ORIGINAL ARTICLE

Extracranial Carotid Artery Stenosis in patients with Ischemic Stroke: a hospital-based study in Shiraz, Iran

ZAHRA BEIZAVI[1], SADEGH IZADI[2], BABAK DANESHFARD[3], ABDOLHAMID SHARIAT[2]
[1]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Clinical Neurology Research Center, Department of Neurology, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Iranian Traditional Medicine Clinical Trial Research Center, Shahed University, Tehran, Iran
Correspondence to Dr. Sadegh Izadi,. Email: izadisad@sums.ac.ir, Tel/Fax: +98 711 612 10 65,

ABSTRACT

Background: Stroke is one of the most important causes of mortality and morbidity in the world and about 15% of strokes are due to large vessels involvements such as extracranial carotid artery disease. It is possible to decline the risk of stroke due to carotid artery stenosis by surgical or non-surgical investigations.
Aim: To assess the extracranial carotid artery in patients with ischemic stroke by color Doppler ultrasonography (CDS).
Materials: This cross-sectional study was done to determine the prevalence of carotid artery stenosis in the ischemic stroke patients. The data were gathered by completing data gathering sheets and review of the patient's charts. The demographic data and those obtained from carotid CDS were gathered and then analyzed using Chi-square, and Logistic Regression test.
Results: Among 200 evaluated ischemic stroke patients, 93(47%) were male and 107(53%) were female. The prevalence of severe stenosis (>70%), moderate stenosis (50%to70%) and mild stenosis (<50%) was 2.5%, 23.9% and26%, respectively. The prevalence of stenosis was 23%, 21% and 27.4% in the age groups of <50 years, 50-70 years, and >70 years, respectively. There was no significant relationship between stenosis and diabetes, ischemic heart disease, hyperlipidemia, or hypertension; however, there was a significant relationship between age and stenosis (P=0.02)
Conclusion: The prevalence of extracranial carotid stenosis in Iran is higher than that of most Asian studies but it is close to western countries' reports.
Keywords: Stroke, Carotid artery, Stenosis, Ultrasonography, Doppler

INTRODUCTION

Ischemic stroke refers to central nervous infarction diagnosed with clinical evidence of neurological deficit attributed to a vascular cause[1]. Basically, ischemic stroke is a major cause of disability and death worldwide. While extracranial carotid diseases, such as carotid occlusion, constitute almost 15% of such causes[2-6]. Studies have demonstrated that the prevalence of extracranial carotid stenosis is more than 5% from age 65 onward, and ultrasonography of the carotid artery for predicting an impending stroke is generally the most important diagnostic technique[7]. B-mode ultrasound is a non-invasive method in evaluation of the peripheral arteries which indicates early presymptomatic disease (8). In view of the relationship between the stenosis of carotid vessels and occurrence of stroke, a number of studies have been conducted in recent years to find a suitable method of research on carotid vessels. As none of these investigations had the adequate standards, invasive and non-invasive methods are still being used depending on the patient's conditions and consultant's discretion[9]. Due to its sensitivity, specific features, lower cost, and accessibility, the ultrasonography of carotid vessels continues to be a suitable method for determining the stenosis[10].

Hypertension, diabetes, ischemic heart disease, hyperlipidemia and smoking are significant risk factors of carotid stenosis and screening carotid ultrasonography is needed in subjects with many risk factors[6,11,12]. Symptomatic carotid stenosis and plaque inflammation is associated with increased risk of stroke recurrence[13]. The use of non-interventional and interventional methods to prevent the occurrence of strokes among patients who had shown no specific symptoms is reported to have produced suitable results[14].

In this study, we investigated carotid vessels atherosclerotic changes based on the CDS findings and the relationship between stenosis and risk factors in stroke patients. The results obtained through the research, conducted in one of the country's largest university centers, helped to identify the treatable reasons behind stroke including stenosis of blood vessels as well as the risk factors.

METHODS AND MATERIALS

This was a hospital-based cross-sectional study conducted during a six-month period between August 2010 and January 2011 in Shiraz Namazee teaching hospital affiliated with Shiraz University of Medical Sciences (SUMS), Shiraz, Iran. Among all ischemic stroke patients admitted in emergency and neurology wards diagnosed on the basis of medical reports, clinical examinations and computed tomography (CT) scans since August 2010 till January 2011, 200 patients were included and underwent ultrasonography of carotid artery. Patients with diagnosis of transient ischemic attack and hemorrhagic stroke were excluded.

