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Investigation of the efficacy of carotid artery doppler USG in evaluating patients admitted to the emergency department with syncope

Investigating the efficacy of carotid artery doppler ultrasonography in evaluating patients with syncope

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Abstract

Aim: In our study, we aimed to investigate the effectiveness of carotid artery doppler ultrasonography (CADU), which is a non-invasive and radiation-free method, as a tool in the differential diagnosis of patients with syncope of primary unknown etiology.

Material and Methods: In this prospective and single-center study, patients aged≥18 years admitted to the emergency department of a tertiary hospital with syncope were included. CADU examinations were performed by two emergency physicians and two experienced emergency residents. Patients were evaluated and scored on the basis of the San Francisco Syncope Rule (SFSR) system. Statistical significance was set at $p<0.05$.

Results: Among the 140 patients included, those with syncope of unknown origin demonstrated higher rates of previous heart failures, significantly elevated levels of BNP, positively correlated with the SFSR score. Furthermore, 25 of the patients were readmitted within 1 month and these patients had significantly higher rates of bilateral carotid artery stenosis. Therefore, using higher cut-off values for measuring carotid stenosis leads to increased specificity when evaluating readmission. This indicated that CADU can be used for ruling out the need for readmission.

Discussion: CADU is an important imaging test in revealing pathological conditions in patients with syncope of unknown etiology and can provide significant results in identifying and excluding patients who could be readmitted within a month. Most studies aim to directly identify the cause of syncope; however, there are limited data to guide clinicians in evaluating and ruling out readmission.

Keywords

Emergency Department, Diagnostic, Doppler Ultrasonography, Carotid Artery, Syncope

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Introduction

Syncope is a common symptom observed in the emergency department (ED) admissions. Although syncope of unknown origin is the most common form, cardiovascular etiologies are the leading causes of mortality [1,2]. Emergency physicians need to make a differential diagnosis in order to distinguish between life-threatening and urgent situations [1,3].

Studies have reported that, in patients with dehydration, carotid artery Doppler USG (CADU) performed after passive mobilization of the foot detected a significant increase in flow time; however, measurements in patients without dehydration did not demonstrate such an increase [4,5]. CADU has, therefore, been suggested as a useful tool in the assessment of the extracranial carotid artery and to determine the direction of blood flow.

Therefore, in this study, we wanted to investigate the efficacy of CADU, a radiation-free and non-invasive method, as a swift decision-making tool to establish a differential diagnosis in patients admitted to the ED with syncope of unknown origin.

Material and Methods

Study Setting and Population

This is a prospective and single-center study conducted on patients who admitted to the ED with syncope of unknown origin between 01.08.2018-01.08.2019 and met the San Francisco Syncope Rule (SFSR) criteria [6]. Patients were excluded from the study if they were under 18 years of age, pregnant, had syncope of known origin, anticoagulant use, and did not provide informed consent. The study also excluded patients who met the study criteria but could not undergo CADU or could not be placed in a suitable position for performing CADU, and those who had lesions in the CADU site of the neck.

Initially, 190 patients were enrolled in the study. Of these patients, we excluded those in whom the primary cause of syncope was determined (n = 23), in whom CADU could not be performed (n = 5), and those who were hospitalized for other pathologies (n = 22). A total of 140 patients were finally enrolled in this study.

Data collection

After the initial assessment of the patient, an assessment based on the SFSR and CADU was performed to assess the presence of carotid artery stenosis, occlusion, and flow measurements. All patients admitted to the ED underwent an assessment of the extra-cranial cerebrovascular system performed by two emergency physicians and two emergency residents other than the principal researcher of the study. This assessment was performed using gray scale imaging, Doppler spectral analysis, and color Doppler imaging (CDI) as described in the American Institute of Ultrasound in Medicine criteria. The investigators included in the study were emergency assistants over 2 years who had previous USG training and had USG experience. Emergency physicians had a minimum experience of 3 years in USG. In addition, prior to the research, a certain number of patients underwent CADU assessment under the supervision of a radiologist experienced in CADU, and the Fleiss kappa coefficient revealed that the interrater agreement was 0.84. Initial examinations of patients were followed by CADU examinations, and patients with carotid stenosis were recommended to undergo a neurologic evaluation. Patients underwent routine assessments outside the scope of the study, with no additional study-specific examinations or interventions. Patients were analyzed in terms of 30-day readmission, and 25 of these patients were readmitted to the ED with syncope. Data related to both admissions were compared.

