Spatial analysis for the epidemiological study of cardiovascular diseases: A systematic literature search

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Abstract

Cardiovascular diseases (CVDs) are the primary cause of death and disability in the world, and the detection of populations at risk as well as localization of vulnerable areas is essential for adequate epidemiological management. Techniques developed for spatial analysis, among them geographical information systems and spatial statistics, as well as cluster detection and spatial correlation, are useful for the study of the distribution of the CVDs. These techniques, enabling recognition of events at different geographical levels of study (e.g., rural, deprived neighbourhoods, etc.), make it possible to relate CVDs to factors present in the immediate environment. The systematic literature presented here shows that this group of diseases is clustered with regard to incidence, mortality and hospitalization as well as obesity, smoking, increased glycaemia, haemoglobin levels, hypertension, physical activity and age. In addition, acquired variables such as income, residency (rural or urban) and education, contribute to CVD clustering. Both local cluster detection and spatial regression techniques give statistical weight to the findings providing valuable information that can influence response mechanisms in the health services by indicating locations in need of intervention and assignment of available resources.

Introduction

In recent years, the application of spatial analysis has gained relevance in epidemiological identification and management of factors associated with disease (Graham et al., 2004; Rezaeian, 2009). Most of these studies rely on spatial statistics to reveal related factors, which therefore play an important role in simplifying decision making, application of interventions and distribution of resources. Although these techniques are particularly useful for infections requiring vectors (Anno et al., 2015; Bergquist, 2017) they have been shown to also be helpful in the study of cardiovascular diseases (CVDs) and other non-communicable disorders (Oliveira et al., 2015; Park et al., 2016; Martínez-Bascuñán and Rojas-Quezada, 2017). Geospatial studies use different techniques to establish correlations, some of which can be complex and difficult to explain to the non-specialist, while the outcome, e.g. a map, can visualize epidemiological situations that can be immediately grasped by the layman. In this type of studies different concepts are used that are worth recognizing. Indeed, different spatial techniques are useful at different levels and they are complementary to each other.

Mapping is a useful approach to empirically identify events associated with health. These results must, however, be carefully interpreted according to the geographical units selected considering the many possible variables at hand. For example, deprivation indices are typically designed for small geographic areas (e.g. neighbourhoods), while approaches used when mapping larger administrative areas, such as district or regions, are likely to mask pockets of deprived neighbourhoods (Exeter et al., 2007, 2014). When attempting to connect health data with an area, it is important to consider geographical units corresponding to the area level chosen for the analysis, e.g. subdividing a large territory such as a city, into small, non-overlapping representative units (Gómez-Rubio et al., 2005). It is also important to choose an area of appropriate size, as very large areas could hide information of interest, while small areas are generally not only homogeneous but also more transparent (Rezaeian et al., 2006; Tonne et al., 2009). Spatially analyses usually use subdivisions which are also administrative units, such as census tracts, census block groups or they use the mail delivery system, i.e. ZIP codes (Ossypuk and Galea, 2007; Arsenault et al., 2013). Naturally, the study area can also be defined arbitrarily (Zhu et al., 2012). For cluster determinations, the required data are the occurring number of events of interest, the expected number of events and the population at risk in each spatial unit of a specific territory (Gómez-Rubio et al., 2005). In addition, it is possible to subdivide this information into various strata (personal such as sex, age, income, etc.) or the general economic strength of each region under study (Gómez-Rubio et al., 2005). Cluster detection is an important epidemiological tool because it can help identifying factors associated with disease. It corresponds to a set of events that are spatially closely related. Positive spatial autocorrelation (SA)
imply that the rates for a given phenomenon tend to be similar for neighbouring areas in comparison to those that are geographically distant (Griffith, 1987; Rezaeian et al., 2007). For example, health variables and underlying related factors tend to be spatially correlated (Lorant et al., 2001; Sofianopoulos et al., 2006), which is due to the high probability that closely situated areas have similar underlying factors related to various phenomena (Rezaeian et al., 2007). It should, in this connection be recognized that there is a difference between the global and the local situation. While the focus when searching for global clusters is on their existence, not location (Aamodt et al., 2007), local cluster analysis aims at quantifying SA and clustering in small geographical units within the study area (Jacquez, 2008). Moran’s I is a commonly used spatial statistic for the detection of global clustering (Moran, 1948), with local indicators of spatial association (LISA) being the statistic of choice for finding local clustering (Anselin, 1995, Bailey and Gatrell, 1995) allowing decomposition of the indicators. Other techniques used for the detection of local clusters are the Getis-Ord Gi static (1992), the geographical analysis machine (Openshaw et al., 1987) and spatial scan statistic (Kulldorff, 1997). Regression techniques are used to determine possible correlations between variables of interest and give information about direction and strength of the relation. A more simple way to assay correlations between variables is to determine the dependent variable and adjust for other possible explanatory factors suggesting evidence for causal association (Jerrett et al., 2003). Others techniques used for estimating spatial regression are ordinary least squares (OLS) (Ford and Highfield, 2016), geographically weighted regression (GWR) (Brunsdon et al., 1996), bivariate LISA (de Andrade et al., 2013; Martinez et al., 2014), the generalized additive model (Hastie and Tibshirani, 1986) and the spatial lag model (Levine, 2003). The present research was undertaken to highlight the application of geospatial analysis for the recognition of factors that determines the spatial distribution of CVD in addition to recognizing the utility of these techniques for the allocation of resources and generation of public policies for CVD.

