Sonographic examination of epiaortic vessels in patients with peripheral vertigo

G. Salvaggio^{a,*}, R. Gargano^b, A. Campisi^a, V. Cantisani^c, P. Ricci^c,
S. Gallina^b, M. Midiri^a, G. Caruso^a

^a *Dipartimento di Biopatologia e Biotecnologie Mediche e Forensi, Sezione di Scienze Radiologiche, Università degli Studi di Palermo, Italy*

^b *Biomedicina Sperimentale e Neuroscienze, Sezione di Otorinolaringoiatria, Università degli Studi di Palermo, Italy*

^c *Dipartimento di Radiologia, Università degli Studi di Roma La Sapienza, Italy*

KEYWORDS

Ultrasound color
Doppler;
Carotid arteries;
Vertigo;
Intima media thickness.

Abstract *Introduction:* To evaluate the utility of echo-color-Doppler ultrasonography (CDU) of extracranial brain-supplying vessels in patients with peripheral vertigo of unknown origin. *Materials and methods:* One-hundred-fifty-six patients (study group; 42 male and 114 female; mean age 61.86 ± 14.14) and 161 patients (control group; 80 male and 81 female; mean age 62.31 ± 13.69) were prospectively evaluated with CDU of extracranial brain-supplying vessels. Plaques in common and/or internal carotid artery (CA), arterial wall intima-media thickness (IMT) of common CA and peak systolic velocity (PSV) and resistive index (RI) of vertebral arteries (VA) were evaluated. Parametric (*t*-test) and non-parametric (Mann–Whitney *U*-test and Kolmogorov–Smirnov test) tests were applied. Logistic regression analysis was performed to provide odds ratio indicating the magnitude of risk of vertigo. Independent variables consisting of characteristics (age, sex), vascular risk factors (hypercholesterolemia, diabetes, hypertension) and CDU variables (IMT, plaque, PSV and RI of VA) were considered.

Results: Plaques were found in 31 (19.8%) patients of study group and in 43 (26.7%) patients of control group. IMT > 1 mm was found in 98 (62.8%) patients of study group and in 125 (77.6%) patients of control group. Statistical tests, applied to PSV and RI, showed no significant difference (*p*-value > 0.05). At logistic regression analysis, vertigo was associated with age, sex, hypercholesterolemia, diabetes, hypertension and IMT (*p* < .01) while plaque, PSV and RI of VA were not significant factors (*p* > .05).

Discussion: IMT is the only CDU variable significantly associated with vertigo, especially in the lower age-classes (35–45 and 45–55) of study group.

Sommario *Introduzione:* Valutare l'utilità dell'eco-color Doppler (CDU) dei vasi epiaortici nei pazienti con vertigine periferica da causa sconosciuta.

Materaili e metodi: Centocinquantasei pazienti (gruppo studio; 42 uomini e 114 donne; età media $61,86 \pm 14,14$) e 161 pazienti (gruppo controllo; 80 uomini e 81 donne; età media

* Corresponding author. Dipartimento di Biopatologia e Biotecnologie Mediche e Forensi, Sezione di Scienze Radiologiche, Università degli Studi di Palermo, Italy.

E-mail address: p.salvaggio@libero.it (G. Salvaggio).

62,31 $\pm$ 13,69) sono stati sottoposti a CDU dei vasi epiaortici. Sono stati valutati i seguenti parametri: presenza di placche ateromasiche a livello dell'arteria carotide (CA) comune e/o interna; spessore medio intimale (IMT) della CA comune; picco di velocità sistolica (PSV) e indice di resistenza (RI) a livello delle arterie vertebrali (VA). Sono stati utilizzati test parametrici (*T*-test) e non parametrici (Mann–Whitney *U*-test e Kolmogorov–Smirnov test). È stata eseguita un'analisi di regressione logistica per fornire un odds ratio indice di grandezza del rischio di vertigine. Sono state considerate variabili indipendenti (età, sesso), fattori di rischio vascolare (ipercolesterolemia, diabete, ipertensione) e variabili CDU (IMT, placche, PSV e RI). **Risultati:** Placche ed IMT > 1 mm sono stati trovati in 31 (19,8%) e 98 (62,8%) pazienti del gruppo di studio e in 43 (26,7%) e 125 (77,6%) pazienti del gruppo controllo. I test statistici, applicati a PSV e RI, non hanno dimostrato differenze significative (*p*-valore > 0,05). Alla regressione logistica le vertigini sono risultate associate ad età, sesso, ipercolesterolemia, diabete, ipertensione e IMT (*p* < 0,01), mentre placche, PSV ed RI non erano fattori significativi (*p* > 0,05).