2.1. Ethical Approval

The study received approval from the university hospital's ethics committee (Ethical approval number: KÜGOKAEK-2018/269).

2.2. Statistical Analysis

Statistical analysis of the research data was performed using the SPSS (21.0 Version) program. Data were analyzed for normality of distribution using the Kolmogorov–Smirnov test. Normally distributed numerical variables were expressed as mean± standard deviation, and those, which were non-normally distributed were expressed as median (min–max). Categorical variables were expressed as numbers and percentages. T-test (for normally distributed numerical variables) and the Mann–Whitney U test (for non-normally distributed numeric variables) were used in independent samples to determine the factors associated with two-category risk groups. Receiver operating characteristic (ROC) analysis was performed on CADU values in evaluating readmission. Values were reported using the area under the ROC curve (AUC) and the confidence interval. Statistical significance was set at $p<0.05$.

Results

Of the 140 patients, 52.9% (n = 74) were women, with a mean age of 51.19±19.39 years. After the patients were evaluated, their SFSR scores were calculated and the subjects were subsequently categorized into groups. All patients had loss of consciousness. The relationship between patients' complaints at admission, chronic disease histories and SFSR scores according to laboratory data is given in Table 1.

Percent stenosis in the right ICA had a significant positive correlation with E-point septal separation (EPSS) at a rate of 34.9% (r = 0.349) and a significant negative correlation with ejection fraction (EF) at a rate of 41.5% (r = −0.415). Right CCA diameter had a significant positive correlation with EPSS at a rate of 16.9% (r = 0.169). Percent stenosis in the left ICA

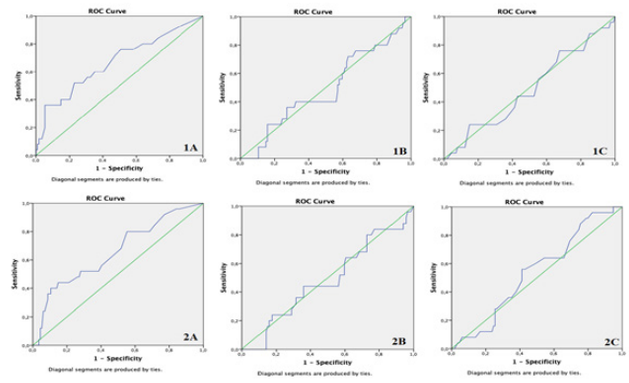


Figure 1. Comparison of CADU parameters in determining re-application within a month. 1A: Right Carotid Stenosis Percentage; 1B: Right CCA Flow Current; 1C: Right CCA Diameter 2A: Left Carotid Stenosis Percentage; 2B: Left CCA Flow Current; 2C: Left CCA Diameter.

had a significant positive correlation with EPSS at a rate of 44.6% (r = 0.446) and a significant negative correlation with EF at a rate of 46.3% (r = −0.463). Left CCA diameter had a significant positive correlation with EPSS at a rate of 19.8% (r = 0.198) and a significant negative correlation with EF at a rate of 18.8% (r = −0.188).