The collected demographic data included information about their age, gender, and risk factors such as hypertension (history of hypertension or systolic blood pressure >140 mmHg and/or diastolic pressure >90 mmHg,

out of the acute phase, treated or not), diabetes (history of diabetes or fasting blood sugar above 126 mg/dL), hyperlipidemia (history of hypercholesterolemia and/or fasting total cholesterol level >200 mg/dL or LDL >130 mg/dL), smoking, and any records of coronary artery diseases. Ultrasonography of the carotid vessels was done by an expert radiologist using B-mode method to examine the anatomy. Also, blood circulation was studied by color Doppler sonography. Worthy of mention is that using B-mode and color Doppler sonography together makes an increase in the accuracy of study.

All data pertaining to carotid vessels ultrasonography were collected including the level of stenosis and its position as well as type of plaque in under 50, 50 to 60-year-old and over 60 patients in both sexes and based on the affected area. The cases in whom the stenosis was lower than 50% with no effect on blood circulation were labeled as mild, while between 50% to 70% and over 70% stenosis considered as moderate and severe, respectively.

Statistical analysis: The acquired data were assessed and analyzed in SPSS version16 made in USA, using Chi-square test and Logistic Regression model. The level of significance was set at $p<0.05$. We also used descriptive statistics including frequency, percentage, mean and standard deviation. Age considered as concomitant and the other risk factors as discrete variables.

RESULTS

From total 200 studied patients, 93(47.0%) were male and 107 (53.0%) female. The mean age of the patients was 68±13; 68±12 for men and 68±14 for women. With regard to risk factors, 124 (62.0%) had hypertension, 58 (29.0%) had ischemic heart disease, 40 individuals (20.0%) had hyperlipidemia, 35 (17.5%) suffered from diabetes, 34 (17.0%) were cigarette smokers, and 11 (5.5%) used hookah.

Table 1 shows the prevalence of stenosis in patients with and without risk factors. Any degree of carotid artery stenosis was associated with the presence of hypertension, diabetes, hyperlipidemia and smoking. Table 2 displays the relationship between stenosis and risk factors. There was no significant relationship between stenosis and hyperlipidemia (p=0.91), diabetes (p=0.83), ischemic heart disease (p=0.30), smoking (p=0.46) or hypertension (p=0.17).

Figure 1 shows the level of extracranial carotid artery stenosis on the basis of gender. In 43.0% of men and 50.5% of women, no stenosis of carotid arteries was witnessed, and severe stenosis was seen amongst only 2.2% of men and 2.8% of women.

Figure 2 shows the level of extracranial carotid artery stenosis on the basis of age. 56.8% of people aged 60 or over, 46.7% of those aged between 50 and 60, and 37.5% of individuals less than 50 years of age had stenosis of carotid vessels to some degree. The results also showed that 37 (25.3%) of over 60 year-old patients had 50% to 70% stenosis while for under 60s it was 10 (19.0%).

Generally, stenosis of more than 70% was observed among 2.5% of the patients, while 23.9% had 50% to 70% stenosis and 27.0% had less than 50. Prevalence of carotid artery stenosis in different portion of carotid arteries is illustrated in figure 3. Comparison of the percentage of carotid artery stenosis between patients that have more than 50% stenosis with patients that have less than 50% stenosis, based on the affected site, showed no significant relationship in the left and right sides. (Internal carotid artery p=0.28, carotid bulb p=0.96, common carotid artery p=0.2)

The echolucency of each plaque was determined on the basis of CDS findings, and hyperechoic plaques were seen to be higher in number on the right side in 57% of individuals with vessel stenosis of more than 50%, while hypoechoic plaques were present in 25% of such patients. On the left side, 60% of individuals with vessel stenosis of more than 50% had hyperechoic plaques and 18% of those patients had hypoechoic plaques.