Discussione: IMT è la sola variabile CDU significativamente associata alla vertigine, specialmente nelle classi di età inferiore (35-45 e 45-55) del gruppo studio.

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Introduction

Vertigo and balance disorders of vestibular origin are one of the most common otolaryngological problems encountered by general practitioners [1]. The studies carried out in recent years show that vertigo may occur in 18% of people over 60 years of age and in 25% of the general population [1]. Vertigo may be caused by a wide spectrum of diseases, ranging from benign to potentially serious conditions. A diagnosis of the organic cause is frequently difficult to achieve and it is often not possible to confirm that some physical dysfunction exists [2]. However, cost efficiencies applied to diagnostic evaluation of this commonly presented symptom predict substantial societal cost savings. Echo-color-Doppler sonography of the extracranial brain supplying vessels is often performed in the evaluations of patients with vertigo of peripheral origin [3]. In our experience, echo-color-Doppler examinations in patients with vertigo show unremarkable results in most cases; moreover, there is an unclear correlation between positive findings at ultrasound examination such as: intima-media thickness, plaque, carotid and vertebral arteries stenosis, peak velocity of vertebral arteries, and the occurrence of vertigo [4–6]. Aim of this prospective case-control study was to evaluate the utility of echo-color-Doppler sonography of extracranial brain supplying vessels in patients with peripheral vertigo of unknown origin.

Materials and methods

Patients

IRB

The study protocol was approved by our institutional review board. Before enrollment, each patient gave written informed consent.

Study group

From June 2006 to March 2007, 260 consecutive patients with balance disorder were referred to our Otolaryngology department. The medical history of each patient was taken and a full neuro-otological examination comprising

otological (otoscopy, stapedius reflex thresholds, pure-tone audiometry and brain stem auditory evoked responses) and vestibular (eye movement examination, hallpike head positioning test, Romberg test and gait assessment, electronystagmography, video-oculography and caloric tests) assessments were performed. On the basis of neuro-otological examination results, patients were classified as affected by dizziness of central (neurological) causes (*N* = 42 patients), Meniere's syndrome (*N* = 12 patients), canalithiasis or cupulolithiasis (*N* = 30 patients), viral labyrinthitis (*N* = 15 patients) and peripheral vertigo of unknown origin (*N* = 161 patients). These 161 patients with peripheral vertigo of unknown origin were referred to Radiology department to perform an echo-color-Doppler sonography of extracranial brain supplying vessels. These patients constituted the study group.

Control group

Control group, consisted of 167 consecutive patients without history of dizziness, was referred to Radiology department to perform an echo-color-Doppler sonography of brain supplying vessels for at least one or a combination of the following conditions: hyperlipidaemia (*N* = 78 patients), hypertension (*N* = 119 patients), transitory ischemic attack (*N* = 11 patients), diabetes (*N* = 45 patients) and atherosclerosis (*N* = 76 patients).

Exclusion criteria

The only exclusion criteria for this study was the lack of identification of the vertebral arteries at echo-color-Doppler sonography. Five patients in the study group were excluded because of the lack of identification of the right vertebral artery (1 patient) and the lack of identification of the left vertebral artery (4 patients). Six patients in the control group were excluded because of the lack of identification of the right vertebral artery (3 patients) and the lack of identification of the left vertebral artery (3 patients).

