Journal of Health Sciences

RESEARCH ARTICLE Open Access

Benefits of low-dose carotid CT angiography in stroke patients

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ABSTRACT

Introduction: Computed tomography angiography (CTA) represents the gold standard as a method for the diagnosis of carotid artery diseases. The current topic is the use of CTA for the evaluation of carotid arteries with a reduction in the dose of contrast agent and dose of ionizing radiation, which, with adequate preparation, would enable the use of this method in some risk groups. The aim of this study was to evaluate the feasibility and image quality of a new low-dose CTA protocol in comparison with a standard protocol.

Methods: Forty patients with recumbent ischemic stroke were included in the study, twenty of whom underwent low-dose CTA, and the remaining twenty underwent a standard CTA protocol of the carotid arteries.

Results: No significant difference was found between the mean values of CT number (Hounsfield unit), signal-to-noise ratio, contrast-to-noise ratio, and subjective assessment of image quality in the comparison of the control and experimental groups. CT dose index, volume, and dose length product were significantly lower in patients who underwent low-dose carotid CTA. There was no significant difference in the degree of carotid stenosis between color Doppler and CTA.

Conclusion: The use of the low-dose protocol for carotid CTA allows the application of this method in risk groups, in which it was previously not possible to perform, with the same image quality in comparison with the standard protocol.

Keywords: Computed tomography angiography; contrast media; signal-to-noise ratio; radiation, ionizing

INTRODUCTION

The arteries of the carotid arterial system are often the site of various pathological conditions such as dissections, pseudoaneurysms, and, by far, the most common, atherosclerotic plaques that lead to stenosis or occlusion. Atherosclerosis is a condition in which fatty deposits (atherosclerotic plaques) accumulate in the walls of the medium and large arteries, leading to reduced or blocked blood flow and, as a result, very often causing an ischemic stroke (1). Despite much more aggressive and effective treatment of stroke today, one-third of patients survive with a residual mild or severe neurological deficit, requiring enormous sums for further treatment and rehabilitation of these patients, and one-third unfortunately end fatally. Therefore, measures and programs for prevention and early diagnosis of this pathological condition are essential. Non-invasive radiological methods that serve us to assess the flow, anatomy, anatomical changes, and pathological conditions of the carotid arteries are primarily extracranial color Doppler ultrasound, computed tomography angiography (CTA), and MR angiography. Color Doppler is a completely non-invasive method that is comfortable for the patient and very cost-effective compared to CTA. The gold standard in the assessment of carotid arteries is CTA, which achieves a high spatial resolution in the analysis of small-caliber arterial blood vessels. However, the disadvantages of CTA are the use of iodine contrast agents and ionizing radiation. Recently, increasing attention has been drawn to the potential harm to patients from ionizing radiation, such as a higher risk of cancer (2,3). According to the results of a large study published in JNCI Cancer Spectrum, the risk of thyroid cancer and leukemia was increased threefold in patients between the ages of 36 and 45 who had undergone a computed tomography (CT) scan of the neck (4). The use of iodinated contrast agents can adversely affect kidney function, especially in patients with impaired renal function, and cause contrast-induced nephropathy (CIN), a serious complication of angiographic procedures (5,6). According to Shams and

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Submitted: 30 September 2023/Accepted: 28 November 2023

DOI: https://doi.org/10.17532/jhsci.2023.2357

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Mayrovitz, The incidence of CIN in patients with initially normal renal function is <5%, in patients with pre-existing renal dysfunction the prevalence is 12-27%, causing prolonged hospitalization, increased morbidity and mortality and additional costs (7). Reducing the X-ray voltage is the most common approach to reducing the radiation dose (8), but this can increase the noise level, which unfortunately also means a poorer quality of the image itself. Recently, more work has been done to solve this problem, and several publications have reported scanning with low tube voltage and with lower doses of the iodine contrast agent without degradation of image quality (9,10). The protocol for the use of low-dose CTA compared to conventional CTA involves a reduction in the dose of iodine contrast agent as well as the dose of ionizing radiation.

