areas is associated with improved overall well-being, including benefits related to both physical and mental health (Bowler et al., 2010; Lee and Maheswaran, 2011; Logan and Selhub, 2012; van den Berg et al., 2010). The mechanisms underlying these associations are not clear, but green space may be associated with lower exposure to ambient air pollution, extreme heat, and noise (Gidlof-Gunnarsson and Öhrstrom, 2007; Laforcezza et al., 2009; Nowak et al., 2006; Su et al., 2009). Proximity to green space may also offer more opportunities for physical activity and social interactions (Bowler et al., 2010; Coombes

et al., 2010; Giles-Corti and Donovan, 2002). Furthermore, access to green space has been associated with lower perceived stress levels and physiologic indicators of stress, as well as cognitive restoration (Hartig et al., 2011; Park et al., 2010; Van Den Berg et al., 2007; Ward Thompson et al., 2012) and lower levels of stress are associated with improved prognosis and quality of life in patients with established cardiovascular disease (Arnold et al., 2012). However, studies of the association between residential proximity to green space and health outcomes have been inconsistent. Discrepancies may be attributed to differences in socioeconomic position and biological susceptibility in the populations studied (Maas et al., 2009a; Mitchell and Popham, 2008).

Stroke remains a leading cause of serious long-term disability and an estimated 6.8 million Americans ≥ 20 years of age have had a stroke (Go et al., 2013; Towfighi and Saver, 2011). Neighborhood-level characteristics and socioeconomic factors have been reported to predict stroke prognosis and mortality across different populations (Addo et al., 2012). There is evidence that environmental factors, including air pollution and living in locations close to high traffic roads, are associated with mortality

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following stroke and other cardiovascular events (Maheswaran et al., 2010; Rosenbloom et al., 2012; Wilker et al., 2013). Evidence also suggests that social isolation (Boden-Albala et al., 2005) and depression (House et al., 2001) are associated with poorer prognosis following stroke. However, whether residential green space is associated with post-stroke mortality has not been studied.

We hypothesized that residential proximity to green space would be associated with lower all-cause mortality following ischemic stroke in a population of stroke survivors living in the greater Boston area. We also hypothesized that the association between residential green space and all-cause mortality may differ by factors related to biological susceptibility, socioeconomic position and residential proximity to high traffic roadways.

2. Methods

2.1. Participants

We identified 1763 patients ≥ 21 years of age admitted to the Beth Israel Deaconess Medical Center (BIDMC) between April 1, 1999 and October 31, 2008, with neurologist-confirmed acute ischemic stroke. The BIDMC is a 650-bed teaching hospital of Harvard Medical School designated as a primary stroke service hospital. We excluded patients with in-hospital strokes or transient ischemic attacks and we restricted analysis to patients living in the greater Boston metropolitan area (defined as living within 40 km of the hospital). This study was approved by the Committee on Clinical Investigations at BIDMC.

Information on demographics, presenting symptoms, medical history and imaging results was abstracted from medical records at the time of hospitalization for stroke. Presumed stroke pathophysiology was characterized as: (1) large-artery atherosclerosis, (2) small-vessel occlusion, (3) cardioembolism, (4) other determined cause or (5) undetermined cause, using the approach developed for the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) (Adams et al., 1999).

2.2. Exposure and covariate assessment

Addresses were geocoded using ArcGIS 9.2 (ESRI, Redlands, CA). Residential green space was determined by Normalized Difference Vegetation Index (NDVI) estimates from satellite images using the National Aeronautics and Space Administration (NASA) Moderate Resolution Imaging Spectroradiometer (MODIS). The NDVI measure is designed to evaluate global distribution of vegetation types, as well as their biophysical and structural properties and spatial/temporal variations (Townshend and Justice, 1995). The index is based on the reflection of visible and near-infrared light by vegetation and is calculated by the difference between near-infrared and visible radiation divided by the sum of near-infrared and visible radiation. The vegetation coverage is likely to be more dense when there is more reflected light in the near infra-red range (Weier and Herring, 2000). Values of NDVI range from -1 to 1 , with higher values indicating more green space. Global NDVI data are provided every 16 days and represent a composite of the previous 16 days with a 250-m spatial resolution as a gridded product in the Sinusoidal projection (Solano et al., 2010).

The ArcGIS GridExtract add-in module was used to assign NDVI grid-cell estimates to each residential address. We used NDVI estimates from the month of July since this month represents the period of most substantial vegetation growth in the greater Boston area and therefore typically reflects the maximum possible green space in each grid cell (Breckle, 2002). We calculated the average NDVI levels for all July estimates between 2000 (when the data first became available from NASA) and 2012 (the end of mortality follow-up period). In each year, there were two July NDVI measures for each cell, providing a total of 26 measures from 2000 to 2012. Estimates were available for all grid cells in all years and there were no missing data.