Table 1: Prevalence of carotid artery stenosis in the patients with and without risk factors

Risk factor	Stenosis (n=115)	No stenosis (n=85)
Hypertension	78(62.9%)	46(37.1%)
No hypertension	37(48.7%)	39(51.3%)
Hyperlipidemia	21(52.5%)	19(47.5%)
No hyperlipidemia	94(58.8%)	66(41.3%)
Ischemic heart disease	32(55.2%)	26(44.8%)
No ischemic heart disease	83(58.5%)	59(41.5%)
Diabetes	19(54.3%)	16(45.7%)
No diabetes	96(58.2%)	69(41.8%)
Hookah	5(54.5%)	5(45.5%)
No hookah	109(57.7%)	80(42.3%)
Cigarette	21 (61.8%)	13(38.2%)
No cigarette	94(56.6%)	72(43.4%)

Table 2: relationship between carotid artery stenosis and risk factors in the ischemic stroke patients

Risk Factors	P value	OR*(95%CI)
Hypertension	0.17	1.55(0.82-2.92)
Hyperlipidemia	0.91	0.95(0.44-2.05)
Ischemic heart disease	0.30	0.70(0.36-1.36)
Diabetes	0.83	1.08(0.49-2.38)
Cigarette	0.15	1.78(0.80-3.94)
Hookah	0.21	0.41(0.10-1.68
Age	0.02	1.02(1.03-1.04)
Sex	0.46	0.79(0.43-1.46

*OR: Odes Ratio, CI: Confidence Interval

Fig.1: Prevalence of carotid artery stenosis by gender in the ischemic stroke patients

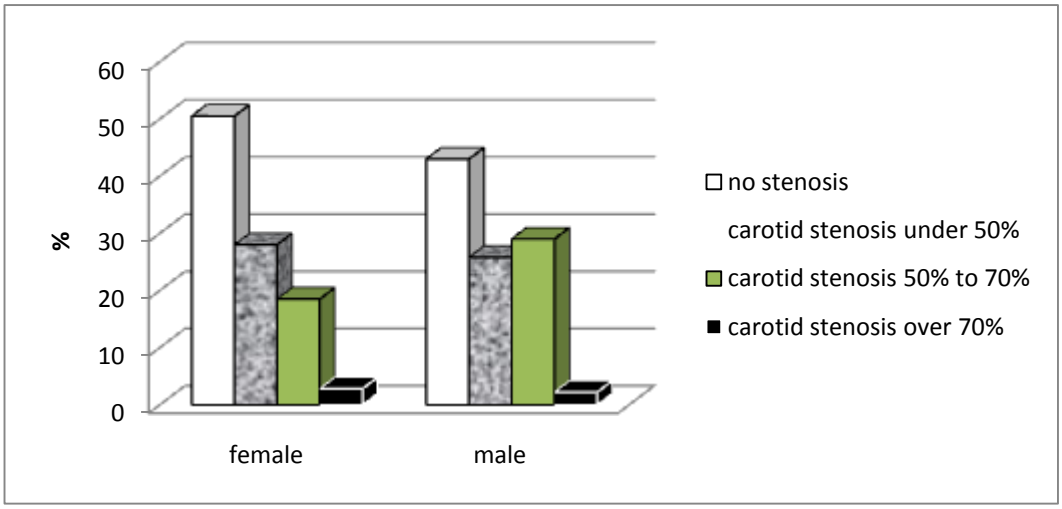


Fig. 2: Prevalence of carotid artery stenosis by age in the ischemic stroke patients