METHODS

Forty patients, including 23 men and 17 women, aged 60-79 years with ischemic stroke, who were treated in the neurology clinic at the Clinical Center University of Sarajevo, were included in the study. All patients with clinically significant stenosis of the internal carotid artery, i.e., stenosis of the artery lumen by more than 50%, previously verified by the ultrasound color Doppler method, and who had survived an ischemic stroke were included in the study. Patients with non-thrombotic ischemic stroke, patients with hemorrhagic stroke or other pathological conditions mimicking ischemic stroke, patients with clinically insignificant stenosis of the internal carotid artery (stenosis of the arterial lumen below 50%), and renal patients with a glomerular filtration rate below 60 mL/min were not included in the study.

The study was conducted at the Clinic for Radiology of the Clinical Center of Sarajevo University, and the conduct of the study was approved by the Ethics Committee of the Clinical Center of Sarajevo University.

The working hypothesis of the study was that low-dose CTA is an equally sensitive diagnostic method for the evaluation of pathological changes in the carotid arteries compared to conventional CTA of the blood vessels of the neck.

In the first phase of the study, an extracranial color Doppler of the carotid arteries was performed in all patients to determine the degree of stenosis and the presence of atherosclerotic plaques. The color Doppler was performed with the GE Voluson 730 device. A linear high-frequency ultrasound probe operating at a frequency of 14 MHz was used. Several parameters were set on the ultrasound device in order to obtain an optimal image. The “gain” was set to −8, which increases the sensitivity of the flow by amplifying the feedback signal. Depth and focus are set to 2-3 cm, depending on the distance of the carotid arteries from the skin. The “pulse repetition frequency” is set to 5 kHz, covering a wide range of velocity scales.

The degree of stenosis was determined by analyzing the flow velocity at the point of greatest stenosis of the internal carotid artery, measuring two parameters: the “peak systolic velocity” and the “end-diastolic velocity.” The degree of stenosis was determined according to the guidelines of the North American Asymptomatic Carotid Endarterectomy Trial (NASCET), published in August 1999 (Table 1) (11).

TABLE 1. North American Asymptomatic Carotid Endarterectomy Trial guidelines for determining the degree of carotid artery stenosis

ICA stenosis (%)	ICA PSV (em/s)	ICA EDV (em/s)	PSV ratio: ICA/CCA
Normal	<125	<40	<2.0
<50%	<125	<40	<2.0
50-69%	125-230	40-100	2.0-4.0
>70%	>230	>100	>4.0
Near occlusion	Variable	Variable	Variable
Total occlusion	Undetectable	Undetectable	Not applicable

PSV: Peak systolic velocity, EDV: End-diastolic velocity

In the next phase of the research, CTA was performed on patients in whom clinically significant stenosis of the carotid arteries was detected by Doppler. The examination was performed in the supination position on a Toshiba Aquilion Prime 160 multislice spiral CT scanner. CTA data acquisition was performed according to an established protocol that included spiral mode, 0.8-s slices, 8 or 16 × 1.25 mm collimation, a pitch of 1.375:1, a slice thickness of 1.25 mm, and a reconstruction interval of 1.00 mm with a FOV (“field of view”) for CTA acquisition of 22 cm. The scan covered the area from the aortic arch to the arteries of the circle of Willis. Only the arterial contrast phase was performed with the intravenous administration of a water-soluble iodine contrast agent. In the control group, i.e., ten patients, CTA of the neck vessels was performed according to the standard protocol, which involved the administration of 100 mL of iodine contrast medium using an automatic injector with a tube voltage of 120 kV. In the experimental group, which included ten patients, low-dose CTA was performed according to the modified protocol. The protocol for low-dose CTA of the neck comprised the administration of 30 mL of iodine contrast medium and a 50 mL test bolus (0.9% sodium chloride), with the tube voltage reduced to 100 kV. Contrast opacification of the blood vessels was measured in the area of the carotid bulb and determined in the Hounsfield unit (HU). The contrast opacity of a blood vessel that is considered minor and sufficient for the assessment of pathological conditions previously verified by Doppler is 200 HU. HU is a universal unit of measurement used in CT examinations to measure the opacity of various tissues.