Materials and Methods

A systematic literature search covering the latest decade of geospatial studies involving CVD was undertaken to investigate the current use spatial statistics and provide an up-to-date overview of this field. PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) and ScienceDirect (https://www.sciencedirect.com/), the two major databases providing access to scientific and medical research, were searched using the following key words: CVD and infarct; CVD and spatial analysis; and CVD and cluster. Inclusion criteria were the following: title or abstract of papers recognizing the use of spatial techniques (including mapping, cluster detection and spatial regression); focus on spatial, ecological studies (since the search term CVD and spatial analysis also yielded results on imaging techniques used for diagnosis that was outside our interest); articles published in the last decade. Exclusion criteria: review articles, work prior to 2007 and articles without abstracts.

Results and Discussion

The territorial distribution of the CVDs is not homogeneous. Publications based on the spatial occurrence of CVD show that this group of diseases is clustered with regard to parameters, such as incidence (Kjaerulff et al., 2016), mortality (de Andrade et al., 2013; Gohari et al., 2015; Gomez-Barroso et al., 2015; van Rheenen et al., 2015; Roberson et al., 2016) and hospitalization (Soares and Nascimento, 2010; Roberson et al., 2016). Likewise, factors directly related to CVD, obesity as measured by the body mass index (BMI) (Mobley et al., 2004; Tamura et al., 2014), smoking (Mobley et al., 2004), increased glycated haemoglobin (HbA1c) levels (Jiwa et al., 2015; Paquet et al., 2016), hypertension (Wang et al., 2014b) and physical activity (Tamura et al., 2014; Cunningham-Myrie et al., 2015) also tend to cluster. These factors and others, like age, income, residency (rural or urban) and education, contribute to CVD clustering (Talbott et al., 2013; Nunes et al., 2013; Ahmad et al., 2015; Caswell, 2016). Spatial analysis facilitates the study of the distribution of factors related to CVD from a spatial, seasonal or temporal viewpoint (Wang et al., 2014a; Roberson et al., 2016). These studies are not only useful, but indeed necessary, since an adequate space-time interpretation of factors involved with a disease allows suitable designation of priorities, resource distribution and policy implementation. Tables 1 and 2 summarize recent studies for cluster detection and spatial correlation with regard to the CVDs.

Table 1. Recent general cardiovascular disease (CVD) studies based on cluster detection and spatial correlation.