All averages below 0.4 ($n=117$) were visually inspected to determine whether the NDVI level was low because it represented a densely urban area with minimal vegetation or whether it represented a grid cell that was predominantly within a body of water. Addresses in regions directly surrounded by water were excluded from analysis since these locations may have different characteristics from low green space areas not directly adjacent to bodies of water, and because residing near a body of water has been associated with positive health benefits distinct from those of green space (White et al., 2013).

Each geocoded address was linked to the corresponding 2000 US census block group and assigned block group level median household income and percentage of adults age ≥ 25 years without high school diplomas. Distance to the nearest high traffic roadway, defined as a roadway with $> 10,000$ vehicles/day, was computed in ArcGIS based on average daily traffic counts provided by the Massachusetts Department of Transportation (2013).

2.3. Outcome assessment

Deaths were determined by Social Security Death Index (SSDI). Participants were censored at the time of death or on June 26, 2012. Follow up time was calculated as the date of symptom onset to censor date.

2.4. Statistical analysis

Cox proportional hazard models were used to calculate hazard ratios (HR) and 95% confidence intervals (CI) for the association between residential green space and all-cause mortality. Quartiles were selected for the primary analysis to evaluate potential nonlinearity and to minimize the influence of outliers in the NDVI distribution. Proportionality of hazards was evaluated by testing interactions with the log of time. We examined the association between all-cause mortality and quartiles of green space, and we conducted a test for trend by evaluating the statistical significance of a linear term using the median green space for each quartile. In the first model, we adjusted for age and sex. In the second model, we further adjusted for race (black, white/unknown), Hispanic ethnicity (yes or no), smoking status (current, former, or never), history of stroke, coronary artery disease, atrial fibrillation, heart failure, diabetes, dyslipidemia, and hypertension, percent of adults in the block group aged ≥ 25 years without a high school diploma (tertiles) and median household income (quartiles). In the third model, we additionally included a term for the natural logarithm of distance to a major roadway as a continuous variable, which has previously been associated with post-stroke mortality in this population (Wilker et al., 2013).

To examine whether the association between green space and post-stroke mortality varied according to major roadway proximity, a cross-product term between quartiles of NDVI and the natural logarithm of residential proximity to a major roadway was included in the model. We also used cross-product terms to test whether the associations with green space differed by factors related to biological susceptibility (age > 75 , diabetes, sex) and socioeconomic indicators of vulnerability (median household income in the lowest quartile and percent of adults aged ≥ 25 years without a high school diploma in the highest tertile) individually in separate models.

We conducted several sensitivity analyses to evaluate the robustness of our findings. In secondary analyses, we treated NDVI as a linear continuous term and scaled the hazard ratios to an interquartile range difference in NDVI (0.22). To explore the best fit of the model of green space and mortality, we also considered models with natural splines that had two, three, and four degrees of freedom in addition to primary analyses with quartiles and secondary analyses treating NDVI as a continuous linear term and evaluated whether models using splines fit the data better using likelihood ratio tests. Instead of using categorical variables, we considered nonlinear associations with socioeconomic factors using natural splines with three degrees of freedom to adjust for median household income and percent of adults aged ≥ 25 years without a high school diploma. We also modeled age using natural splines with two degrees of freedom rather than as a linear continuous variable. We allowed baseline mortality rates to vary by age in separate models. In addition, because people who survive to a particularly old age may reflect a different subgroup of the population, we conducted an analysis excluding the 3 participants > 100 years of age. Finally, since stroke severity might be related to access to green space, models were adjusted for length of hospital stay (continuous and then as > 4 vs ≤ 4 days) as an indicator of stroke severity.

Analyses were conducted using SAS Version 9.3 (Cary, NC) and R (RSTUDIO V 0.97, R Version 3.01, Survival Package). Plots were created in Stata (Version 12, College Station, Texas). All p -values are two sided and $p < 0.05$ is considered statistically significant.

3. Results

Of the 1763 patients initially assessed, there were 1705 eligible who lived within 40 km of the Medical Center with recorded date and time of stroke. Complete covariate data and green space measures were obtained for 1675 participants (98%). We excluded 30 participants with residential addresses located in NDVI grid cells made up mostly of water (2% of participants with NDVI measures), leaving a total of 1645 participants. There were 929 deaths over up to 13.2 years of follow up, with a median follow up of 5 years. Population characteristics by quartiles of residential green space are presented in Table 1. Participants living in the lowest quartile of green space tended to be slightly younger, more likely to be black or Hispanic, lived in areas with higher percentages of individuals ≥ 25 years without a high school diploma and had lower median incomes. History of stroke and hypertension were highest in this group as well. The green space measures in our data ranged from

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