The NASCET guidelines were also used to measure carotid stenosis on CT. The degree of stenosis was determined according to the formula in which the diameter of the largest arterial stenosis (B) and the diameter of the post-stenotic part (A) were measured (Figure 1).

The objective image quality is determined by the parameters signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR). The SNR is used in radiology and serves to measure the real signal, which reflects the real anatomy, in relation to the so-called “noise,” which indicates, for example, random quantum patterns, and the lower it is, the “grainier” and poorer the quality of the CT image. The SNR is the quotient of the signal in the lumen of the blood vessel on the native series and the standard deviation of the background noise (Formula 1), while the CNR is the difference between the signal of the contrast-enhanced blood vessel and the signal of the tissue in the background divided by the standard deviation of the background noise (Formula 2).

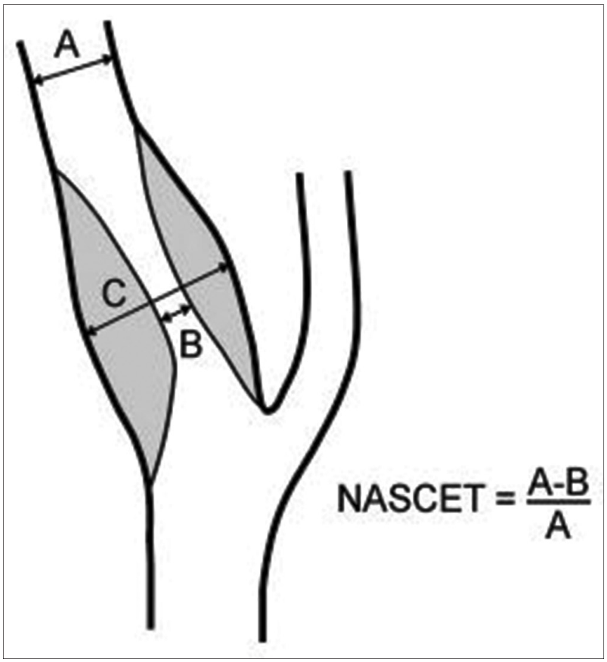

FIGURE 1. North American Asymptomatic Carotid Endarterectomy Trial formula for carotid stenosis measurement on CT (12).

$$\mathrm{SNR} = \frac{\text{Avg pixel values in Signal ROI}}{\text{Std Background ROI}}$$

Formula 1. Formula for calculating SNR

$$\mathrm{CNR} = \frac{\text{Avg Signal ROI} - \text{Avg Background ROI}}{\text{Std Background ROI}}$$

Formula 2. Formula for calculating CNR

The radiation dose during a CT scan is determined by the "CT dose index-volume" (CTDIvol) and the "dose length product" (DLP) values, and the specified value is automatically calculated by the CT scanner according to the scan parameters. The resulting values are then archived in a dose information page and a structured report called "Digital Imaging and Communications in Medicine," or DICOM for short. The unit of measurement for CTDIvol is mGy, and for DLP, it is mGy*cm.

Two readers with several years of experience in the interpretation of CTA images, who were blinded to all clinical information about the subjects, independently reviewed the CTA images and subjectively rated them: the graininess of the image, the sharpness of the arterial contour, and the artifact of the stripes on a scale from 1 to 4.

RESULTS

The study comprised a total of 40 patients, who were divided into two separate groups. The first group of patients was scanned using a voltage of 100 kV, and the second group used a voltage of 120 kV. All other scanning parameters were kept constant between the two groups.

The average age of the patients in the first group (120 kV) was 70 years, while the average age of the patients in the second group (100 kV) was 72 years (Table 2). However, the age difference between the two groups was not statistically significant (Student's t test, $p = 0.425$).

According to the one-sample binomial test, male and female patients are equally likely to occur ($p = 0.200$). However, it should be noted that the study included 23 (57.5%) male and 17 (42.5%) female patients. No significant differences were found in the frequency of male and female patients between the two groups (Fisher's exact test, $p = 1.000$).

