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Research Article

Spatial Analysis of Geographic Distribution and Accessibility of Suspected Acute Stroke Patients Transferred to Acute Stroke Centers by Emergency Medical Services in Tehran, Iran: A Cross-Sectional Study

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Abstract

Objectives: We intended to map the geographical distribution of patients with acute stroke who called the Tehran EMS center based on the geographic information of the incident location on a map. The distributions of these centers and patients' access within a standard period were evaluated.
Methods: A cross-sectional study based on the registered data was conducted on suspected acute stroke patients > 18 years of age that were transferred by EMS. The analysis was performed based on pointing the patients' locations and locating the hospitals in ArcGIS software plus a review of the polygons and focal points.
Results: Totally, 1,606 patients suspected to stroke with a mean age of 64.89 ± 17.48 years were evaluated, of whom 947 (58.6%) were male. The mean time of arrival of an ambulance in the patient's location from the EMS station was 11.94 ± 6.67 minutes, and the longest time was 69.32 minutes. The mean time from the patient's location to the stroke center was 17.79 ± 11.42 minutes (range 2.4 - 83.70 minutes). Stroke centers in Tehran are not distributed in a balanced manner, and they are concentrated on the central and northern parts of Tehran, limiting access to hospital services.
Conclusions: The multiplicity of hospitals in the west and center of Tehran led to an increase in access times in eastern Tehran. It emphasizes the necessity of revision of service locating, especially because the east of Tehran has a denser texture than the west.

Keywords: Emergency Medical Services, Geographic Information Systems, Health Services Accessibility, Stroke

1. Background

Stroke is the second most common cause of death and the third leading cause of disability in the world that imposes significant financial costs on patients' families, communities, and health systems. Only in the United States, both direct and indirect costs of stroke are estimated at nearly $33.6 billion annually, of which $17.5 billion is related to direct medical costs, and these costs are projected to almost triple in the next two decades (1-3).

Although it is now possible to treat acute ischemic stroke (AIS) through intravenous thrombolysis and endovascular thrombectomy, the success of recanalization is a time-dependent process; the sooner it is performed, the better are the results (4-9). It is claimed that saving one minute in the treatment process will give an average of 1.8 days of healthy life to a patient with AIS, and every 15 minutes of reduction in treatment delay will lead to adding one month of life without disability. Nevertheless, since these patients usually arrive late to the hospital, only a small percentage of them are candidates for recanalization treatment (5, 10-12).

The possibility of reperfusion treatment and other advances in AIS management over the past two decades have highlighted the role of the Emergency Medical Service (EMS) in improving stroke care, and now the EMS system is playing a vital role in the survival chain of AIS patients (8, 13-16). This system is responsible for the rapid detection of acute stroke symptoms, the stabilization of vital signs, the transfer of the patient to the appropriate hospital, and informing the destination hospital's stroke team (13, 17-19). However, the system also faces challenges and obstacles in the way of fulfilling this responsibility, including routing the distance from the ambulance station to the patient's location to the destination hospital. Appropriate strategies in this regard play a critical role in reducing the delay in initiating thrombolytic therapy for patients with AIS (1, 9-11, 13). The use of Geographic Information System (GIS) and spatial analysis of information can provide good strategies for managing AIS patients. In spatial analysis, the first step is to identify and describe the spatial patterns. After finding the patterns, we can probably explain the causes of pattern formation (20). The ultimate goal of a GIS is to support decision-making based on geographic data, and its primary function is to get information obtained from combining different layers of data gathered through different ways and different perspectives. Using this system, the current situation of the distribution of resources for the treatment of AIS patients is reviewed, and their measure and method of access in a standard period with available facilities are evaluated.

In Iran, the system "724" (providing specific services for acute stroke patients seven days a week/24 hours a day) and the code SAMA (emergent stroke) have been established since July 2015. These systems aim to rapidly identify and screen patients suspected to acute stroke and create a link and better coordination between the pre-hospital system and stroke centers for quicker transference (via air or ground) of patients with a suspected stroke. Currently, a few centers in Tehran can provide proper medical services to AIS patients. Besides, they do not have a predetermined geographical distribution that can affect the timing of providing services to the patients.

2. Objectives

In this study, we intended to map the geographical distribution of patients with acute stroke who called the Tehran EMS Center based on the geographic information of the incident location on a map and then calculating the distance of the patients' location to the definite stroke center. The distributions of these centers and patients' access within a standard period were evaluated. It is hoped that this study could provide managers and authorities with a perspective of timely access of patients to equipped hospitals treating stroke in decision-making and management policies for optimizing the distribution and allocation of stroke facilities.

3. Methods

3.1. Study Design

This is a cross-sectional study based on registered information (724 Registry of Tehran EMS Center) that was designed and carried out using relevant information for six months from 06/22/2018 to 12/21/2018. The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences and assigned the code: IR.TUMS.VCR.REC.1397.973. To conduct the study, permission was obtained from the Security of Tehran EMS center. The confidentiality of information was preserved, and all items were used anonymously.

3.2. Study Population

The study population consisted of all patients older than 18 years, suspected of having an acute stroke, calling the Tehran EMS to be transferred to the hospital, with activated SAMA code, and recorded information in the Tehran EMS Information Registry System during the study period. The case was excluded if there was a history of trauma, incomplete patient record, and death before the arrival of EMS personnel. In this study, using a census method, all eligible patients during the six-month study period were enrolled.

3.3. Definitions

The city of Tehran is the largest metropolis of Iran, with a population of 8.7 million, according to the 2016 census. Regarding Tehran's administrative, political, social, and economic status, more than 14 million people enter and leave the city daily from the suburb. Thus, Tehran's population during the day is nearly 22 million. This population is covered by the Tehran EMS, which provides emergency services to citizens through 216 EMS stations throughout Tehran. Statistics of Tehran EMS show that there are more than 17,000 calls to the dispatch unit daily, with 9,000 requests for an ambulance. Tehran has numerous health centers including more than 150 private and public hospitals throughout the city, but EMS patients are transferred almost always to public ones. Thus, only 10 hospitals are capable of providing specialized services to stroke patients that are called Stroke centers. The pattern of dispersion of

109 enrolled EMS stations and Stroke centers in Tehran is shown in Figure 1.