<table>
<thead>
<tr>
<th>Place</th>
<th>Level of study</th>
<th>Cluster detection</th>
<th>Spatial correlation</th>
<th>Main findings</th>
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<tr>
<td>State of Paraná, Brazil</td>
<td>City</td>
<td>GCD¹ by Moran’s I / LCP¹ by LISA</td>
<td>Bivariate Moran’s I</td>
<td>IHD² clusters positively correlated with old age, illiteracy and urban development</td>
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<td>Madrid, Spain</td>
<td>Census tract</td>
<td>GCD¹ by Moran’s I / LCP¹ by LISA</td>
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<td>Clustered CVD leading to death (men and women)</td>
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<td>Alberta, Canada</td>
<td>Provincial health care network</td>
<td>LCP¹ by Getis-Ord Gi and spatial scan statistics</td>
<td>Not done</td>
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<tr>
<td>Florida, USA</td>
<td>County</td>
<td>GCD¹ by Moran’s I / LCP¹ by LISA</td>
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<tr>
<td>Vale do Paraíba, Brazil</td>
<td>Municipality</td>
<td>GCD¹ by Moran’s I / LCP¹ by LISA</td>
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<td>Tehran, Iran</td>
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<td>Not done</td>
<td>Clusters of death due to acute heart disease, cerebrovascular disease and hypertension</td>
<td>Gohari et al., 2015</td>
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</table>

¹Global cluster detection; ²Local cluster detection; ³Ischemic heart disease; ⁴Acute myocardial infarction.
### Table 2. Recent specific cardiovascular disease (CVD) studies based on cluster detection and spatial correlation.

<table>
<thead>
<tr>
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<th>Place</th>
<th>Level of study</th>
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<th>Spatial correlation</th>
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<td>Census tract</td>
<td>GCD by Moran’s I</td>
<td>OLS and GWR</td>
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<td>South Africa</td>
<td>District</td>
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<td></td>
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<tr>
<td></td>
<td>Lausanne, Switzerland</td>
<td>District, neighbour-hood</td>
<td>LCD by Getis-Ord Gi</td>
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<td>Two temporal BMI-related clusters. Adjusting for neighbourhood-level income attenuated cluster presence</td>
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<td></td>
<td>King County, USA</td>
<td>Neighbour-hood</td>
<td>LCD by LISA and spatial scan statistics</td>
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<td>Taiwan</td>
<td>Township</td>
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<td>Climate and pollution</td>
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<td>Houston and Travis, USA</td>
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<td>Ludhiana, India</td>
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aGlobal cluster detection; bLocal cluster detection; cOrdinary least squares; dGeographically weighted regression; eBody mass index; fParticulate matter, size 2.5 µm; gPhysiological equivalent temperature; hParticulate matter, size 10 µm; iOut-of-hospital cardiac arrest (OHCA); jCardiopulmonary resuscitation.
Factors of importance for cardiovascular disease spatial distribution patterns

Socioeconomic status

The nexus between socioeconomic status and CVD is well documented (Backholer et al., 2016). Spatial analysis has provided valuable information for a better understanding of this relation. In Australia, population with high risk for CVD trend to clustering in more disadvantaged areas (Bagheri et al., 2015). In Harris, Texas, geographically weighted regression showed a correlation between high CVD mortality and social deprivation at the neighbourhood level (Ford and Highfield, 2016). Results were similar in a study of an area in Strasbourg, France, where high-risk clusters for myocardial infarction (MI) was seen to accumulate in economically deprived areas despite good access to health amenities (Kihal-Talantikite et al., 2017). By mapping the level of income and risk of acute myocardial infarction (AMI) hospitalization and mortality during two time intervals (in 1999 and in 2013), a study covering all of USA at the county-level showed that although cardiovascular risk tends to decrease in all income strata, a low earnings level generates latency in this trend (Spatz et al., 2016). Socioeconomic deprivation can promote CVD clustering with other health conditions, like preterm birth for women, since the first condition is a risk factor for the second (Kramer and Williamson, 2013).