TABLE 2. Sex and age distribution of patients included in the study. Number of patients (*N*), mean ($\bar{x}$) and standard deviation (σ) of patients' age in two evaluated groups

kV	Sex						Total		
	Male			Female					
	Age (years)			Age (years)			Age^a (years)		
	N	$\bar{x}$	σ	N	$\bar{x}$	σ	N	$\bar{x}$	σ
Group									
120	11	69	6	9	72	7	20	70	6
100	12	74	7	8	70	9	20	72	8
Total	23	72	7	17	71	8	40	71	7

^{a}The age distribution is normal (Kolmogorov-Smirnov test, *P*=0.200)

Figure 2 shows the location of the stenosis (left or right) in two groups of patients. In total, seventeen patients (43%) were diagnosed with stenosis of the right internal carotid artery and twenty-three (57%) with stenosis of the left internal carotid artery. The distribution of stenosis localization in the two groups of patients studied was not significantly different (Fisher's exact test, $p = 0.262$).

The boxplot in Figure 3 shows the degree of stenosis at different locations for two patient groups. No significant difference was found between the mean values of the degree of stenosis in two groups (Mann-Whitney U test, $p = 0.142$) or between two locations (Mann-Whitney U test, $p = 0.745$). The median ($\tilde{x}$) of the degree of stenosis is 70%, with an interquartile range (ΔQ) of 15%.

The data analyzed show that the two groups of patients studied were similar in terms of gender and age as well as the status of the diagnosed ACI stenosis (location and grade).

Table 3 shows the mean ($\bar{x}$) and standard deviation (σ) of CT number, SNR, CNR, and subjective image quality (IQ) for two groups of patients scanned using two different imaging techniques, one with 120 kV and high-concentration contrast agents and the other with 100 kV and low-concentration contrast agents.

The data indicate that there are no significant differences between the two groups for any of the variables in Table 3. The average CT number is 484 HU (σ = 85 HU), the SNR is 3.9 (σ = 0.6), the CNR is 20.5 (σ = 2.2), and the subjective IQ grade is 3.9 (σ = 0.4).

Figure 4 shows the differences in CTDIvol and DLP for two patient groups. As can be seen in the boxplot in Figure 3, the CTDIvol and DLP are significantly lower in patients scanned using an anode voltage of 100 kV (student's t test, $p < 0.05$).

Figure 5 shows the differences in the degree of stenosis as measured by the different diagnostic modalities. As shown in the boxplot in Figure 3, there is no significant difference between stenosis grade measured by color Doppler ultrasound and computed tomography angiography (Related-Samples Wilcoxon Signed Rank Test, $p = 0.220$).

DISCUSSION

Current literature describes a small but non-negligible risk of radiation-induced cancer in patients undergoing computed tomography (13,14). Therefore, the reduction of

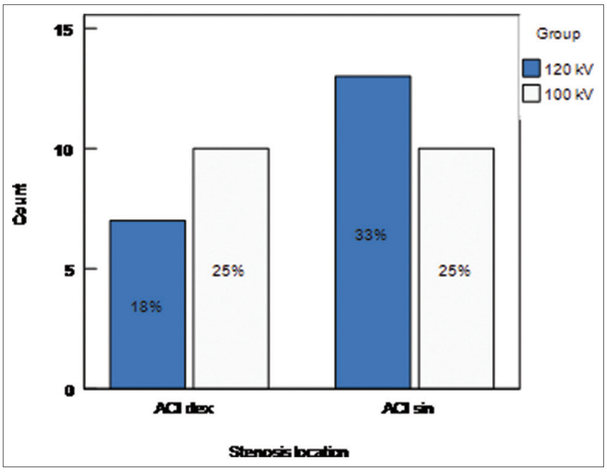

FIGURE 2. Distribution of stenosis location (right or left) in two patient groups.