The population distribution in Tehran is unbalanced. Thus, to model access to Tehran EMS, the service area of an EMS station was determined, and the number of residents in each area was extracted. Figure 2 shows the pattern of population distribution in the service area of Tehran EMS stations.

3.3.1. SAMA Code (Plan 724)

The American Stroke Association recommends that all patients with acute stroke be transferred to the nearest primary stroke centers or hospitals with similar facilities (14). According to this recommendation, in Iran, the system of "724" (providing 24/7 specific services for AIS patients) and the code SAMA (emergent stroke) have been established since July 2015. The goal is to quickly identify and screen patients with suspected acute stroke and establish a more coordinated link between the pre-hospital system and acute stroke centers for faster transmission (via air and ground) of the patient to thrombolytic facilities. For this purpose, after a client calls 115 (the EMS phone number in Iran), the Emergency Medical Dispatcher (EMD) conducts targeted interviews with the caller based on the current algorithm, and then the nearest EMS station is announced. Then, emergency medical technicians immediately activated the SAMA code after they performed a rapid neurologic examination using the face-arms-speech-time (FAST) tool and confirmed the diagnosis of stroke if less than three hours have passed since the onset of symptoms. Necessary actions are taken and the definite hospital (stroke center) is informed for patient transfer via the Dispatch Unit. At the hospital, patients are referred to as an emergency medicine physician to continue the diagnostic and treatment processes. According to the announcement of the Deputy Minister of Health and Medical Education of Iran, this plan is obligatory and the patient information must be recorded in the databank of the ministry since 2016.

3.3.2. Access Time

Distance access is substantial in spatial pattern analysis. Direct line distance, network distance, or access time can be used to measure distance. This study used time distances. Two distances are important, including the time interval between the station (ambulance location) and the patient location and the distance between the patient location and the referral stroke center. The distribution of Tehran's EMS stations is almost high and covers almost all of Tehran's neighborhoods, but the number of referral stroke centers is low, and they are concentrated in the central part of Tehran. Therefore, it is important to pay attention to the time distance between the EMS station and the patient's location and the time the patient is dispatched to the Stroke Center. Designed maps of the areas were separately marked by hot and cold spots. Hot spots are areas that do not have proper access, and cold spots are areas that have good access.

3.4. Data Collection

Data were extracted from the patients' records and the Tehran EMS registry system using a researcher-made checklist. The checklist included the following two main sections:

1) The first section contained demographic information and possible variables affecting the correct diagnosis, including:

A) Demographic information of patients including age and gender

B) The time information of the emergency: date and time of the call, time of the onset of symptoms, time of dispatch activation, time of dispatch, time of arrival in the patient's location, time of delivery to the hospital.

C) Information related to the patient's chief complaint, associated symptoms, and medical history.

D) Information related to dispatch (SAMA activation) and distribution of patients to centers for the system 724.

2) The second section contained the location information of the emergency and hospitals of Plan 724.

Location information of the Emergency is recorded in two ways in the Tehran EMS registry system: first, via Global Positioning System (GPS) installed on some ambulances and second, through location tracking via tablets available for technicians to record information. These data are routinely loaded and recorded in the GIS system of the Tehran EMS center.

3.5. Statistical Analysis

To analyze the data, in the first step, the recorded information about stroke in the EMS database, which was available in the SqlServer format, was extracted. The database records the call time, dispatch time, EMS station, patient's location, time of arrival in the patient, the transfer time (from the patient's location to the hospital), and the route of EMS departure. Four layers are used as geodatabases:

1) Location information of EMS station layer: For recording station's location information and its descriptive characteristics

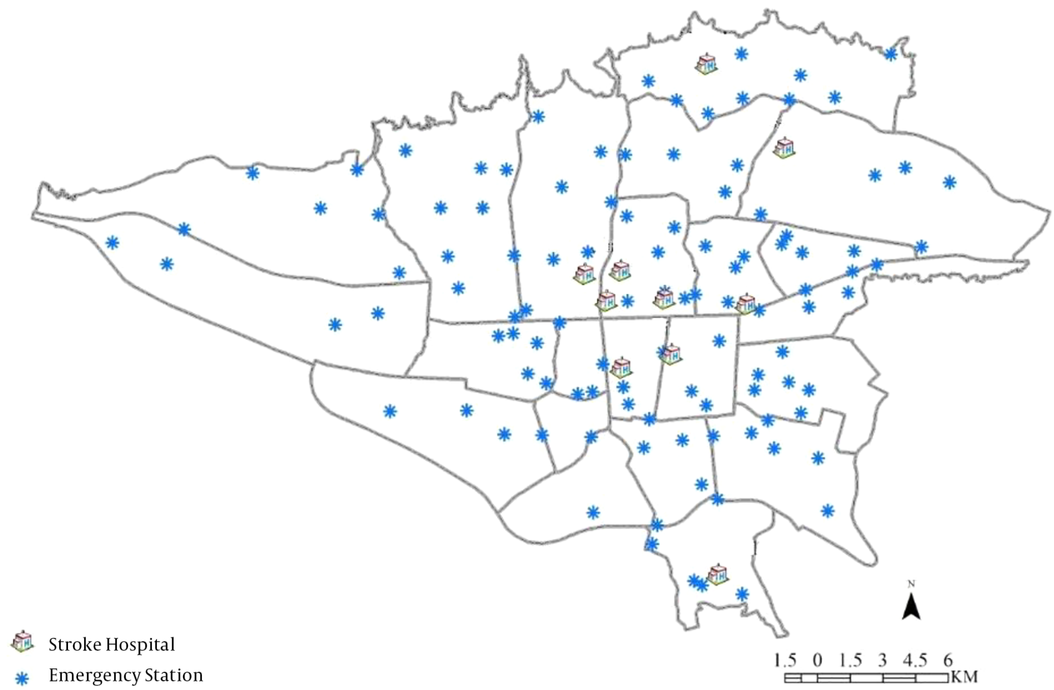

Figure 1. Spatial distribution of emergency stations, hospitals, and stroke centers in Tehran

2) Patient information layer: For recording patients' demographic characteristics, call time, the arrival time of the EMS, dispatch time to the hospital, and hospital arrival time.