Risk analysis show a spatial correlation between deprivation and premature mortality due to diseases of the circulatory system (Juhász et al., 2010; Boruzs et al., 2016). The risk factors tend to cluster together in socioeconomic disadvantage areas (Weimann et al., 2016), e.g., the BMI clusters found in disadvantaged areas where there is also increased CVDs (Mobjley et al., 2004; Joost et al., 2016). Property values refers to probable price of a given property at a given time and is thus related to the regional economy (Coffee et al., 2013; Leonard et al., 2016). High and low obesity clusters were attenuated after adjusting for age, gender, race, education and income; however they disappeared once neighbourhood residential property values and residential density were included (Drewnowski et al., 2007; Huang et al., 2015).

Socioeconomic status can determinate the opportunity of access to health services. Clusters of people dying from heart disease at home before any attempt at transport were observed in areas with lower socioeconomic and household resources (Pathak et al., 2011). Using disease mapping at the district level and risk analysis with rapid inquiry facility (RIF) techniques, one study showed that people living in highly deprived areas showed a low relative frequency of prescriptions of statin treatments (Boruzs et al., 2016).

Education level

Pedigo and colleagues found that neighbourhoods from eastern Tennessee, USA belonging to a high-risk clusters of stroke and MI mortality tended to have high populations with low education level (Pedigo et al., 2011). A study carried out in Brazil consistent with this finding reports a spatial cluster for ischemic heart disease (IHD) mortality correlating with illiteracy in the study population in question (de Andrade et al., 2013).

Alcohol intake

The connection between heart disease and high alcohol intake is not uncommon, which fact is in agreement with a study from Chile, where one study region, identified as being at a high risk for CVD-related deaths associated with alcohol consumption (Castillo-Carniglia et al., 2015). These results are supported by the finding of two clusters in the areas of Valparaiso and Biobio characterized by high alcohol intake; indeed, the alcohol consumption in the latter has been one of the highest in the country for over 45 years (Castillo-Carniglia et al., 2015).

Rural vs urban residency

Both rural and urban areas have characteristic particularities that may influence the development of CVD. A recent study in Peru highlighted the presence of clusters for obesity in urban children, while in the rural areas the prevalence of obesity was low (Hernandez-Vasquez et al., 2016). A study conducted in Tennessee using the Besag, York and Mollié (BYM) model found rural residency a determinant of for MI and stroke (Odoi and Busingye, 2014). There are geographical clusters among the rural population in Taiwan characterized by underutilization of cardiovascular drugs, which is related to a low presence of specialists in cardiology in some areas (Cheng et al., 2011). Rural living could thus select for inadequate access to health services, hindering the timely management of diseases. In this respect, spatial regression analysis carried out in Taiwan have revealed that mortality related to cold or heat waves is more pronounced in the rural areas due to less access to medical facilities and resources than are available metropolitan areas (Wu et al., 2011).