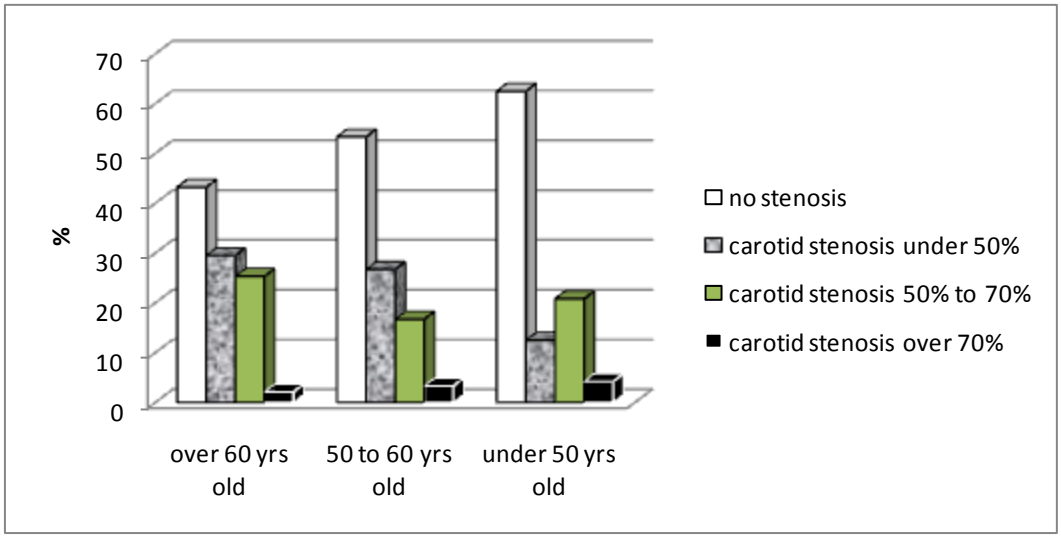
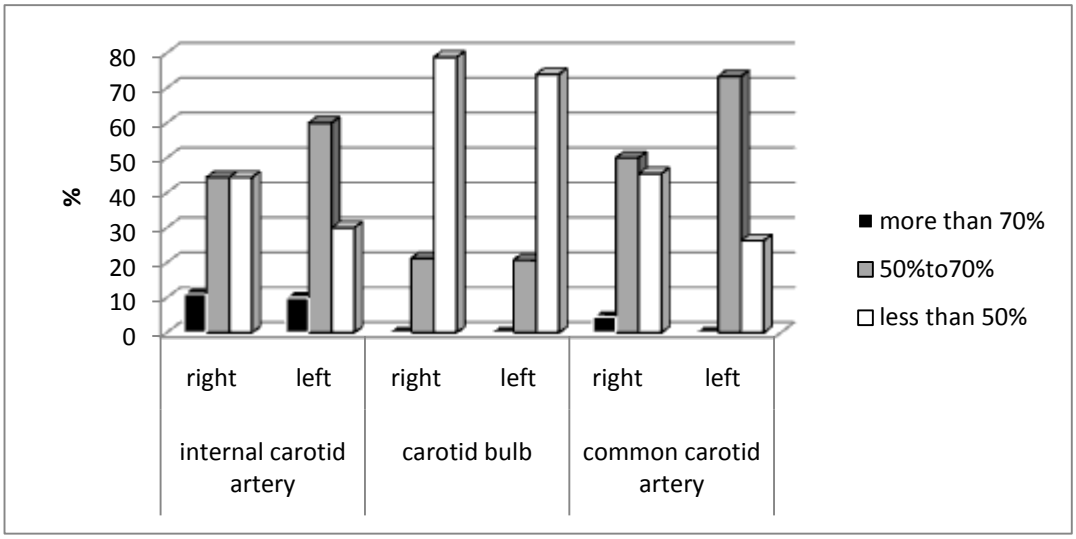


Fig. 3: Prevalence of carotid artery stenosis in the different portions of carotid arteries in the ischemic stroke patients



DISCUSSION

In this study, 93 men and 107 women were included while 57.0% of men and 49.5% of women suffered from different degrees of stenosis in their blood vessels. The moderate-to-severe stenosis among men was 31.2% and it was 21.3% for women. Serena et al, in their research in Spain, showed that 28% of ischemic stroke cases were related to carotid arteries[15].

In a research done by Ghaffarpur et al, stenosis of internal carotid arteries was studied and severe stenosis was reported in 20% of cases, while 36% suffered from mild stenosis and 44% had moderate stenosis[16].

In another study conducted in Taiwan, the moderate-to-severe stenosis of internal carotid artery was reported to be only 8% of stroke patients, whereas the figure in Western countries is about 20%. In this study, the impact of race on the vessels' affected area was researched. They reported that atherosclerotic engagement of the intracranial vessels among Asian and Black populations was higher than that of extracranial ones, whereas among the country's white population, the engagement of extracranial vessels was higher[17].

In this study, the level of extracranial carotid vessels involvement, as compared with that of other studies conducted in Asia, was higher and the figures obtained about stenosis of the carotid vessels are closer to those in Western countries. This can be due to westernization of lifestyle in Iran in recent years. On the one hand, in view of the fact that to treat severe stenosis of vessels (over 70%), there is a need for interventions in the form of stenting or endarterectomy, only 2.5% of patients suffered from severe stenosis; if they have other criteria, one of the above methods of intervention ought to be adopted in order to treat the stenosis and reduce the likelihood of stroke in them.

Furthermore, 22.5% of patients suffered from moderate stenosis of the carotid vessels which the chance of stroke recurring in them is high; thus, in addition to medical treatment, they should be monitored periodically through ultrasonography so that in case of a rise in vessel stenosis, some form of vessel intervention may be adopted.