3) Hospital information layer: For recording information about all hospitals and medical centers in Tehran, the type of hospital, and stroke centers.

4) Information layer of Tehran transportation network: For recording information from the Tehran transportation network including the type of route, route direction, and route length for use in network analysis and extraction of service areas.

After generating layers using spatial analysis tools, we explored ESDA's exploratory spatial data analysis (ESDA). The analytical tools used in this study are as follows:

Spatial Autocorrelation: It measures the relationship of a variable with itself on the space. Is there a relationship between features with neighbors? Spatial autocorrelation can be positive or negative (21, 22). Moran's I id used to measure the spatial autocorrelation. This measure calculates the difference of each feature from its neighbors to compute the similarity and relationship of each feature with its neighbors and evaluates whether the pattern expressed is clustered, dispersed, or random (23-25).

High/low Clustering: We used the Getis-Ord General G measure. This metric determines whether there is a high cluster or a low cluster. In other words, is there a concentration of high values or low values?

Hot-Spot (Getis-Ord Gi*): The Getis-Ord Gi*, also known as the hot-spot analysis, is a tool for analyzing the location-related clustering in attributes of spatial data. This method is an extension of local high/low clustering and measures Getis-Ord Gi for each feature individually (22, 26-28).

Service Area: It covers all accessible streets and routes in the study area that covers with EMS stations (29-31).

The analysis was based on pointing the patients' location and stroke centers on ArcGIS software and surveying polygons and focal points. The distance between the patient's locations and the destination Stroke Center was calculated using current analyzers for ArcGIS software. Two methods were used to compute the times: recorded times in the Tehran EMS information system for cases transferred, and the estimated times via ArcGIS analyzers. Based on the shortest and longest distance gone, the grouping of patients was done according to the distances traveled; besides, near and far areas to hospitals were identified. To

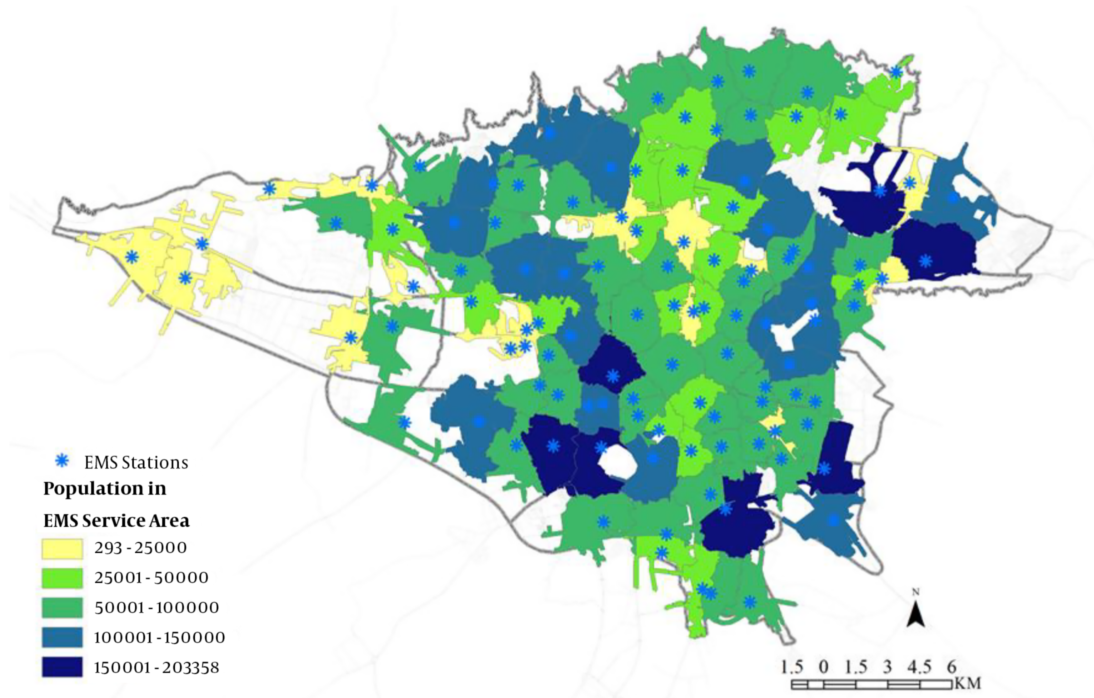

Figure 2. Spatial distribution of population in the service area of Tehran EMS stations

evaluate patients' access within the defined time (< 3 h), the transport time to a stroke center was recorded according to the registered information and GIS data, and patients were divided into three groups.

4. Results

4.1. Total Statistics

During the study period, 1,606 patients suspected to stroke with a mean age of 64.89 ± 17.48 years were evaluated, of whom 947 (58.96%) were male, and 659 (41.03%) were female. Regarding the time of calls, the minimum number of calls was distributed in 3 - 4 AM with 14 cases and the maximum number of calls in 6 - 7 PM with 122 cases. Totally, 40.7% (n = 658) of calls were made before noon (12:00 midday) and 59.3% (n = 958) of calls in the afternoon. The dispersion pattern of the patients, EMS stations, and stroke centers in Tehran are shown in Figure 3.

Figure 4 shows the proportion of suspected stroke patients per 10,000 people covered in the service area of each EMS station. This indicator reveals the demand for services. As shown on the map, the proportion of patients with suspected stroke is higher in the central part of Tehran and it decreases by approaching the perimeter.

4.2. From the EMS Station to the Patient's Location

According to the findings of the present study, the mean arrival time of an ambulance in the patient's location from the EMS station was 11.94 ± 6.67 minutes and the longest time was 69.32 minutes. Figure 5 shows the spatial pattern of the arrival time of EMS in the patient's location while the areas are marked by hot and cold spots separately.