Study population

The final study population (Table 1) consisted of 156 patients with peripheral vertigo [study group; 42 male and 114 female; mean age 61.86 years $\pm$ 14.14 (standard deviation)] and 161

Table 1 Study population.

patients without history of dizziness [control group; 80 male and 81 female; mean age 62.31 ± 13.69 (standard deviation)]. The medical records of the study and control groups were reviewed by a radiologist (-) for factors related to hypercholesterolemia (cholesterol = 200 mg/dl), diabetes [plasma glucose (FPG) level >126 mg/dl on two separate occasions] and hypertension (systolic pressure = 160 mmHg; diastolic pressure = 90 mmHg).

Examination Technique

In all patients, gray scale and color-Doppler sonography of extracranial brain supplying vessels (common carotid arteries, internal carotid arteries and vertebral arteries) were performed by using an HDI 5000 (ATL, Bothell, WA) equipped with a 4- to 7-MHz linear array transducer. Color-Doppler examination was performed with a pulse repetition frequency (PRF) of 2500–3500; color gain was adjusted for each patient by increasing amplification until random artifacts appeared and then reducing it until they disappeared. Wall filter settings were low (100Hz). Echo-color-Doppler sonography of extracranial brain supply vessels was performed in a dimly lighted room with a comfortable temperature (22–24 °C) in the supine position with the head slightly hyperextended.

Image analysis

The echo-color-Doppler images obtained in each patient were acquired and interpreted by two radiologists (- -), (-) with 18 and 8 years of experience performing echo-color-Doppler, respectively, in order to identify the following findings: the presence of plaque in common and/or internal carotid artery, the arterial wall intima-media thickness of common carotid artery and the peak systolic velocity and resistive index determined in both vertebral arteries. The intima-media thickness of common carotid artery was calculated 1.0 cm proximal to the carotid bulb and analyzed quantitatively offline by computer (HDI-Lab system

software; ATL Ultrasound). Intima-media thickness was obtained from gray-scale images in the plaque free section. Care was taken to ensure that the distal common carotid artery arterial wall was parallel to the transducer plane to eliminate any artifacts as a result of angulation. A short cine-loop of images of each common carotid artery was recorded and stored in a proprietary format specific to Philips machines, which retains most of the raw ultrasound data with little post-processing. All images were analyzed in the intima-media thickness “plug in” of HDI-Lab (Philips Medical Systems). An “area-of-interest” box was then placed over the deep common carotid artery wall and intima-media thickness was calculated. The intima-media thickness was measured from the intima–lumen interface (the anterior line of high reflectivity) to the media–adventitia interface (posterior line of high reflectivity) by the HDI-Lab system [7]. The mean value was also calculated from the left and right carotid artery. An intima-media thickness of less than 1 mm was considered normal [8]. Peak systolic velocity and resistive index were determined in both vertebral arteries at C1–C2 level in the neutral head position and in full range rotation. Parameters were taken in the vertebral artery contralateral to the direction of rotation. Duplex measurement of angle-corrected flow velocities was done with the sample volume expanded over the entire vessel diameter. Visual control of the maximal luminal width and acoustic control of an optimum time frequency Doppler signal made certain that the sample volume passed through the center of the vessel. We aimed to keep the angle of insonation as low as possible, in most cases about 60°.

Statistical analysis

All data were initially entered into an Excel database (Microsoft, Redmond, WA) and tabulated in a spreadsheet (STATISTICA's version 6.0 and R software version 1.8). Data analysis was carried out by comparing the peak systolic velocity and the resistive index of study and control groups. Parametric (*t*-test) and non-parametric (Mann–Whitney *U*-test and Kolmogorov–Smirnov test) tests were used to evaluate if there was any significant difference between the groups with regard to the peak systolic velocity and resistive index. The Pearson correlation coefficient (*r*) between peak systolic velocity and between resistive index of vertebral arteries in the neutral head position and in full range rotation of study population was evaluated. Logistic regression analysis was performed to provide odds ratio (adjusted relative risk estimates) indicating the magnitude of risk of vertigo. Independent variables consisting of characteristics (age, sex), vascular risk factors (hypercholesterolemia, diabetes, hypertension) and echo-color-Doppler variables (intima-media thickness, plaque, peak systolic velocity and resistive index of vertebral arteries). Results were considered statistically significant at $p < .05$.