SFSR scores were correlated with the CADU results of the patients, and significantly more severe stenosis in the right ICA (12.5±13.4 vs 28.9±21.7; p<0.001) and left ICA (12.8) in patients with heart failure (12,8±13.7 vs 32.5±18.8; p<0.001) and a significantly higher diameter (CCA) in the left common carotid artery (6.6±1.1 vs 7.3±1.0; p= 0.020) were present. CADU data were analyzed for the presence of pathological findings on electrocardiography (ECG), and the percentage of stenosis in the left ICA in patients with pathological findings on ECG (14.1±14.7 vs 45.7±17.6; <0.001) and a significantly higher diameter in the left CCA (6.6±1.1 vs 7.9±0.6; p=0.045) was significantly higher than in those without. Patients with dyspnea had a significantly lower diameter in the right CCA (6.7±1.0 vs 5.9±0.8; p=0.013).

Patients discharged were evaluated for 30-day readmission along with clinical data. A total of 17.9% of the patients were subsequently readmitted. Dizziness and dyspnea were significantly higher in readmitted patients. Readmission was significantly higher in patients with CHF, CAD, and chronic renal failure. Mean laboratory parameters at readmission were compared with levels measured at the time of initial admission; mean levels of creatinine, potassium, and BNP were significantly higher, whereas sodium was significantly lower. In addition, the percentage of stenosis in the right and left ICA was significantly elevated in readmitted patients. No significant difference was observed in terms of other parameters. Furthermore, readmitted patients had significantly higher EPSS and significantly lower EF (Table 2).

The ROC analysis for CADU parameters performed in determining the readmission status is presented in Figure 1. This analysis showed a significant difference in the percentage of stenosis in the bilateral carotid in readmitted patients. AUC was 0.656 for percent stenosis of the left carotid artery (95% CI; 0.535–0.777; p = 0.015) and 0.668 for percent stenosis of the right carotid artery (95% CI; 0.541–0.794; p = 0.009). Other parameters did not differ significantly. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratio (LR) of CADU parameters for readmission are given in Table 3. These values suggest that percent stenosis

Table 1. Distribution of clinical data of cases according to SFSS

Parameter			San Francisco Syncope Scores			p
			0 n (%) / Mean ±SD	1 n (%) / Mean ±SD	2 n (%) / Mean ±SD	
Complaints	Dizziness	No	53 (79,1)	12 (17,9)	2 (3,0)	0.030
		Yes	43 (58,9)	23 (31,5)	7 (9,6)	
	Dyspnea	No	90 (73,8)	26 (21,3)	6 (4,9)	0.002
		Yes	6 (33,3)	9 (50,0)	3 (16,7)	
	Palpitation	No	82 (70,7)	28 (24,1)	6 (5,2)	0.316
		Yes	14 (58,3)	7 (29,2)	3 (12,5)	
Chronic Disease History	CHF	No	93 (74,4)	26 (20,8)	6 (4,8)	<0.001
		Yes	3 (20,0)	9 (60,0)	3 (20,0)	
	CAD	No	87 (71,9)	30 (24,8)	4 (3,3)	0.001
		Yes	9 (47,9)	5 (26,3)	5 (26,3)	
	CRF	No	93 (70,5)	31 (23,5)	8 (6,1)	0.149
		Yes	3 (37,5)	4 (50,0)	1 (12,5)	
Laboratory Data	Creatinine (mg/dL)		0,9±0,3	1,2±1,1	1,2±0,7	0.035
	Sodium (mEq/L)		137,9±4,1	137,9±2,2	136,7±1,5	0.600
	Potassium (mEq/L)		4,2±0,5	4,3±0,5	4,4±0,5	0.294
	BNP (pg/mL)		35,2±47,8	132,7±419,9	263,0±312,0	0.004
KADU Parameters	Right ICA Stenosis (%)		12,7±13,2	17,7±19,8	16,0±13,8	0.238
	Right CCA Flow Current (mL/min)		472,5±160,6	466,7±156,2	420,0±140,8	0.637
	Right CCA Diameter (mm)		6,7±1,1	6,6±1,0	6,4±0,9	0,256
	Left ICA Stenosis (%)		13,0±13,2	16,7±16,8	26,6±25,1	0.028
	Left CCA Flow Current (mL/min)		562,1±161,8	511,1±219,0	479,1±140,8	0.265
	Left CCA Diameter (mm)		6,9±1,1	6,7±1,2	6,6±1,0	0.672