The mean, standard deviation, the minimum, and maximum spatial and time distance traveled from EMS stations to the patient's location are shown in Table 1.

Table 1. Average Time Interval and Distance Traveled by Ambulances of EMS Station to Reach a Suspected Stroke Case

	Mean ± SD	Min	Max
Distance	1389.26 ± 955.98	182.32	7258
Time	11.94 ± 6.67	2	69.31

To design the spatial pattern of ambulance allocation at each EMS station to a patient, the movement radius (location distance without time) of ambulances from each EMS station to the incident scene (the studied patient's location) was determined. The result is shown on a spider map in Figure 6.

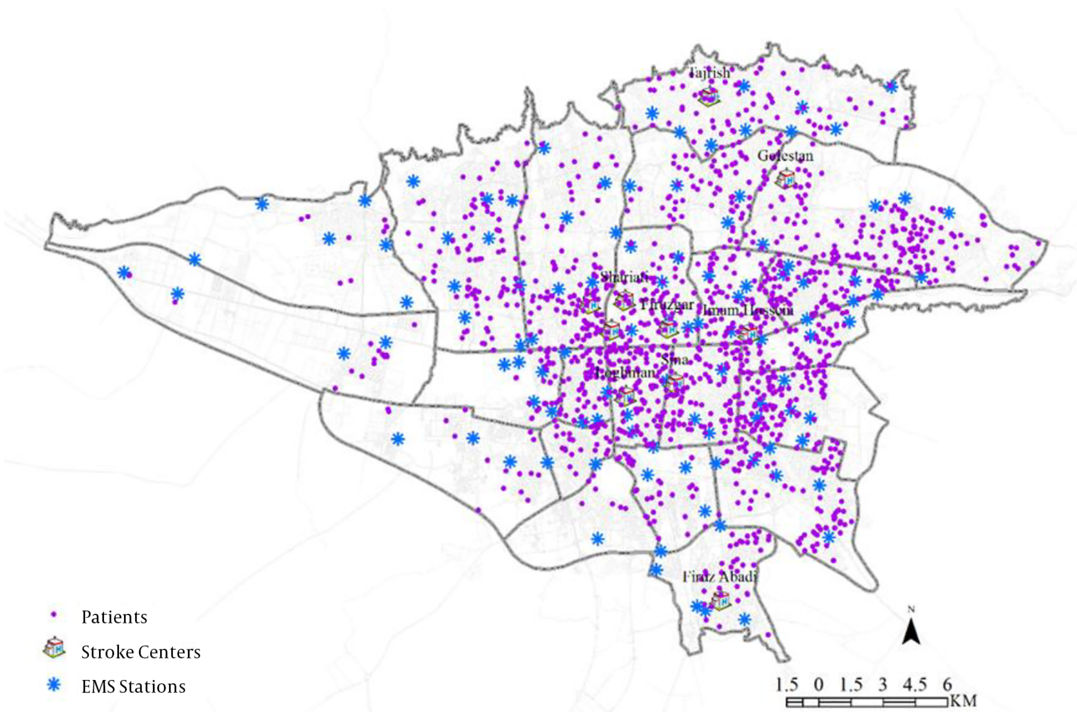

Figure 3. The dispersion pattern of patients, EMS stations, and stroke centers in Tehran

4.3. From the Patient's Location to the Stroke Center

According to the findings, the mean time interval from the patient's location to the stroke center was 17.79 ± 11.42 minutes (range = 2.4 - 83.70 minutes). In addition, the spatial pattern of access to clinical centers in Tehran was not balanced. There were few referral hospitals for stroke patients in Tehran. On the other hand, their spatial distribution was not desirable, and most of these hospitals were located in the central part of Tehran, where there was an intense physical pattern with narrow pedestrian crossings. Tehran's commercial, cultural, political, and administrative centers are concentrated in this part, thus, it often has high traffic and makes it difficult to access the hospital. This is well reflected in Figure 7. As can be seen, central Tehran has better access to health services, but in the east of Tehran, there is a long distance from the hospitals, and the traffic is heavy; thus, the access is poor, and there are hot spots. In other words, time access is generally longer in this area.

5. Discussion

5.1. General Information

From the maps in Figure 4, the spatial distribution of patients suspected to stroke was not balanced in Tehran; it was more in some areas, and less in others and the most intense concentration was observed in the center of Tehran. The spatial distribution of patients with suspected stroke in Tehran could follow three patterns: clustered, random, or dispersed. Spatial analysis of the present study data showed that the spatial pattern of suspected stroke patients in Tehran was not random and followed the cluster pattern. Numerous factors such as demographic characteristics of the resident population, air pollution, and type of area use (residential, office-commercial, workshop, etc.), and even the cultural and economic status of the resident population can be influential in this regard. For example, some people prefer to go to private medical facilities, while according to Iran's policy, EMS patients usually cannot be transferred to private centers. Therefore, people may transfer their patients to private centers by a private ambulance or car. The population distribution may be one of the possible influencing factors in this regard. For this purpose, the population of Tehran in various areas was surveyed and