Results

Plaque and intima-media thickness

Plaques were found in 31 (19.8%) patients of study group and in 43 (26.7%) patients of control group. Intima-media

thickness > 1 mm was found in 98 (62.8%) patients of study group and in 125 (77.6%) patients of control group. Age distribution of patients with intima media thickness > 1 mm of study and control group is shown in Table 2.

Peak systolic velocity and resistive index

In patients with vertigo, the mean peak systolic velocities in neutral head position of the right and left vertebral arteries were $44.15 \text{ cm/s} \pm 10.08$ (range, 21.50–65.90 cm/s) and $44.10 \text{ cm/s} \pm 9.96$ (range, 22.20–65.70 cm/s), respectively. The corresponding mean peak systolic velocities in the control group were $44.34 \text{ cm/s} \pm 11.20$ (range, 22.30–65.00 cm/s) and $44.13 \text{ cm/s} \pm 10.64$ (range, 20.50–61.40 cm/s). In full rotation range, the mean peak systolic velocities of the right and left vertebral arteries were $44.04 \text{ cm/s} \pm 9.82$ (range, 20.80–66.80 cm/s) and $44.23 \text{ cm/s} \pm 9.91$ (range, 22.90–66.00 cm/s) in patients with vertigo and $44.46 \text{ cm/s} \pm 11.05$ (range, 21.00–65.60 cm/s) and $44.26 \text{ cm/s} \pm 10.65$ (range, 21.70–62.00 cm/s) in control group. In study group, the mean resistive index in neutral head position of the right and left vertebral arteries were 0.668 ± 0.08 (range, 0.20–0.90) and 0.660 ± 0.09 (range, 0.22–1), respectively. The corresponding mean resistive index in the control group were 0.670 ± 0.08 (range, 0.20–0.94) and 0.662 ± 0.09 (range, 0.22–0.90). In full rotation range, the mean resistive index of the right and left vertebral arteries were 0.667 ± 0.08 (range 0.24–1) and 0.658 ± 0.09 (range, 0.24–1) in the study group and 0.669 ± 0.08 (range, 0.24–0.94) and 0.660 ± 0.09 (range, 0.24–0.91) in control group. The *t*-test, Mann–Whitney *U*-test and Kolmogorov–Smirnov test applied to peak systolic velocities and resistive index in neutral head position and in full rotation range showed that the difference of the location parameter between the two groups was not

statistically significant (p -value > 0.05). These results are summarized in Tables 3 and 4. Pearson correlation coefficients were 0.995 [p -value < 0.01 ; 95% CI (0.994–0.996)] and 0.997 [p -value < 0.01 ; 95% CI (0.996–0.997)] for peak systolic velocity and 0.92 [p -value < 0.01 ; 95% CI (0.90–0.93)] and 0.92 [p -value < 0.01 ; 95% CI (0.92–0.95)] for resistive index of right and left vertebral arteries in neutral head position versus full range rotation, respectively. Correlation coefficients confirmed that the variables correlate strongly and positively.

Logistic regression analysis

At logistic regression analysis, vertigo was associated with age, sex, hypercholesterolemia, diabetes, hypertension and intima-media thickness ($p < .01$) while plaque, peak systolic velocity and resistive index of vertebral arteries were not significant factors ($p > .05$). Results of logistic regression analysis are showed in Table 5.