CHF: Congestive Heart Failure; CAD: Coronary Artery Disease; CRF: Chronic renal failure; ICA: Internal Carotid Artery; CCA: Common Carotid Artery; BNP: Brain natriuretic peptide; SD: Standard Deviation

Table 2. Distribution of clinical data for the first admission and at 30-day readmission

Parameter			Re-Application Status		
			No (n=140) n (%) / Mean ±SD	Yes (n=25) n (%) /Mean ±SD	p
Complaints	Dizziness	No	68 (48,6)	6 (24,0)	0.023
		Yes	72 (51,4)	19 (76,0)	
	Dyspnea	No	122 (87,1)	15 (60,0)	0.001
		Yes	18(12,9)	10 (40,0)	
	Palpitation	No	115 (82,1)	22 (88,0)	0.472
		Yes	25 (17,9)	3 (12,0)	
Chronic Disease History	CHF	No	125 (89,3)	17 (68,0)	0.005
		Yes	15 (10,7)	8 (32,0)	
	CAD	No	122 (87,1)	16 (64,0)	0.004
		Yes	18 (12,9)	9 (36,0)	
	CRF	No	132 (94,3)	19 (76)	0.003
		Yes	8 (5,7)	6 (24)	
Laboratory Data	Creatinine (mg/dL)		0,91±0,36	1,15±0,56	0.010
	Sodium (mEq/L)		138,13±2,62	136,56±6,27	0.047
	Potassium (mEq/L)		4,16±0,43	4,40±0,69	0.027
	BNP (pg/mL)		50,13±102,42	179,91±502,40	0.012
KADU Parameters	Right ICA Stenosis (%)		12,33±12,67	22,08±22,26	0.003
	Right CCA Flow Current (mL/min)		490,52±155,98	430,80±150,49	0.083
	Right CCA Diameter (mm)		6,67±1,01	6,53±1,02	0.540
	Left ICA Stenosis (%)		11,28±11,08	18,34±16,25	0.022
	Left CCA Flow Current (mL/min)		493,27±180,34	495,48±137,00	0.954
	Left CCA Diameter (mm)		6,61±1,08	6,67±1,18	0.822
ECO Evaluation	EPSS		9,15±7,57	15,48±11,73	0.001
	EF		63,30±10,27	54,36±16,61	0.001

CHF: Congestive Heart Failure; CAD: Coronary Artery Disease; CRF: Chronic renal failure; ICA: Internal Carotid Artery; CCA: Common Carotid Artery; BNP: Brain natriuretic peptide; EPSS: E-Point Septal Separation; EF: Ejection Fraction; SD: Standard Deviation

Table 3. Sensitivity, specificity, NPV, PPV and LR values of ECDU findings in the evaluation of re-admission