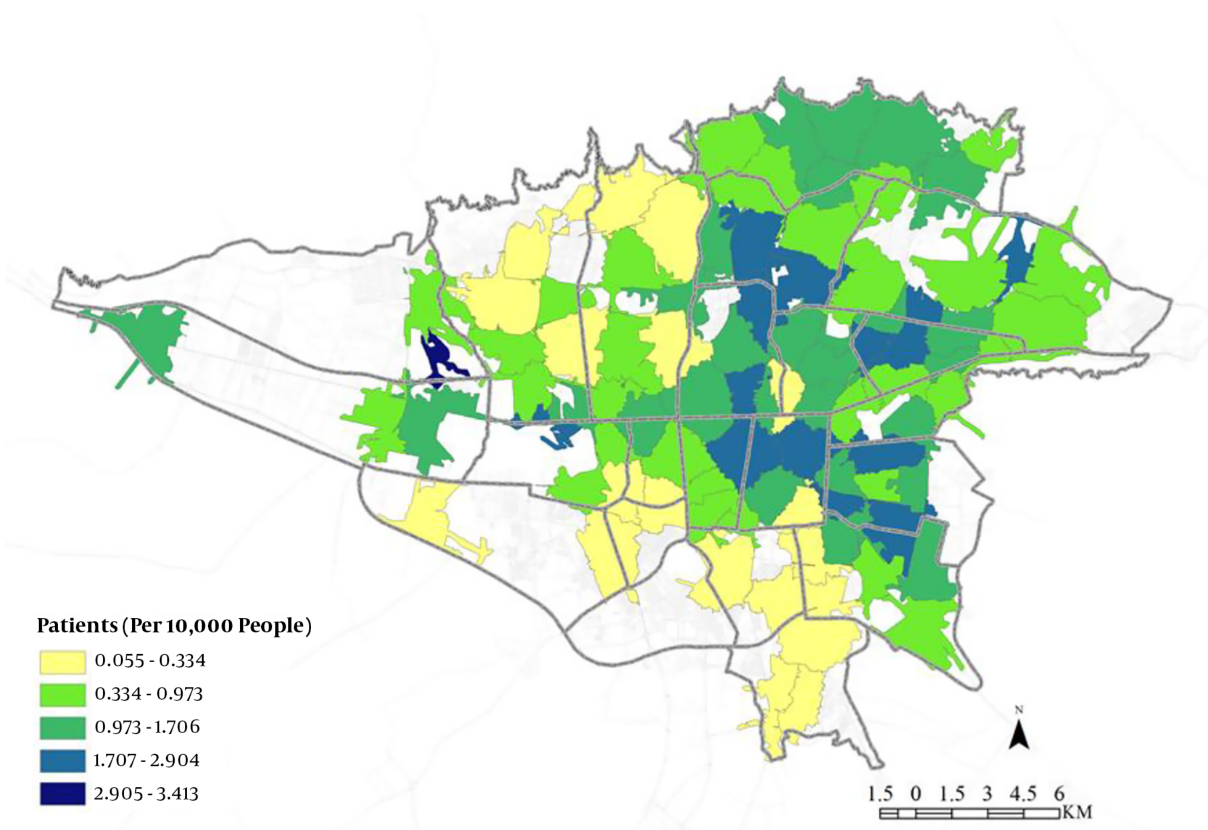

Figure 4. The spatial pattern of the proportion of suspected stroke patients per 10,000 people in Tehran

showed in Figure 4. The analysis of the map indicated that most of the population was located in districts 2, 5, 4, and 15 of Tehran municipality, but this pattern was not very consistent with the distribution of patients, as the east-west axis indicated a greater concentration of patients in the eastern part of Tehran than in the western one. However, in the north-south axis, the concentration was almost in the center.

5.2. From the EMS station to the Patient's Location

One of the important results of this study was the distance traveled by ambulances. As seen, there was no predetermined movement radius for an ambulance mission in Iran. Thus, if an EMS station lacked an ambulance at the time of a call and another station's facility would inevitably be used, it would lead to travel irrational distances in some cases. The location of EMS stations in Tehran has not been prearranged for a variety of reasons; thus, the stations' distances and their covered areas are not standard. On the other hand, for many reasons, there are many non-emergent missions in Tehran in which many ambulances are involved rather than they perform essential tasks such as the transference of a suspected stroke patient to the hospital; this may lead to frustration, waste of time, and energy of the staff. It is essential to inform the public at large and promote culture to avoid the misuse of free EMS, and even if needed, penalize the unnecessary uses of the EMS, like in some other countries. Designing a smart application or software that has ready access to all EMS databases and is capable of calculating the time and space distance to choose the best option for dispatching to the patient's location may help alleviate this problem.

5.3. From the Patient's Location to the Stroke Center

Access to hospitals is important in the control and management of stroke patients. For this purpose, the spatial pattern of stroke centers' dispersion was designed (Figure 7). As the research findings showed, the spatial pattern of access to clinical centers in Tehran was not balanced. There are a few referral hospitals in Tehran for stroke patients and their spatial distribution was not desirable, as most of these hospitals were located in the cen-