Discussion

To date, only few papers are present in literature with the aim of investigating the utility of color-Doppler sonography in patients with peripheral vertigo; moreover, only few studies show an association between balance disorder and plaque [9,10]. Gutmann et al. [9] analyzed the frequency of pathological Doppler examination results of 150 patients with vertigo, hearing loss and tinnitus. They reported that patients with vertigo bear a greater risk for stenosis of the extracranial arteries (28%) compared to an asymptomatic population (1%). Authors concluded that the early attribution of stenosis to a malfunction of the inner ear helps to avoid invasive examinations of cervical vessels. Sanguigni et al. [10] performed an echo-Doppler ultrasonography of supra-aortic branches in patients affected by coronary artery disease, either partially symptomatic or asymptomatic for carotid artery stenosis. A significant carotid stenosis ($>50\%$) was demonstrated in 51/184 subjects (27.7%); 21 subjects (41.2%) were partially symptomatic (dizziness, vertigo, lipothymia, etc), while 30 subjects (58.8%) were completely asymptomatic. The authors' data suggest that carotid disease can develop in a significant proportion of patients, even though completely asymptomatic. Our study confirms the findings reported by Gutmann and Sanguigni since we found that the percentage of patients with plaques was higher in control group (26.61%) respect to study group (19.39%). These data show an unclear relationship between vertigo and plaque; therefore, further investigations are necessary.

In our knowledge, there are no previous studies about the relationship between intima-media thickness of peripheral vessels and vertigo; whereas, several studies report association of intima-media thickness in peripheral vasculature to the presence and severity of coronary artery disease [11–13].

Ultrasound measurements of intima-media thickness occurrence in the carotid arteries were used as indicator of coronary atherosclerosis in several previous studies [11,14]. Similarly, intima-media thickness could be used as indicator of intracranial vessels atherosclerosis, e.g. vasculature of the areas of cochleovestibular structures.

Table 2 Age distribution relative to intima-media thickness in study and control group.

Table 3 Resistive index value of vertebral artery (VA) in study and control group. *t*-test, Kolmogorov–Smirnov (K-S) test and Mann–Whitney (M – W) test results.

Resistive index	Study group	Control group	<i>p</i> -value Test <i>t</i>	<i>p</i> -value Test K-S	<i>p</i> -value Test M-
RightVA Neutral head position	0.668 ± 0.08	0.670 ± 0.08	> 0.05	<i>p</i> > .10	> 0.05
LeftVA Neutral head position	0.660 ± 0.09	0.662 ± 0.09	> 0.05	<i>p</i> > .10	> 0.05
RightVA Full rotation range	0.667 ± 0.08	0.669 ± 0.08	> 0.05	<i>p</i> > .10	> 0.05
LeftVA Full rotation range	0.658 ± 0.09	0.660 ± 0.09	> 0.05	<i>p</i> > .10	> 0.05

Perfusion of the areas of cochleovestibular structures was investigated by Koyuncu et al. [15] using 99m Tc - HMPAO single photon emission computerized tomography (SPECT) in 20 young patients (average age 36 years) with vertigo presumed to have peripheral vestibular abnormalities.

Eleven of 20 patients demonstrated hypoperfusion in SPECT: Authors concluded that high grade hypoperfusion of these patients showed that vascular abnormality occurred in the young patients. In our study, even if the percentage of intima-media thickness > 1 mm was lower in study group (61.8%) respect to control group (78%), the analysis of age distribution showed that intima-media thickness > 1 mm was most represented in lower age-classes (35-45 and 45-55) of study group than in control group. These results, according to Koyuncu et al. [15], could suggest a vascular etiology of vertigo in these age-classes (35–55 years). The last evaluated imaging findings were peak systolic and resistive index as calculated within the vertebral arteries. Peak systolic velocity and resistive index were evaluated at C1-C2 because this level is reported to be the most common site of narrowing of the vertebral artery secondary to cervical movement and also the most frequent site of pathology in manipulative incidents [16–19]. Comparing the peak systolic velocity and the resistive index of study and control groups in neutral head position and in full range rotation, no statistical differences were found; these results indicate that these parameters are useless in the identification of vertigo etiology. The analysis of correlation matrix relative to peak systolic and resistive index shows that the measurements of these parameters in neutral head position and in full range rotation have a high correlation (>0.90). These results indicate that there is only