Parameter	Sensitivity (%95 CI)	Specificity (%95 CI)	NPV (%95 CI)	PPV (%95 CI)	LR+ (%95 CI)	LR- (%95 CI)
Right ICA Stenosis >%25	40	84,2	86,5	35,7	2,53	0,71
	(21,1-61,3)	(76,2-90,4)	(82,2-89,9)	(22,7-51,3)	(1,33-4,8)	(0,5-0,9)
Right ICA Stenosis >%30	36	93,9	86,9	56,3	5,86	0,68
	(17,9-57,5)	(87,8-97,5)	(83,2-90)	(34,6-75,8)	(2,41-14,2)	(0,5-0,9)
Right CCA Flow Current <300 Ml/Dk	20	85	83,1	23,8	1,43	0,93
	(6,8-40,7)	(28,2-71,8)	(79,9-85,8)	(11,2-43,6)	(0,58-3,54)	(0,75-1,15)
Right CCA Flow Current <250 Ml/Dk	8	94,7	82,4	25	1,52	0,97
	(1-26)	(88,9-98)	(80,6-84,2)	(6,7-60,9)	(0,33-7,1)	(0,86-1,1)
Right CCA Diameter <6 mm	24	67,5	80,2	13,9	0,74	1,13
	(9,4-45,1)	(58,1-76)	(75,9-83,9)	(7,1-22,5)	(0,35-1,56)	(0,88-1,46)
Right CCA Diameter <5 mm	8	93,9	82,3	22,2	1,3	1
	(1-26)	(87,8-97,5)	(80,4-84,1)	(11,9-25,4)	(0,3-5,9)	(0,9-1,1)
Left ICA Stenosis >%25	40	85,9	86,7	38,5	2,85	0,7
	(21,1-61,3)	(78,2-91,7)	(82,5-90,1)	(24,4-54,8)	(1,47-5,52)	(0,5-0,97)
Left ICA Stenosis >%30	36	89,5	86,4	42,8	3,42	0,72
	(17,9-57,5)	(82,3-94,4)	(82,5-89,6)	(26,2-61,3)	(1,62-7,23)	(0,53-0,97)
Left CCA Flow Current <300 Ml/Dk	16	88,6	82,8	23,5	1,4	0,95
	(4,5-36,1)	(81,3-93,8)	(80-85,2)	(9,9-46,4)	(,5-3,9)	(0,79-1,14)
Left CCA Flow Current <250 Ml/Dk	12	95,6	83,2	37,5	2,74	0,92
	(2,6-31,2)	(90,1-98,6)	(81-85,2)	(13,3-70,1)	(0,7-10,7)	(0,8-1,1)
Left CCA Diameter <6 mm	24	69,3	80,6	14,6	0,78	1,1
	(9,4-45,1)	(59,9-77,6)	(76,4-84,3)	(7,5-26,6)	(0,37-1,65)	(0,9-1,4)
Left CCA Diameter <5 mm	4	92,9	81,5	11,1	0,57	1,03
	(0,1-20,4)	(86,6-96,9)	(80,1-82,9)	(1,6-48,8)	(0,1-4,4)	(0,9-1,13)

ICA: Internal Carotid Artery; CCA: Common Carotid Artery; CI: Confidence Interval; NPV: Negative Predictive Value; PPV: Positive Predictive Value; LR: Likelihood Ratio

in the right and left ICA could be considered as a diagnostic test in readmissions. When the cut-off value for right ICA stenosis increased from 25% to 30%, sensitivity decreased from 40 to 36, whereas specificity increased from 84.2 to 93.9. When the cut-off value for left ICA stenosis increased from 25% to 30%, sensitivity decreased from 40 to 36, whereas specificity remained almost the same.

Discussion

Syncope is a manifestation of transient cerebral hypoperfusion and may be attributable to various causes. This manifests as a sudden-onset, reversible loss of consciousness [7,8]. The cause of syncope varies by population. Soteriades et al. conducted a study to evaluate the incidence and prognosis of syncope caused by specific etiologies among participants in the Framingham Heart Study and reported the most frequently identified causes as vasovagal (21.2%), cardiac (9.5%), and orthostatic (9.4%); in 36.6%, the cause was unknown [9]. In addition, it is important to know that the elderly population has multiple comorbidities and poorer clinical outcomes. Therefore, older adults need early diagnosis to identify causes such as cardiac syncope associated with high mortality and morbidity to swiftly start a treatment.

Technological advances over the last 20 years have resulted in an increase in grayscale resolution in doppler USG such as in CDI, considerably improving the quality of CADU assessment. The increased use of doppler USG has also enabled operators of CADU to specialize [10]. USG is fast, portable, reproducible, non-invasive, inexpensive and easily accessible, which makes it an advantageous method in CADU assessments, as in other areas of use.