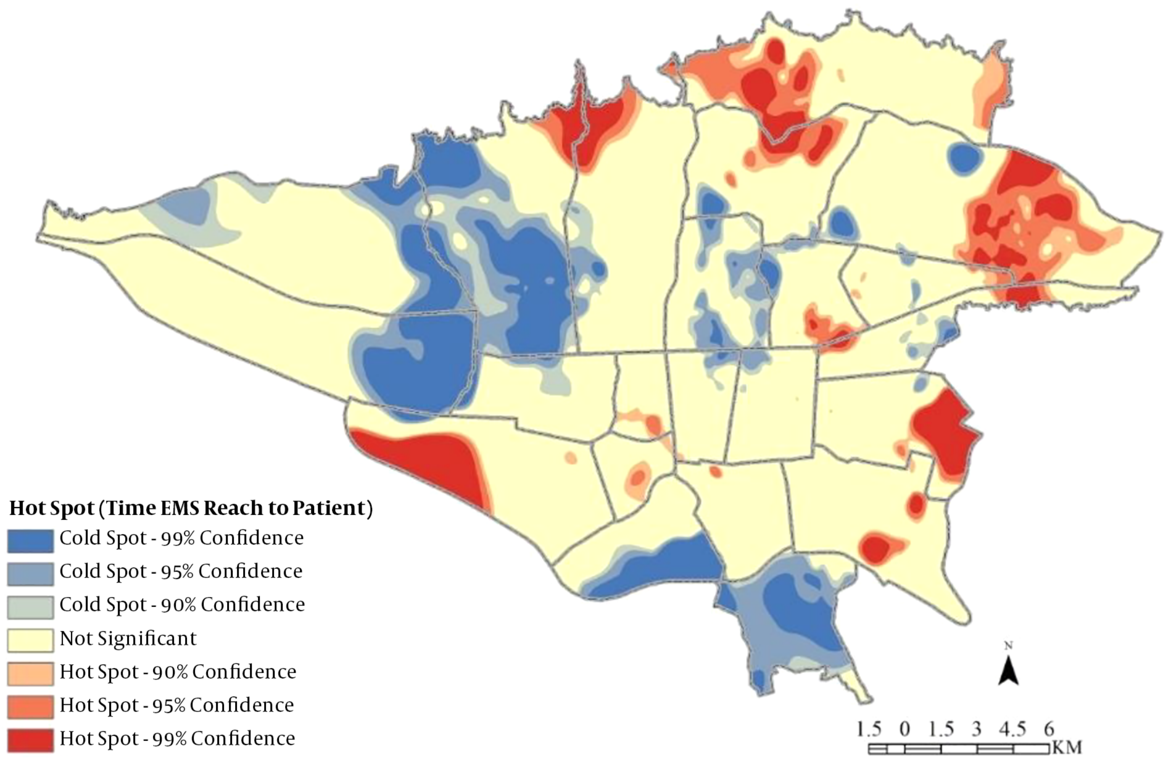

Figure 5. The spatial pattern of the arrival time of an ambulance in the patient's location

ter of Tehran. This part of the city has an intense physical pattern structure, the streets are narrow, and the administrative, commercial, cultural, and political organizations are concentrated in this part of the city, resulting in heavy traffics in the region. These factors limit access to hospital services, which sometimes causes ambulances to travel considerable distances to get to the hospital; this would certainly take a considerable amount of time, given that the city's current traffic situation takes a long time. This is well reflected in Figure 6. As can be seen, the center of Tehran had better access to health services, but in the east of Tehran, which was far from the hospitals and the traffic was heavy, the access was poor and there were hot spots. In other words, in this area, time access was generally longer.

Analysis of the spatial pattern of access to stroke centers from the patient's location revealed important points. Spatiotemporal analysis of access patterns to health centers showed that this pattern was not random but clustered. The mean arrival time in the hospital varied among areas, ranging from < 5 min to > 30 min, which was illustrated by the line pattern. The arrival time in the hospital was affected not only by the distribution of hospitals but also by the state of the transport network and the traffic in particular. Therefore, we conducted a spatial-temporal analysis of access time to the hospital; for this purpose, the maps of cold and hot spots were used. As shown in Figure 7, the modeling showed that the center of Tehran was within the range of cold spots. In general, the central part toward the north of Tehran had good access. However, the more we approached the peripheries from the center, the poorer was the access, so that the east of Tehran had the longest access time. This points to the need for reconsidering the settlement of services, especially in the eastern part of Tehran that has a more compact texture than the western part.

5.4. Limitations

The strength of this study was that it applied the role of traffic and time access, not just distance. Given that the project was implemented in six months and climate change may have an impact on the prevalence and occurrence of stroke, it is proposed to conduct a longer study to

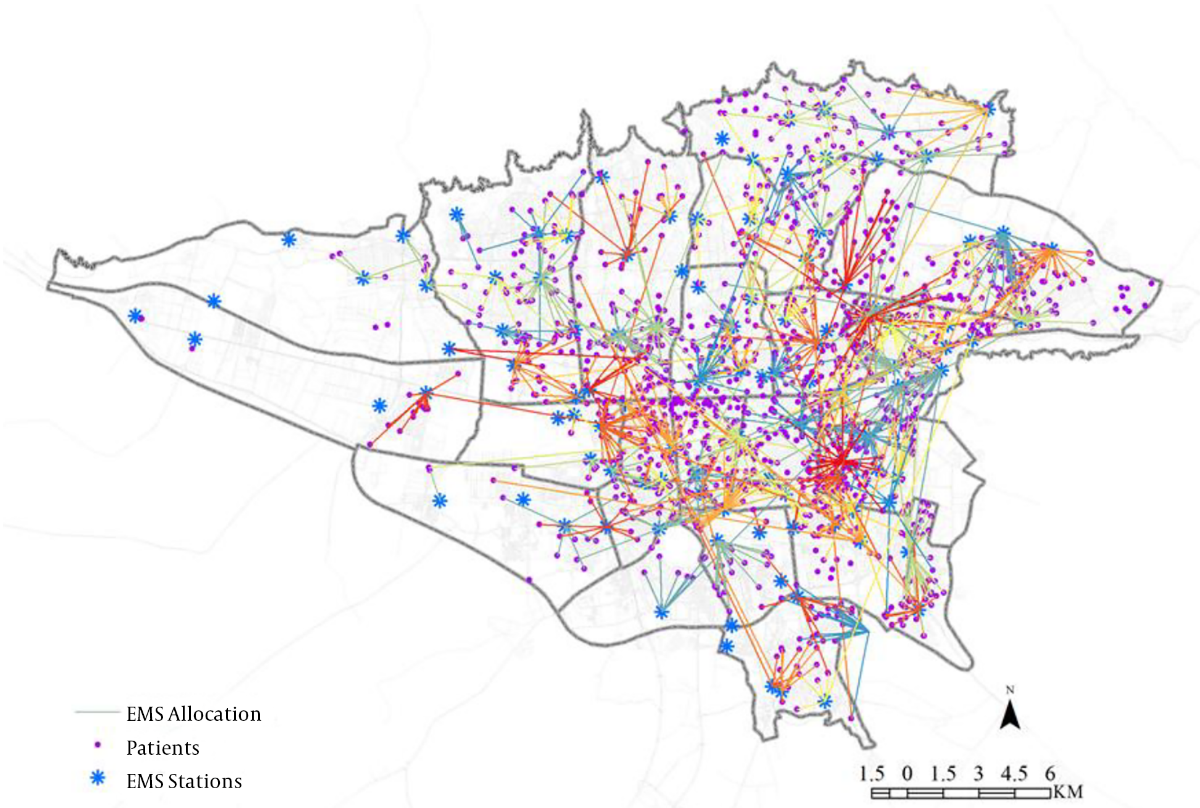

Figure 6. The movement radius of ambulances from each EMS station to the incident scene

survey the trend and spatial patterns in different seasons of a year. Spatial statistics analysis requires accurate spatial information, and gathering the spatial data was one of the most important and time-consuming constraints in this research. It is necessary to organize the acute stroke system, use a smart and integrated system to accurately record incidents based on the GPS data, report to managers accurately to plan and prioritize the distribution of specific resources and collect complete and comprehensive information for each incident in a shared database. Besides, the reasons for more strokes in some areas should be investigated by eliminating the effect of population density and evaluating other baseline characteristics such as mean age, risk factor, culture, etc.