Environmental influence

Temperature

Intermediate-term temperature changes, such as heat and cold waves, can lead to rises immortality by inducing physiologic stress resulting in increased platelet counts, hypercholesterolemia and an enhanced tendency for blood coagulation (Keatinge et al., 1984; Keatinge et al., 1986; Neld et al., 1994). An Australian study based on global and local Moran’s I showed increased spatial clustering of CVD during the warmer months, and a weak correlation between AMI and age during the warmer months was detected by Loughnan et al. (2008). A cluster of high general mortality in elderly people, a susceptible group for CVD, was detected after a heat wave in Sydney, Australia (Vaneckova et al., 2010), while Chen et al. (2015) tell us that a heat wave contributed to increased stroke mortality in Nanjing, China. A retrospective study carried out in Cuiabá and Várzea Grande, Brazil, reported a period with higher temperature variations and low humidity coinciding with the appearance of a cluster of high CVD (Rodrigues et al., 2015). However, although there thus seems to be a strong relation between high temperatures and impaired health in CVD patients, the opposite has also been seen, i.e. Roberson et al. (2016) report hospitalization for stroke coupled with a high risk for mortality in winter. The individual energy balance model, discussed by Höppe (1999) and Matzarakis et al. (1999) in the context of a physiologic- equivalent temperature (PET), may have a bearing on this outcome. PET is defined as the air temperature (in an ambient indoor setting) at which the heat budget of the human body is balanced. This approach enables a comparison of the integral effects of complex thermal conditions outside (not only decided by air temperature, but also by humidity, wind speed, cloud cover, etc.) with the indoor experience. On hot summer days, for example, the PET value may be much higher than the air temperature, while on a windy day in winter considerably lower. Indeed, an ecological study identified a cluster of high mortality correlated with a changed PET score both in cold and warm seasons (Thach et al., 2015).
Air pollution and noise

Fine particulate matter in the air, a common problem in modern cities, predisposes the development of respiratory and cardiovascular diseases in urban populace. The correlation between air pollution and CVD is well known (Brunekreef et al., 2009; Dehbi et al., 2016). PM_{2.5} and PM_{10} are particles of different sizes suspended in the air, which are derived from industrial activity, combustion, and diesel emission (Ogundeji et al., 2016). Spatial analysis can improve the understanding and detection of pollution emission. Using satellite-derived data for optical PM_{2.5} detection, it is possible to find spatial CVD clusters in areas where there are high levels of pollution confirming that CVD is spatially related to the concentration of particles (Aina et al., 2014; Chen et al., 2016; Weber et al., 2016). High concentrations of both PM_{2.5} and PM_{10} have been shown to be spatially correlated to mortality due to CVDs (Tonne et al., 2009; Lim et al., 2014; Rodrigues et al., 2015), and clusters of AMI events close to industry installations, specifically steel industry, have been reported (Namayande et al., 2016).

A study carried out in Barcelona, Spain suggests that areas with high traffic noise can be just as dangerous as pollution for MI mortality. In addition, increased OLS indicate a connection between noise and conditions, such as Type II diabetes mellitus in men and mortality due to hypertension in women (Barcelo et al., 2016). In France, an ecological study showed a spatial correlation between mortality due to IHD, MI, and stroke mentioning 161 communes exposed to high noise levels related to the three main airports in the country (Evrad et al., 2015).

Water

Ecological studies are useful to detect neighbourhood determinants with impact on health. For example, the quality of drinking water has been shown to influence the progress of CVD. The number of cardiovascular, coronary and cerebrovascular disease increased in municipalities with high arsenic concentrations in the drinking water (Medrano et al., 2010), and an association between arsenic water content and stroke admissions in a analysis based on zip codes and binomial regression models (Lisabeth et al., 2010).

Support from health-related resources

Bystander cardiopulmonary resuscitation

Cardiopulmonary resuscitation (CPR) performed by a bystander (B-CPR) is defined as CPR performed by any person who is not part of the organized emergency-response system in a community (Bradley and Rea, 2011). The prevalence of this knowledge in a population speaks of its level of development (Bradley and Rea, 2011). Spatial analysis has been useful to identify and improve the management of this technique in the population (Nasse et al., 2014). Taking in account clusters of out-of-hospital cardiac arrest (OHCA) and the prevalence of B-CPR in a community, populations at high risk for OHCA can be estimated (Lerner et al., 2005; Sasson et al., 2010; Sasson et al., 2012; Nasse et al., 2014). Nasse and colleagues (2014) have proposed a standardized approach to improve the detection of such populations using three different spatial analytic methods. When two out of three of these methods identify a location with high OHCA incidence and low B-CPR, this location is definitely at high risk. Income is an important determinant of the prevalence of B-CPR as OHCA victims in census tracts characterized by high income are more likely to receive B-CPR than others (Sasson et al., 2011; Root et al., 2013). This disproportion is increased among African American neighbourhoods, which are therefore promising targets for community-based interventions at the neighbourhood level.