Numerous studies have investigated the use of CADU scan in determining the cause of syncope. Daniella et al. have reported that CADU rarely detected the cause of syncope. However, other reports have stated that it can be used for diagnostic purposes, including the detection of early atherosclerosis or serious diseases that require evaluation of carotid artery revascularization, or for optimizing treatment of known atherosclerosis [11]. Nicholous et al. have stated that CADU is ineffective in establishing the cause and treating syncope [12]. Morrison et al. conducted a study that used CADU in 96% of the patients admitted with syncope, and found that it could only diagnose <5% among the ≥60% patients with early stenosis [13]. These studies were solely based on the structural evaluation of the carotid artery (stenosis and occlusion, among others). However, our study complemented the structural evaluation with examination of flow and the arterial diameter. The results of our study suggest that higher SFSR scores were correlated with lower diameters and decreased flow in bilateral carotid arteries. Although no significant intergroup difference was observed, we think that this was attributable to the number of patients included in the study. Studies with more patients can elicit clearer results on this topic. Furthermore, we think that using CADU examination in conjunction with SFSR can be useful in the diagnostic evaluation of syncope patients.

CADU is not likely to serve as a diagnostic test that can be used alone to determine the cause of syncope. Determining the

cause of syncope, an episode requires the use of high-value tests. A study by Mendu et al. in 2009 reported that CADU was performed in 267 of 2106 high-risk elderly patients admitted with syncope and early abnormal findings were detected in 122 patients; however, CADU could determine the cause of syncope in only 2 patients [14]. A syncope study by Schnipper et al. in 2005 reported that, of 4199 patients admitted with syncope or presyncope, 140 were scheduled for neurovascular testing, 109 of whom were scheduled for CADU, which resulted in detecting lesions underlying syncope in only 2 patients [15]. Likewise, in our study, CADU does not seem to have revealed the cause in any of the 140 high-risk patients admitted with syncope. Another study by Scott et al. in 2014 analyzed CADU results performed on 313 outpatients with syncope over a period of 5 years at Brigham and Women's Hospital, excluding those with focal neurological deficits or carotid stenosis. They found that in 48 (15.4%) of 313 patients with stenosis ≥50%, carotid ultrasound did not diagnose the cause. Moreover, seven patients underwent a change in medications and one patient subsequently underwent carotid atherectomy, however, even this was a casual finding for the practitioner [16]. Against the background of these studies, using CADU to reveal the cause of syncope is likely to be seen as an extra workload and an economic loss.

The data from our study showed that patients with syncope who had a history of CHF had significantly higher percent stenosis in bilateral ICA than those without a history of CHF. In addition, percent stenosis in bilateral ICA demonstrated a significant positive correlation with EPSS and a negative correlation with EF. In the light of this data, we believe that performing CADU in selected patients with syncope who have a history of CHF, high EPSS and low EF minimizes loss of economic resources and time. Again, based on the results of ROC analysis performed for CADU values, we suggest that the use of higher cut-off values for right and left ICA stenosis could provide higher specificity, thereby making it a potential diagnostic test in evaluating readmission in patients with syncope as well as in differential diagnosis. We could not compare our results with other studies due to the lack of similar studies; further studies with more patients should be conducted to validate these results.

Finally, several studies have argued that performing CADU in patients admitted with syncope would cause loss of time and economic resources. However, recent technological developments and ensuing progress in medical education have prompted most healthcare institutions to incorporate USG training into the curricula for clinical training, including clinical training for emergency medicine in Turkey. In our study, CADU examinations were performed by emergency clinicians, and this system eliminates the problem of potential loss of time and economic resources attributed to CADU.

Limitations of the study

The limitation of the study is that, although the number of patients included in the study seems sufficient, we think that a study with a higher number of patients could yield clearer results.

Conclusion

In patients with syncope, CADU examination alone probably does not identify the underlying cause. Our results show that CADU examination in selected patients with syncope who have a history of CHF, high EPSS and low EF could be useful in revealing carotid artery pathologies. When coupled with higher cut-off values of CADU, increased specificity could also help rule out readmission.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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