5.5. Conclusions

Spatial analysis of data showed that the spatial pattern of patients suspected of stroke in Tehran was not random but adhered to a cluster pattern. Access time analysis indicated that the pattern was not random but formed a cluster. Regarding the analysis of the patient's transfer time to the hospital, the pattern suggested a significant difference from the east to the west of Tehran. The multiplicity of hospitals in the west and center of Tehran led to an increase in access times in eastern Tehran. The hot spot maps confirmed these patterns, and emphasized the necessity of revision of services locating, especially because the east of Tehran has a denser texture than the west.

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Footnotes

Authors' Contribution: Conception and design of the study: PHK, HF, and PS. Acquisition of data: HF, MB, and PHS. Data analysis and interpretation: HF and AR. Drafting of the article: PHS, and AR. Critical revision of the article: PHK, HF, PS, and MB. All the authors provided final approval

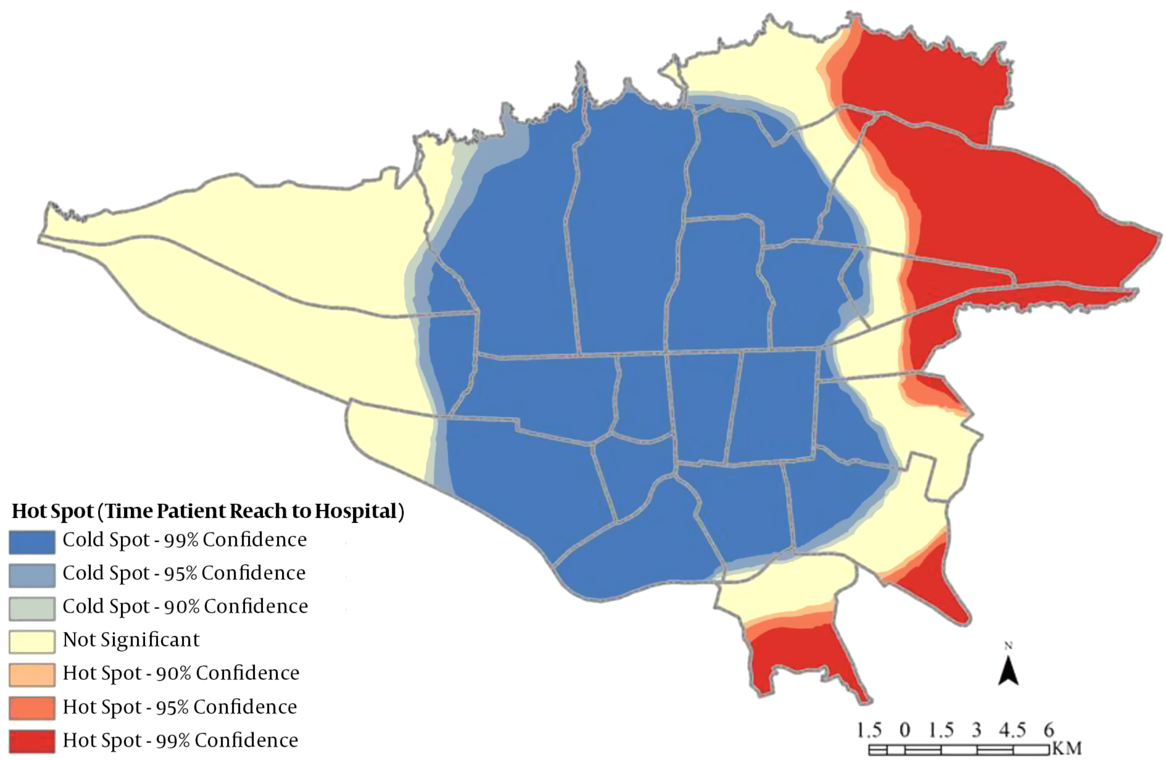

Figure 7. The spatial pattern of patient arrival in the reference hospital

of the version to publish and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interests: All the authors declare that they have no conflict of interest regarding the performed study.

Ethical Approval: The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences and assigned code: IR.TUMS.VCR.REC.1397.973. To conduct the study, permission was also obtained from the Security of Tehran EMS Center. The confidentiality of information was preserved and all items were used anonymously.

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References

1. Johnson W, Onuma O, Owolabi M, Sachdev S. Stroke: a global response is needed. *Bulletin of the World Health Organization*. 2016;**94**(9):634. doi: 10.2471/BLT.16.181636. [PubMed: 27708464].
2. Meretoja A, Kaste M, Roine RO, Juntunen M, Linna M, Hillbom M, et al. Direct Costs of Patients With Stroke Can Be Continuously Monitored on a National Level. *Stroke*. 2011;**42**(7):2007–1. doi: 10.1161/STROKEAHA.110.612119. [PubMed: 21527757].
3. Ovbiagele B, Goldstein LB, Higashida RT, Howard VJ, Johnston SC, Khavjou OA, et al. American Heart Association Advocacy Coordinating Committee and Stroke Council. Forecasting the future of stroke in the united states: a policy statement from the American heart association and American stroke association. *Stroke*. 2013;**44**(8):2361–75. doi: 10.1161/STR.0b013e31829734f2. [PubMed: 23697546].
4. Del Zoppo GJ, Higashida RT, Furlan AJ, Pessin MS, Rowley HA, Gent M. PROACT: a phase II randomized trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke. *Stroke*. 1998;**29**(1):4–11. doi: 10.1161/01.STR.29.1.4. [PubMed: 9445320].
5. Wahlgren N, Ahmed N, Dávalos A, Ford GA, Grond M, Hacke W, et al. Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *The Lancet*. 2007;**369**(9558):275–82. doi: 10.1016/S0140-6736(07)60149-4.
6. Berkhemer OA, Fransen PS, Beumer D, Van Den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *New England Journal of Medicine*. 2015;**372**(1):11–20. doi: 10.1056/NEJMoa1411587. [PubMed: 25517348].
7. Baratloo A, Forouzanfar MM, Hashemi B, Safari S, Delavar Kasmaei H, Rouhipour A, et al. Tissue Plasminogen Activator: A Literature Review. *Arch Neurosci*. 2016;**3**(1). en. e30452. doi: 10.5812/archneurosci.30452.
8. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic

stroke. *New England Journal of Medicine*. 2008;**359**(13):1317–29. doi: 10.1056/NEJMoa0804656. [PubMed: 18815396].