Access to health resources

Swift and easy access to health establishments can determine outcome and adherence to treatment with regard to the CVDs. Ecological analyses based on spatial approaches support prioritizing target areas that require improved health service coverage. Using descriptive mapping it is possible characterize travel time and population coverage for cardiac interventional services, enabling direct, visual detection of areas (or populations) with low-level access (Graves, 2011; Clark et al., 2012). Mapping has also has been used to identify areas with poor ambulance response times (Earnest et al., 2012). Principal component analysis (PCA) allows condensing variables related to a given phenomenon and sorting them into a hierarchal diagram. Using this technique to combine variables associated with disease burdens and access to health services, Hames et al. (2016) detected areas of high medical vulnerability by GIS mapping and z scoring at the census tract level. In addition to mapping, the study of interaction with social vulnerability by bivariate analysis proved useful for the detection of vulnerable areas for an old-people group among the general population (Hames et al., 2016). However, the situation can sometimes be more complex as revealed by a study conducted in Denmark where the existence of a strong correlation between individuals with a low AMI mortality rate and personal initiative was revealed (Ersboll et al., 2016). While a fatal AMI was seen among only 12.0% of individuals having asked for a medical check-up the year before the AMI, the outcome was fatal in as much as 78% in those who had not. In this study, a high population ratio to practicing doctors (GP) or a long distance to a GP could not explain the increased odds of a fatal outcome of AMI in individuals without such contact. In the Indian city of Ludhiana, on the other hand, clusters of poor outcome after stroke have been found to occur in locations far from major medical facilities (Pandian et al., 2016).

Geographical and socio-economic factors can determine access to health services. Both the personal health state, car ownership and distance to service are determinates for predicting access to health services. GWR was useful to weigh the effects of these variables on health access indicating locations where the predictive strength of the independent variables was higher or lower than the global trend (Comber et al., 2011). Spatial analysis has also been a valuable tool in the study of health resource distribution, for example when identifying population at risk by the multi-criterion two-step floating catchment area (MC2SFCA) method, which enables measuring healthcare accessibility, thus facilitating the allocation of automated external defibrillators (Lin et al., 2016). Indeed, GIS plays an important role in the development of algorithms for this purpose as well as for improving cardiac diagnostic resources (Kaffash-Charrandabi et al., 2015; Ferguson et al., 2016). In England, ecological studies based on mapping and detection of clusters for the proportion of observed medical diagnoses have been useful for the determination of areas where CVDs are under-diagnosed (Soljak et al., 2011). The use of GWR to assess whether a linear regression relationship between observed and expected prevalence of CVD exist allowed the detection of areas where more general practitioners would be needed.

Adherence to prescribed medical treatment

Spatial analyses of people on medicines for CVD has showed clustering for drug adherence (Cheng et al., 2011; Erickson and
Lin, 2014). By application of GIS technology, Hoang et al. (2011) found a cluster of strong adherence for acute coronary syndrome treatment round a university hospital, and White et al. (2016) described a cluster of low prevalence for hypertension, which was related to the presence of a physician known to provide adequate primary health care.

**Conclusions**

Studies that use spatial analysis in health have been useful to understand the implication of environmental factors in the development of CVD. To obtain reliable results, it is important to use adequate statistical and geospatial analysis tools, as well as an adequate definition of the geographical units used. In the spatial distribution of CVD, the socioeconomic level, the level of urbanity and education of the population have an important influence. These variables determine the level of access and link to health services. Environmental variables, such as temperature, humidity and contamination also determine the distribution of CVD. In this way, the application of spatial study helps to recognize particularly vulnerable areas where intervention can take place facilitating the allocation of health resources and/or applying prevention policies for these diseases.

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