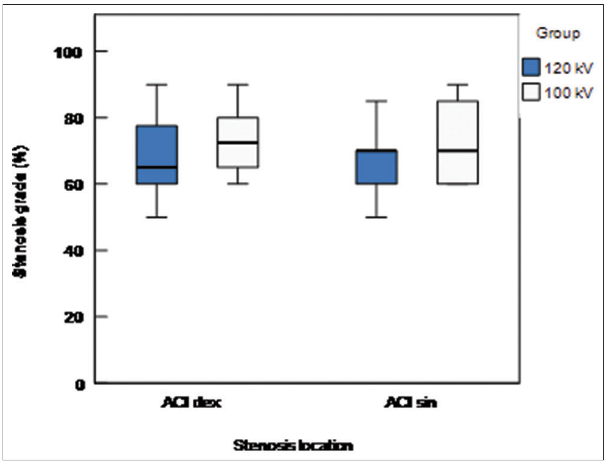

FIGURE 3. Stenosis grade in different locations for two patient groups.

radiation dose during imaging has become an important issue. It is obvious that low-dose protocols should also be used for CTA. The standard dose, i.e., the effective dose of ionizing radiation applied during an examination of the CTA of blood vessels in the neck, is 4 mSv, which is equivalent to 16 months of radiation compared to the natural background radiation we are exposed to on a daily basis (15). Various techniques and strategies aim to reduce the radiation dose delivered during CT imaging and the dose of the iodinated contrast agent. However, the main disadvantage of the low-dose protocol was the increased image noise caused by the lower photon flux.

With the introduction of multidetector CT scanning with thinner collimation and faster data acquisition time, a lower dose of contrast agent and high diagnostic accuracy became possible (16). CTA with lower radiation exposure has been reported to be as good as conventional CTA (17-19); however, radiation exposure remains the real disadvantage of CTA. Especially in CTA of the neck vessels, the tube voltage reduction approach seems promising. First of all, the examined head-neck volume usually does not show the volume and inter-individual differences, as, for example, in abdominal examinations, where body proportions and obesity more often limit the degree of possible tube voltage reduction.

TABLE 3. Mean ($\bar{x}$) and standard deviation (σ) of CT number, SNR, CNR, and subjective IQ grade for two patient groups

kV	CT number (HU)[a]		SNR[a]		CNR[a]		Subjective IQ grade[b]	
	$\bar{x}$	σ	$\bar{x}$	σ	$\bar{x}$	σ	$\bar{x}$	σ
Group								
120	470	71	3.9	0.7	20.3	2.0	3.9	0.4
100	498	97	3.8	0.5	20.8	2.4	3.9	0.4
Total	484	85	3.9	0.6	20.5	2.2	3.9	0.4

[a]No significant difference between mean values was found (Student's t test, *P*>0.05); [b]No significant difference between distributions in two group was found (Independent-samples Mann-Whitney *U* test, *P*>0.05), SNR: Signal-to-noise ratio, CNR: Contrast-to-noise ratio, IQ: image quality

Our study demonstrates the clinical feasibility of a protocol for low-dose CTA of the carotid artery with a reduction of the iodine contrast agent dose from 100 mL to 30 mL and the X-ray tube voltage from 120 kV to 100 kV. Previous studies have described higher image noise in low-dose protocols, which was compensated by higher attenuation to improve SNR/CNR (13,15). However, the results of our study showed that the 100 kV examination protocol provided comparable or even slightly lower image noise than the standard protocol. The latest CT scanners are equipped with X-ray tubes that are optimized for high tube currents, especially at low tube voltages. The low image noise in this study could therefore be explained by the technical advantages of the device. The objective assessment of the image quality, i.e., the image noise, was carried out using the parameters SNR and CNR. These parameters were on average equal or higher in the low-dose protocol than in the standard protocol, which meant better image quality with less noise (Table 3).