9. Strbian D, Ringleb P, Michel P, Breuer L, Ollikainen J, Murao K, et al. Ultra-early intravenous stroke thrombolysis: do all patients benefit similarly? *Stroke*. 2013;**44**(10):2913–6. doi: 10.1161/STROKEAHA.111.000819. [PubMed: 23970791].
10. Barber PA, Zhang J, Demchuk AM, Hill MD, Buchan AM. Why are stroke patients excluded from TPA therapy? An analysis of patient eligibility. *Neurology*. 2001;**56**(8):1015–20. doi: 10.1212/WNL.56.8.1015. [PubMed: 11320171].
11. Tong D, Reeves MJ, Hernandez AF, Zhao X, Olson DM, Fonarow GC, et al. Times from symptom onset to hospital arrival in the Get with the Guidelines–Stroke Program 2002 to 2009: temporal trends and implications. *Stroke*. 2012;**43**(7):1912–7. doi: 10.1161/STROKEAHA.111.644963. [PubMed: 22539544].
12. Meretoja A, Keshtkaran M, Saver JL, Tatlisumak T, Parsons MW, Kaste M, et al. Stroke thrombolysis: save a minute, save a day. *Stroke*. 2014;**45**(4):1053–8. doi: 10.1161/STROKEAHA.113.002910. [PubMed: 24627114].
13. Jauch EC, Saver JL, Adams Jr HP, Bruno A, Connors JJ, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2013;**44**(3):870–947. doi: 10.1161/STR.0b013e318284056a. [PubMed: 23370205].
14. National Institute of Neurological Disorders; Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *New England Journal of Medicine*. 1995;**333**(24):1581–8. doi: 10.1056/NEJM199512143332401. [PubMed: 7477192].
15. Hacke W, Donnan G, Fieschi C, Kaste M, Broderick JP, Brott T, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet*. 2004;**363**(9411):768–74.
16. Goldstein JN, Thomas SH, Frontiero V, Joseph A, Engel C, Snider R, et al. Timing of fresh frozen plasma administration and rapid correction of coagulopathy in warfarin-related intracerebral hemorrhage. *Stroke*. 2006;**37**(1):151–5. doi: 10.1161/01.STR.0000195047.21562.23. [PubMed: 16306465].
17. Jauch EC, Cucchiara B, Adeoye O, Meurer W, Brice J, Gentile N, et al. Part 11: adult stroke: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2010;**122**(18 suppl 3):S818–28. doi: 10.1161/CIRCULATIONAHA.110.971044. [PubMed: 20956227].
18. Meretoja A, Kaste M. Pre-and in-hospital intersection of stroke care. *Annals of the New York Academy of Sciences*. 2012;**1268**(1):145–51. doi: 10.1111/j.1749-6632.2012.06664.x. [PubMed: 22994234].
19. Baratloo A, Rahimpour L, Abushouk AI, Safari S, Lee CW, Abdalvand A. Effects of telestroke on thrombolysis times and outcomes: a meta-analysis. *Prehospital Emergency Care*. 2018:1–13. doi: 10.1080/10903127.2017.1408728. [PubMed: 29345529].
20. Haining RP, Haining R. *Spatial data analysis: theory and practice*. Cambridge: Cambridge university press; 2003. doi: 10.1017/CBO9780511754944.
21. Griffith DA. *Spatial econometrics: Methods and models*. Taylor & Francis; 1989. Contract No.: 0013-0095.
22. Ord JK, Getis A. Local spatial autocorrelation statistics: distributional issues and an application. *Geographical analysis*. 1995;**27**(4):286–306. doi: 10.1111/j.1538-4632.1995.tb00912.x.
23. Mitchel A. The ESRI Guide to GIS analysis, Volume 2: Spartial measurements and statistics. *ESRI Guide to GIS analysis*. 2005.
24. Kalkhan MA. *Spatial statistics: geospatial information modeling and thematic mapping*. United States: CRC press; 2011. doi: 10.1201/9781439891117.
25. Fotheringham AS, Brunsdon C, Charlton M. *Quantitative geography: perspectives on spatial data analysis*. United States: Sage; 2000.
26. Getis A. Local spatial statistics: an overview. *Spatial analysis: Modelling in a GIS environment*. 1996:261–77.
27. Anselin L, Getis A. Spatial statistical analysis and geographic information systems. *The Annals of Regional Science*. 1992;**26**(1):19–33. doi: 10.1007/BF01581478.
28. Fischer MM, Getis A. *Handbook of applied spatial analysis: software tools, methods and applications*. Germany: Springer Science & Business Media; 2009.
29. Lee JG, Selvakumar A, Alvi K, Riverson J, Zhen JX, Shoemaker L, et al. A watershed-scale design optimization model for stormwater best management practices. *Environmental Modelling & Software*. 2012;**37**:6–18. doi: 10.1016/j.envsoft.2012.04.011.
30. Bajjali W. *ArcGIS for environmental and water issues*. Germany: Springer; 2017. doi: 10.1007/978-3-319-61158-7.
31. Yang C. *Introduction to GIS programming and fundamentals with Python and ArcGIS®*. United States: CRC Press; 2017. doi: 10.1201/9781315156682.