Handheld Versus Conventional Ultrasound for Assessing Carotid Artery in Routine Volunteers

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Research Article

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Abstract

Objective: The study aimed to estimate the feasibility and accuracy of carotid intima-media thickness (CMT) and hemodynamic parameters measurement in a handheld ultrasound device.

Methods: Utilizing an ex vivo pig carotid artery sample, CMT was measured with a handheld ultrasound and compared with histopathology. Then we performed a carotid ultrasound on 25 volunteers using a handheld ultrasound device and a conventional ultrasound system. After a week, these volunteers were scanned again by the same observer. Assessments of the max IMT, mean IMT and hemodynamic parameters (PSV, EDV, PI, RI, S/D, ACCEL, AT, TAMEAN) were compared. Intraclass correlation coefficient (ICC) was used to assess inter-device agreement. Repeatability and correlation of mean IMT were analyzed by Bland–Altman Plots and linear correlation analysis.

Results: The mean IMT measured from the common carotid artery by handheld ultrasound showed good agreement (ICC=0.79) with conventional ultrasound. Furthermore, we obtained good repeatability and a consistent trend in the mean value of IMT before and after ($r = 0.680$, $P < 0.01$). In addition, the max IMT and the hemodynamic parameters (PSV, EDV, S/D, ACCEL, TAMEAN) showed moderate agreement (ICC=0.73, 0.52, 0.58, 0.70, 0.61, 0.51, respectively). The PI, RI and HR values were excellent agreement with conventional ultrasound (ICC=0.80, 0.84, 0.94).

Conclusion: About the basic assessment of carotid, the images and parameters obtained using handheld ultrasound showed a moderate to excellent agreement with conventional ultrasound. The handheld ultrasonic devices can be widely used as a diagnostic tool for carotid artery structure and hemodynamics examination.

Background

Cardiovascular disease is the leading cause of death all over the world ^[1]. The root cause of cardiovascular and cerebrovascular events is atherosclerosis (AS), a chronic, inflammatory disease characterized by plaque formation on the intimal surface of the artery ^[2]. As the main clinical cause of stroke, carotid atherosclerosis is considered to be directly related to treatment effect, prognosis and recurrence, and may be an independent predictor of important adverse cardiac events ^[3]. Many studies revealed that carotid ultrasound could further evaluate and predict the risk of cardiovascular and cerebrovascular diseases by measuring carotid intima-media thickness (CMT) ^[4–6]. The increased CMT reflects the early stages of AS and cardiovascular risk. Recently, with its perspective, availability and portability, handheld ultrasound equipment is expected to become the second "Stethoscope" for general practitioners' outvolunteer, ward, site and family follow-up. This study investigated the feasibility and repeatability of a handheld ultrasound device in assessing CMT and carotid hemodynamic parameters measurements compared with a conventional ultrasound device representative of this class of devices.

Materials And Methods

Tissue mimicking ultrasound phantom

The ultrasound phantom used KS107BD (L) system (Institute of acoustics, Academy of Sciences, China). These phantoms were filled with ultrasonically tissue-mimicking materials (TM materials). In TM materials, speed of sound was $1540 \pm 10 \text{ m/s}$, and acoustic attenuations were $0.70 \pm 0.05 \text{ dB/cm/MHz}$ (23 ± 3). Phantoms contained monofilament nylon targets and simulated tumor, cyst and stone. The longitudinal resolution and the axial resolution at different depths (2cm, 3cm, 4cm and 5cm, respectively) were measured by handheld ultrasound (STORK, China) and conventional ultrasound (Insight 37CT, SASET, China). The measurements were repeated 4 times, and took the average value.

Ex Vivo carotid Phantom

One freshly excised pig carotid was acquired from a local butcher shop. An acoustic absorber was placed on the bottom layer of the mold, and 0.9% normal saline was poured into the mold that contained the carotid sample, which was suspended by using a stitching thread, as shown in Figure 1. A handheld device (STORK, China) equipped with a 4-12MHz linear probe was used. We used the automatic detection of IMT ultrasound technique for measuring IMT on our model by five times. The operator was blinded to the actual size of each model.