In a research carried out by Grønholdt et al, it was shown that there were higher risks of stroke with hypoechoic plaques as compared to hyperechoic ones in patients with more than 50% vessel stenosis[18]. Also, Wang et al showed that 55.2% of stroke patients had atherosclerotic plaque in their carotid blood vessels while 37% of those plaques were unstable and could lead to embolic stroke without creating considerable stenosis in vessels[19]. Additionally, the research conducted by Espagnoli et al indicated that the stenosis level in carotid vessels is not by itself sufficient to identify patients with high risk of stroke; rather the type of plaque and its stability level should also be taken into account[20].

In our present research, the plaques identified on both right and left sides were mostly of hyperechoic type rather than hypoechoic. Since the formation of blood clot and thrombosis on the hypoechoic plaque is more likely and it is a predictor of recurrence of stroke[11], treatment by antiplatelet and Statins reduced the likelihood of blood clot formation and subsequently the occurrence of stroke.

In line with other studies, the prevalence of carotid vessels stenosis increases with advanced age[5,12,21,25]. In addition, stenosis was shown to be more prevalent among men (57%) than women (49.5%).

A study done by Iemolo F et al. revealed carotid artery stenosis is more seen in women compared with men, whereas the prevalence of carotid plaque area is more observed in men[22]. In a study conducted by Smith et al., it was revealed since the life expectancy of women is higher and incidence of stroke is more in older age, the number of cases in women is more than men (23). But in another study, it was shown that 55% of cases in USA are male (24). There are different criteria such as hormone effects and life expectancy in determination of the correlation between gender and carotid stenosis (26). Also, different types of study can be related to the difference of the results[27,28].

Controlling modifiable risk factors and lifestyle is essential for preventing stroke. Considering the fact that most of all stroke occurring each year are first stroke, individuals with risk factors can be identified for specific management and modification of these risk factors[6]. Suanprasert et al revealed that well-controlled risk factors are very important for protection of recurrent ischemic stroke[29].

In our study, there was a significant relationship between hypertension and stenosis and all the patients had at least one risk factor. This information helps us for policy purposes because it is possible that improved risk factors have significantly lowered the population's stroke rate[30].

Similar to other parts of the world, investigations in Iran show that hypertension as a modifiable risk factor is the most prevalent risk factor for stroke (17, 25, 31). It should be controlled either by lifestyle measures or pharmacological means. For improving the control of modifiable risk factors, a careful patient follow-up is required.

In a research done by Hicks et al, smoking was known as a risk factor for progression of moderate asymptomatic carotid artery stenosis, but age, gender and hypertension were not significant predictors of progression to severe stenosis (32). In our research, the level of tobacco smoking was 22.5%, and smoking was ranked after hypertension, ischemic heart disease, hyperlipidemia, diabetes, therefore smoking as one of the risk factors of atherosclerosis has been proposed to identify high risk patients.

It should be mentioned that this study was a hospital-based study that has less accuracy in comparison to population-based studies. The other limitation of this study is inter-observer bias of evaluation of carotid ultrasonography and missing of some data regarding the patient's history.

CONCLUSION

The level of extracranial involvement in this study is similar to that of Western countries and higher than another study in Asia. The present study showed that in this region, as in other regions, hypertension is the most prevalent risk factor outweighing all other risk factors. In view of this issue, by informing the public and encouraging more precise policy-making on the part of health officials to control those risk

factors especially hypertension, stenosis of carotid vessels and occurrence of stroke is likely to be markedly reduced.

Acknowledgement: This study was supported financially by a research grant from Shiraz University of Medical Sciences and this article was extracted from thesis of Zahra Beizavi, medical student of SUMS. The authors would like to thank Dr. Nasrin Shokrpour at Center for Development of Clinical Research of Nemazee Hospital for editorial assistance.

Conflict of Interest: Nothing to declare.

