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4-Dimensionally Guided 3-Dimensional Color-Doppler Ultrasonography Quantifies Carotid Artery Stenosis With High Reproducibility and Accuracy

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ABSTRACT

OBJECTIVES The purpose was to analyze the agreement and binary accuracy of the degree of internal carotid artery stenosis (ICAS) as determined by 4-dimensionally (4D) real-time gray-scale guided 3-dimensional (3D) color-Doppler ultrasonography (3DC-US) (4D/3DC-US) compared with catheter angiography (CA) and duplex ultrasonography (DUS). This study hypothesized that 4D/3DC-US is noninferior to CA and DUS in grading ICAS in selected patients.

BACKGROUND Clinical stratification in patients with ICAS largely depends on a patient's symptomatic status and the degree of stenosis.

METHODS Screening with 4D/3DC-US was prospectively performed in 93 study patients (with 122 ICASs), thus yielding 80 patients for analysis (with 103 ICASs) after excluding patients with insufficient image quality, previous revascularization, and contraindications to CA. The ultrasound examination (10 MHz) consisted of consensus conform DUS examination and independent real-time 4D-guided gray-scale views for orientation followed by static 3DC-US NASCET (North American Symptomatic Carotid Endarterectomy Trial) percent stenosis quantification using off-line multiplanar rendering. Multiplanar selective CA of the same ICASs was quantified with dedicated software in a blinded fashion.

RESULTS Quantitative CA of 103 stenoses with a mean degree of 65 ± 17% was compared with 4D/3DC-US, with a resulting concordance correlation coefficient of 0.89 and a standard deviation of differences (SDD) of 8.1% at a bias of +1.7%. Binary 50% and 70% stenosis detection with 4D/3DC-US revealed a sensitivity of 97% and 87%, respectively, and a specificity of 92% and 84%, respectively. Interobserver SDD for CA of 52 stenoses (7.2%) did not differ from SDD for 4D/3DC-US and CA ($p = 0.274$). Accuracy of 50% stenosis detection by 4D/3DC-US was tendentially higher compared with DUS (96% vs. 91%).

CONCLUSIONS The 4D/3DC-US method provides reliable and accurate stenosis quantification and binary classification with good diagnostic accuracy compared with CA and DUS. (J Am Coll Cardiol Img 2017;■:■-■) © 2017 by the American College of Cardiology Foundation.

Atherosclerosis of the carotid arteries is a well-characterized cause of stroke and transient ischemic attacks. The risk of neurovascular events increases with the degree of internal carotid artery stenosis (ICAS), thus making accurate diagnostic assessment of ICAS, in addition to symptomatic status, essential for risk estimation in a patient (1-3). The accurate diagnosis of angiographically

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ABBREVIATIONS AND ACRONYMS

4D = 4-dimensionally

4D/3DC-US = 4-dimensionally real-time gray-scale-guided 3-dimensional color-Doppler ultrasonography

CA = catheter angiography

CCC = concordance correlation coefficient

DUS = duplex ultrasonography

ICAS = internal carotid artery stenosis

MLD = minimal lumen diameter

MPR = multiplanar rendering

SDD = standard deviation of differences

3D = 3-dimensional

3DC-US = 3-dimensional color-Doppler ultrasonography

2D = 2-dimensional

US = ultrasonography

defined >50% ICAS in symptomatic patients and >70% ICAS in asymptomatic patients is important because these cut levels are established criteria for therapeutic stratification (1). Furthermore, diagnosis of ICAS stenosis progression by duplex ultrasonography (DUS) is a significant predictor of neurovascular events during follow-up in asymptomatic patients (4,5). Additionally, there is a clinical need for completely noninvasive ICAS imaging technologies that do not have the nephrotoxic side effects of angiographic contrast agents (1).

DUS has numerous pitfalls when quantification of stenosis is attempted by spectral blood velocity parameters (1,6,7). In particular, for stenoses within the low (<50%) to moderate (50% to 70%) range, intrastenotic velocity increases only slowly relative to the luminal loss, thereby resulting in a lack of diagnostic accuracy that often requires additional morphological estimation of plaque stenosis in B-mode or color-Doppler ultrasonography (US) images according to the NASCET (North American Symptomatic Carotid Endarterectomy Trial) method (6–10). To improve detection of moderate stenoses, US societies suggested combining spectral DUS with visual stenosis estimation within 2-dimensional (2D) US images (6,7). However, direct measurement of stenotic lumen reduction within 2D color-Doppler US images delivered inconsistent results and may not improve accuracy when this method is used alone (8,9). It was hypothesized that 3-dimensional (3D) sonomorphometry could be an important innovation and enhance validity of direct stenosis measurement.

Previously, 3D color-Doppler US (3DC-US) of ICAS was evaluated in reconstructed images using resource-intensive approaches such as freehand 2D color-Doppler scanning and post hoc 3D reconstruction from serial slices using interpolation algorithms (11–13). Stenosis grading with 3DC-US using a dedicated volume probe generating static 3D images for immediate online and post hoc off-line multiplanar rendering (MPR) of relevant vessel segments is an innovative approach. The static 3DC-US volumetric images can be acquired after a quick topoanatomic orientation with real-time 4-dimensionally (4D) guided gray-scale imaging using the same probe. The possibility of remote interpretation of 3D raw data provided by a sonographer implies advantages similar to those of teleradiology and may be clinically applicable to 3DC-US, while bearing in mind observer dependency and other limitations of US (1). Our intention was to assess the diagnostic features of 4D real-time guided 3DC-US (4D/3DC-US) by measuring the NASCET percentage of lumen reduction in comparison with catheter angiography (CA) and DUS (10,14). We hypothesized that the percentage of stenosis grades measured within 3D multiplanar-rendered 3DC-US volume datasets would allow grading of ICAS at an equivalent accuracy compared with these modalities.

We conducted this multimodality imaging study in a prospective, controlled, and blinded fashion by providing patients with a clinically relevant indication for exact stenosis quantification before possible revascularization (1).

MATERIAL AND METHODS

ENROLLMENT OF PATIENTS AND DATA COLLECTION. Consecutive ambulatory patients with suspected carotid artery stenoses were offered participation in our prospective bicentric multimodality imaging study at the University of Freiburg and the University Heart Center of Freiburg-Bad Krozingen in Germany, independent of other studies on patients with carotid artery stenosis (15). US imaging and all analyses were performed in individual patients with a symptomatic indication or relevant carotid plaque stenosis with suspected progression on prescreening. CA was clinically justified and offered to patients with an indication to undergo carotid artery revascularization eventually according to a multidisciplinary clinical board decision.

All therapeutic procedures and decisions were performed independent of this research study protocol. All patients received a neurological examination at baseline. Pre-screening of 216 eligible patients was performed with 2D DUS, followed by clinical and US screening with 4D/3DC-US; the final study examinations were performed using 4D/3DC-US, DUS, and angiography was performed after anonymization (Figures 1 and 2). The study recordings were independently analyzed (Figures 1 and 2). A total of 101 study patients had given written informed consent and were informed about the potential angiographic risk, including irreversible cerebral ischemic events (1,15). Inclusion criteria were informed consent and good US image quality (Figure 1). Study exclusions were made on the basis of clinical (n = 8) and imaging (n = 13) criteria (Figure 1). Other pre-specified exclusion criteria that did not apply were pregnancy, asymptomatic status in patients younger than 50 years of age, mental illness other than dementia, suspected nonatherosclerotic stenosis, and other