minimal change to peak systolic velocity and resistive index with cervical rotation. This result is in agreement with Zaina C et al [4]. In their study, peak velocity at C1-2 level were measured in the artery contralateral to the direction of rotation, in the positions of neutral, 45° and end range rotation. No change in peak velocity at C1-2 level between the initial neutral measurement and the measurements at 45° and end range rotation was found (*P* > .05). However, in that study, subject sample comprised young asymptomatic volunteers (mean age 32.7 years, SD 8.8 years) and perhaps they report that it is not unexpected to observe a non-significant change in vessel haemodynamics. Our study showed the same results of study of Zaina et al. [4] despite our sample comprised symptomatic and asymptomatic subjects with a wide range of age. The results of this study suggest that no further information are given by cervical rotation relative to resistive index and peak systolic velocity in the vertebral arteries. Nevertheless, with regard to logistic regression analysis show that independent variables (age, sex), vascular risk factors (hypercholesterolemia, diabetes, hypertension) and only one echo-color-Doppler variable such as intima-media thickness are significant for the risk of vertigo. Conversely, no statistical significance was found for plaques, peak systolic velocity and resistive index of vertebral arteries. Particularly, age is marginally significant and its significance level increases by excluding its interactions with hypercholesterolemia and hypertension. This means that there is a confounding effect between age and some variables that could lead to assign to age a greater weight in the explanation of vertigo. Moreover, logistic regression model shows that the likelihood of vertigo increases 4 time in

Table 4 Peak systolic velocity value in cm/seconds of vertebral artery (VA) in study and control group. *t*-test, Kolmogorov–Smirnov (K-S) test and Mann–Whitney (M – W) test results.

Peak systolic velocity	Study group	Control group	<i>p</i> -value Test <i>t</i>	<i>p</i> -value Test K-S	<i>p</i> -value Test M-W
RightVA Neutral head position	44.15 ± 10.08	44.34 ± 11.20	> 0.05	<i>p</i> > .10	> 0.05
LeftVA Neutral head position	44.10 ± 9.96	44.13 ± 10.64	> 0.05	<i>p</i> > .10	> 0.05
RightVA Full rotation range	44.04 ± 9.82	44.23 ± 9.91	> 0.05	<i>p</i> > .10	> 0.05
LeftVA Full rotation range	44.46 ± 11.05	44.26 ± 10.65	> 0.05	<i>p</i> > .10	> 0.05

Table 5 Estimation coefficient, standard error and *p*-value of the coefficients of logistic regression.

Variables	Estimation coefficient	Standard error	<i>p</i> -value
Intercept	2.889	0.617	2.86e-06***
Sex (male)	−0.983	0.255	0.000117***
Age	−0.019	0.010	0.050867*
Hypercholesterolemia	−2.754	0.536	2.85e-07***
Intima-media thickness > 1 mm	−1.305	0.329	7.10e-05***
Diabetes	−0.545	0.383	0.155124*
Hypertension	−0.854	0.288	0.003035**

Significant level: ***(α OSS < 0.001).

**(αOSS < 0.01).

*(αOSS < 0.1).

patients with intima-media thickness (>1 mm), 2.6 times in female [despite in our sample female was most represented (73.07%)], 16 times in patients with hypercholesterolemia, 2.3 times in patients with hypertension and 1.7 times in patients with diabetes. Our study has some biases. The first is that only a single measurement of resistive index and peak systolic velocity of vertebral arteries was taken in the neutral head position and in full range rotation in order to perform an echo-color-Doppler examination as it is performed routinely. Several authors [20] reported that peak systolic velocity at C1-2 showed poor reliability if a single measurement was taken and they suggest to use the mean of three measures to considerably reduce the size of a change required to reach statistical significance.

A second limitation is that patients were not stratified for independent variables (age and sex) and vascular risk factor (hypercholesterolemia, diabetes, hypertension). In the current analysis, we could not determine if different cardiovascular risk classes may have a different rule on the vertigo etiology.

Conclusion

According our findings, we conclude that intima-media thickness is the only echo-color-Doppler variable significantly associated with vertigo. Echo-color-Doppler of brain supplying vessels may be used to integrate intima-media thickness values with vascular risk factors and other relevant clinical information to determine the vertigo etiology.

Conflict of interest statement

The authors have no conflict of interest.

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