REFERENCES

1. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A,et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association.Stroke.2013; 44(7):2064-89. doi: 10.1161/STR.0b013e318296aeca. PubMedPMID:23652265.
2. Daneshfard B, Izadi S, Shariat A, Toudaji MA, Beyzavi Z, Niknam L. Epidemiology of stroke in Shiraz, Iran. Iranian journal of neurology. 2015;14(3):158–163. PubMedPMID: 26622981.
3. Rahme R, Abruzzo TA, Ringer AJ. Acute ischemic stroke in the setting of cervical carotid occlusion: a proposed management strategy. World Neurosurg. 2011 Dec; 76(6 Suppl):S60-5. doi: 10.1016/j.wneu.2011.08.016. PubMed PMID: 22182272.
4. Matthew L. Flaherty, Brett Kissela, Jane C. Khoury, Kathleen Alwell, Charles J. Moomaw. Carotid Artery Stenosis as a Cause of Stroke. Neuroepidemiology. 2013; 40(1): 36–41. doi:10.1159/000341410. PubMed PMID: 23075828.
5. Lim YJ, Kim YW, Choe YH, Ki CS, Park SK. Risk Factor Analysis for Development of Asymptomatic Carotid Stenosis in Koreans. J Korean Med Sci. Feb 2006; 21(1): 15–19. doi: 10.3346/jkms.2006.21.1.15. PubMed PMID: 16479058
6. Rundek T, Sacco RL. Risk Factor Management to Prevent First Stroke. Neurol Clin. Nov 2008; 26(4): 1007–ix.doi: 10.1016/j.ncl.2008.09.001. PubMed PMID: 19026901.
7. Eckstein HH, Kühnl A, Dörfler A, Kopp IB, Lawall H, Ringleb PA. The diagnosis, treatment and follow-up of extracranial carotid stenosis: a multidisciplinary German-Austrian guideline based on evidence and consensus. Dtsch Arztebl Int. 2013; 110(27-28):468-76. doi: 10.3238/arztebl.2013.0468. PubMed PMID: 23964303.
8. Ebrahim S, Papacosta O, Whincup P, Wannamethee G, Walker M, Nicolaides AN. Carotid Plaque, Intima Media Thickness, Cardiovascular Risk Factors, and Prevalent Cardiovascular Disease in Men and Women . Stroke. 1999; 30: 841-850 doi: 10.1161/01.STR.30.4.841.
9. Johnson MB, Wilkinson ID, Wattam J, Venables GS, Griffiths PD. Comparison of Doppler ultrasound, magnetic resonance angiographic techniques and catheter angiography in evaluation of carotid stenosis. Clin Radiol. 2000; 55(12):912-20. doi.org/10.1053/crad.2000.0518. PubMed PMID: 11124070.
10. Nederkoorn PJ, van der Graaf Y, Hunink MG. Duplex Ultrasound and Magnetic Resonance Angiography Compared With Digital Subtraction Angiography in Carotid Artery Stenosis.Stroke.2003;34(5):1324-32.doi:10.1161/01.STR.0000068367.08991.PubMed PMID:12690221.
11. Ederle J, Brown MM. Stroke prevention. Herz. 2008 Nov;33(7):518-23. doi: 10.1007/s00059-008-3167-4.PubMed PMID: 19066748.
12. Alkali NH, Bwala SA, Akano AO, Osi-Ogbu O, Alabi P, Ayeni OA. Stroke risk factors, subtypes, and 30-day case fatality in Abuja, Nigeria. Niger Med J. 2013 Mar;54(2):129-35. doi: 10.4103/0300-1652.110051. PubMed PMID: 23798800.
13. 13.Marnane M, Prendeville S, McDonnell C, Noone I, Barry M, Crowe M, et al. Plaque inflammation and unstable morphology are associated with early stroke recurrence in symptomatic carotid stenosis. Stroke. 2014 Mar;45(3):801-6. doi: 1161/STROKEAHA.113.003657. PubMed PMID: 24481971.
14. 14.Cruz-Cosme C, Segura T. Severe asymptomatic carotid stenosis: a neurological perspective. Rev Neurol. 2012; 1; 55(5):283-96. PubMed PMID:22930140.
15. Serena J, Irimia P, Calleja S, Blanco M, Vivancos J, Ayo-Martín O. Ultrasound measurement of carotid stenosis: recommendations from the Spanish Society of Neurosonology. Neurologia. 2013; 28(7):435-42. doi: 10.1016/j.nrl.2012.07.011. PubMed PMID: 23040716.