On the other hand, the administration of 30 mL of iodine contrast agent with ultrafast acquisition of the device resulted in satisfactory blurring of the carotid arteries, which is the second criterion of objective assessment of image quality. All images in both groups were diagnostic, which means that the threshold for contrast opacification of the blood vessel, which according to several authors is 200 HU (20,21), was exceeded. The average contrast opacification of the carotid bulb was 498 HU in the low-dose protocol and 470 HU in the standard protocol, which means that the voltage of the X-ray tube with low kV settings and reduced contrast dose can produce a contrast attenuation of >400 HU in the arterial system (22). It is known that lowering the tube voltage in CTA increases intravascular contrast opacification due to increased intravascular iodine attenuation at low voltage, as the mean energy of X-ray photons approaches the k-edge of iodine, which is 33.2 keV (23). Excessive contrast agent permeability of blood vessels could lead to poorer image quality. By reducing the iodine contrast agent dose to 30 mL in the low-dose protocol, the problem of excessive contrast agent opacity was solved, resulting in an ideal opacity of the blood vessel lumen with an average value equal to that of the standard protocol. Several similar protocols have been described in the literature. Thomas et al. (24) used 70 mL of iodinated contrast agent (400 mg I/mL) at a flow rate of 5 mL/s and achieved a mean arterial enhancement of 410 HU (range 215 HU-670 HU)

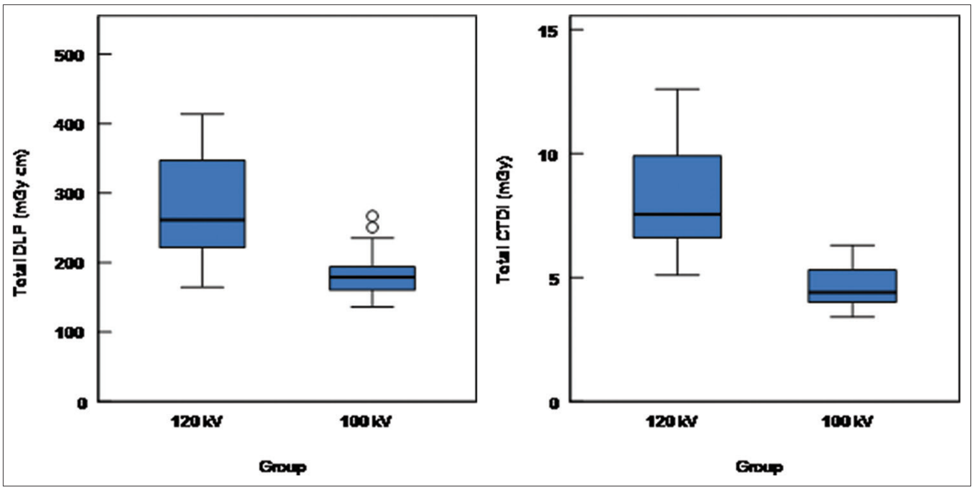

FIGURE 4. Dose length product and volume computed tomography dose index for two groups of patients.

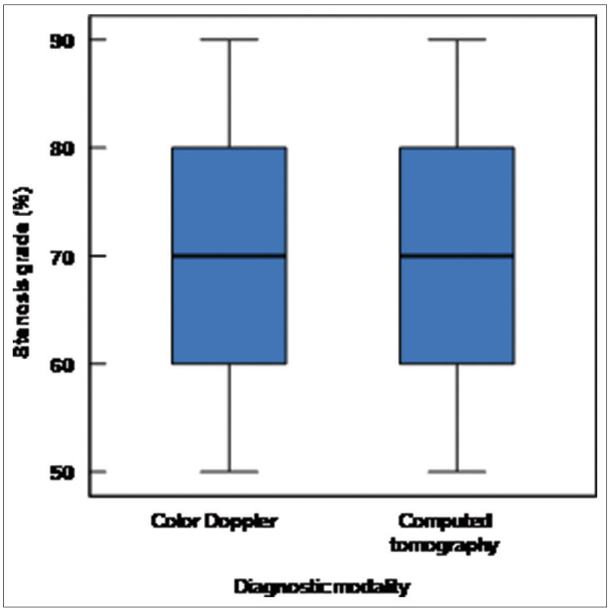

FIGURE 5. Stenosis grade as measured on different diagnostic modalities.

using a 64-slice dual-energy CT system. Fujikawa et al. (25) performed 60-mL and 80-mL CM with high iodine concentration (370 mg I/mL) on a 16-MDCT and achieved a mean arterial enhancement of 210.7 HU-383 HU and 310.3 HU-368.5 HU, respectively.