16. Ghafarpoor M, Harirchian M, Khamseh F, Razazian N. Evaluation of internal carotid arteries stenosis in patients with transient ischaemic attack in Imam Khomeini Hospital. Tehran University Medical Journal1999; 57(1): 53-58. Persian.
17. Tan TY, Chang KC, Liou CW, Schminke U. Prevalence of Carotid Artery Stenosis inTaiwanese Patients with One Ischemic Stroke. Journal of Clinical Ultrasound2005; 33:1-4. PubMed PMID: 15690439.
18. Grønholdt ML, Nordestgaard BG, Schroeder TV, Vorstrup S, Sillesen H. Ultrasonic echolucent carotid plaques predict future strokes. Circulation. 2001; 3:104(1):68-73. doi: 10.1161/hc2601.091704 PubMed PMID:11435340.
19. Wang B, Sun S, Liu G, Li Y, Pang J, Zhang J, et al. Correlation between aortic/carotid atherosclerotic plaques and cerebral infarction. Exp Ther Med 2013; 6(2):407-410.doi: 10.3892.2013.1129 PubMed PMID:24137198.
20. Spagnoli LG, Mauriello A, Sangiorgi G, Fratoni S, Bonanno E, Schwartz RS, et al. Extracranial thrombotically active carotid plaque as a risk factor for ischemic stroke. JAMA. 2004; 20:292(15):1845-52. PubMed PMID:15494582.
21. Savji N, Rockman CB, Skolnick AH, Guo Y, Adelman MA, Riles T, et al. Association between advanced age and vascular disease in different arterial territories: a population database of over 3.6 million subjects. J Am Coll Cardiol. 2013 Apr 23;61(16):1736-43. doi: 10.1016/j.jacc.2013.01.054. PubMed PMID:23500290.
22. Iemolo F, Martiniuk A, Steinman DA, Spence JDSex differences in carotid plaque and stenosis. Stroke. 2004 Feb;35(2):477-81. doi: 10.1161/01.STR.0000110981.96204.64 PubMed PMID:14739419.
23. Smith DB, Murphy P, Santos P, Phillips M, Wilde M. Gender differences in the Colorado Stroke Registry. Stroke. 2009 Apr;40(4):1078-81. doi:10.1161/STROKEAHA.108.541730. PubMed PMID: 19211487.
24. Johnson M, Bakas T. A Review of Barriers to Thrombolytic Therapy: Implications for Nursing Care in the Emergency Department. J Neurosci Nurs 2010;42:88-94. PubMed PMID:20422794.
25. Roy-O'Reilly M, McCullough LD. Sex differences in stroke: The contribution of coagulation. Exp Neurol. 2014 Feb 19. pii: S0014-4886(14)00056-9. doi: 10.1016/j.expneurol.2014.02.011. PubMed PMID:24560819.
26. Wang J, Ning X, Yang L, Tu J, Gu H, Zhan C, et al. Sex Differences in Trends of Incidence and Mortality of First-Ever Stroke in Rural Tianjin, China, From 1992 to 2012. Stroke. 2014 Apr 15. PubMed PMID:24736241.
27. Suwanwela NC. Stroke Epidemiology in Thailand. J Stroke. 2014 Jan;16(1):1-7. PubMed PMID:24741559.
28. Suanprasert N1, Tantirithisak T.Impact of risk factors for recurrent ischemic stroke in Prasat Neurological Institute. J Med Assoc Thai. 2011 Sep;94(9):1035-43. PubMedPMID 21970191.
29. Fang MC, Perraillon MC, Ghosh K, Cutler DM, Rosen AB. Trends in Stroke Rates, Risk, and Outcomes in the United States, 1988-2008. Am J Med. 2014 Mar 25. pii: S0002-9343(14)00271-X. doi: 10.1016/j.amjmed.2014.03.017. PubMed PMID:24680794.
30. Ma AJ, Dong Z, Li G. Prevalence rates and risk factors on stroke among 50 - 79 years-olds in Beijing. Zhonghua Liu Xing Bing Xue Za Zhi. 2012 Jul; 33(7):645-8. PubMed PMID: 22968008.
31. Iranmanesh F, Salehi M, Bakhshi H, Arab R.Silent stroke and related risk factors. Journal of Gorgan University of Medical Sciences.2013; 15: no1. Persian.
32. Hicks CW, Talbott K, Canner JK, Qazi U, Arhuidese I, Glebova NO, et al. Risk of Disease Progression in Patients with Moderate Asymptomatic Carotid Artery Stenosis: Implications of Tobacco Use and Dual Antiplatelet Therapy. Ann Vasc Surg. 2014 Feb 12. doi: 10.1016/j.avsg.2014.02.007. PubMed PMID: 24530720.