Currently, the radiation doses in CT scans are usually indicated by two values: CTDIvol and DLP. CTDIvol is an index of the average radiation output of the scanner, is measured in mGy, and reflects the specific selection of scan parameters in a single cross-sectional scan in relation to the radiation dose. Therefore, CTDIvol is used to measure the output radiation dose on only one cross-section and allows the user to compare the output radiation dose from different CT scanners. DLP is the product of CTDIvol and the length of the scanned field, measured in centimeters, and the unit of measurement is mGy * cm (26). The average values of CTDIvol and DLP in the experimental group were significantly lower than the values in the control group (Figure 4). It can therefore be concluded from the results of the parameters determined that reducing the tube voltage to 100 kVp in low-dose CTA also significantly reduces the radiation dose of the X-ray tube. Similar results were obtained by Lenfant et al. (27), who in their study using iterative reconstructions in CTA of blood vessels of the neck with a tube voltage of 120 kV, 100 kV, and 80 kV determined different values of the CTDIvol and DLP parameters, which were significantly lower in the groups with lower tube voltage with almost the same image quality and the same noise level (CTDIvol 120 kV-4.8 ± 1.1, 100 kV-4 ± 1.1, 80 kV-2.3 ± 0.2; DLP 120 kV-197.1 ± 51.2, 100 kV-150.7 ± 37.8, 80 kV-90.4 ± 9.4).

The subjective evaluation was performed by two experienced radiologists who assessed the graininess of the images, the contours of the arterial walls, artifacts, and the overall impression of the image quality. The results of the subjective assessment of the low-dose and standard protocols were similar, with no significant differences (Table 3).

Color Doppler is used as the initial diagnostic method because it is readily available, inexpensive, and noninvasive. However, as it is partly a subjective method, it is sometimes recommended to perform an additional diagnostic evaluation, and the best option in this case is CTA. In our study, we primarily investigated the correlation between color Doppler and CTA findings in assessing the degree of carotid stenosis. When comparing these two diagnostic methods, we observed a significant correlation between the degree of carotid stenosis assessed by Doppler and CTA (Figure 5). The study by Rustempasic and Gengo (28) also showed a linear correlation in the assessment of the degree of carotid stenosis by color Doppler and CTA ($r = 0.536$; $p < 0.05$).

The differences in terms of gender and age were not significant. The average age of the patients was 69 years, which is consistent with previously conducted studies on patients with carotid stenosis. There was also no significant difference between the mean values of the degree of stenosis in the two groups. Therefore, we can safely assume that the patient groups are comparable and that no age-, gender-, or disease-related differences should affect the overall outcome of the study.

This study also has some limitations. Firstly, the sample size was still small. Second, it is difficult to extrapolate these study results to CTAs of other parts of the body. The larger diameter of the soft tissues in the chest and abdomen could overload the capacity of the X-ray tubes, which could lead to increased image noise and artifacts.

CONCLUSION

The use of CTA of the neck vessels with lower doses of X-rays and iodine contrast agent, with appropriate preparation, makes it possible to use this method in kidney patients and patients with previous severe allergic reactions to the contrast agent, in whom this examination could not previously be performed. The method also reduces the risk of developing CIN and the risk of cancer caused by excessive doses of radiation. In the low-dose neck CTA protocol, the voltage of the X-ray tube is reduced from 120 kV to 100 kV and the dose of iodine contrast medium from 100 mL to just 30 mL.

On the other hand, there is also an economic justification and a "cost advantage" for this method, as three times less contrast medium is used during an examination than with the conventional method, and the reduction in the voltage of the X-ray tube extends its service life.

Color Doppler ultrasound is an excellent method for diagnosing pathological conditions of the carotid arteries and should be used as a cost-effective, non-invasive and painless method as the first diagnostic modality in the diagnosis of the carotid arteries.

DECLARATION OF INTEREST

Authors declare no conflict of interests.

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