Pathological Examination

Hematoxylin and eosin (HE) staining: The pig carotid was sealed in 10% formalin solution and embedded in paraffin, which was then cross-sectioned for a transverse section of tissues of about $3 \mu\text{m}$ in thickness. The section was then HE stained to observe IMT. The level of IMT in each slice was measured by Leica Cyclone software. We randomly selected five slices, measured each slice three times, and took the average value of IMT.

Study population

This study enrolled 25 volunteers (at Jiading Branch of Shanghai First People's Hospital, Shanghai, China). These volunteers underwent a scan using both the handheld ultrasound and a conventional ultrasound and repeated the scan after a week. One junior sonographer (with more than 3 years of experience in diagnostic ultrasound) performed all the exams. The order of the second visit was arranged by random. The observer was unaware of volunteers' clinical information or status. Furthermore, each volunteer who underwent examination with the handheld ultrasound was performed after informed consent. Clinical investigations were performed according to the Declaration of Helsinki. Each participant signed the informed consent form for this study. This study protocol was approved by the medical ethics committee of Shanghai General Hospital (2019KY009-4) and registered on the official website of China Clinical Trial Registration Center (ChiCTR2000035937).

Ultrasound examinations

The volunteers underwent the examination in a supine position and breathed calmly. The enrolled volunteers underwent carotid ultrasound scans by the handheld ultrasound device (STORK, China) equipped with a 4-12MHz linear probe and a conventional ultrasound device (LOGIC P9, GE Healthcare) with a 3-12MHz linear probe. The IMT of the common carotid artery was measured at 1.5cm proximal to the carotid bifurcation. The max IMT, mean IMT were measured on the far wall along the common carotid artery and analyzed by internal automatic software. The length of the automatic sampling frame is about 15mm; the measurement of the CIMT was obtained using a micrometer-scale value. The CIMT and the hemodynamic parameters were measured in longitudinal planes. In addition, hemodynamic parameters, i.e., peak systolic velocity (PSV), end diastolic velocity (EDV), artery systolic-diastolic ratio ($S/D=PSV/EDV$), resistive index ($RI=(PSV-EDV)/PSV$), mean flow velocity (MFV), pulsatility index ($PI=(PSV-EDV)/MFV$), acceleration time (AT), blood flow acceleration (ACCEL), time averaged mean velocity (TAMEAN) of carotid arteries were acquired and recorded using the Doppler ultrasound technique. The values of hemodynamic parameters were measured and calculated with a mean value obtained in 3 continuous cardiac cycles (Figure 2).

Statistical analysis

SPSS 19.0 (IBM, Armonk, NY, USA) statistical analysis software was used. The continuous data were expressed as mean $\pm$ SD, and compared using a paired sample t-test. Non-normally distributed data were analyzed by Wilcoxon signed-rank test. Intraclass correlation coefficient (ICC) was used to assess inter-device agreement. The Bland-Altman plot and linear correlation analysis were used to assess repeatability and correlation of mean IMT. $P<0.05$ represented that the difference was statistically significant.

Results

1. Tissue mimicking ultrasound phantom

Targets at four different depths were evaluated in this study. There were no difference in the longitudinal resolution and the axial resolution by using handheld ultrasound and conventional ultrasound (Table 1).

Table 1
Comparisons of conventional and handheld ultrasounds values in ultrasound phantoms
($\bar{x} \pm s$)

Item	Conventional ultrasounds	Handheld ultrasounds	t/Z value	p value
Longitudinal resolution (cm)				
2cm	1.01±0.02	1.01±0.03	-0.111 ^a	0.919 ^a
3cm	0.99±0.02	0.99±0.01	1.567 ^a	0.215 ^a
4cm	1.02±0.02	1.01±0.03	0.000 ^b	1.000 ^b
5cm	1.01±0.02	1.00±0.02	-2.449 ^a	0.092 ^a
Axial resolution (cm)				
2cm	4.15±0.10	4.20±0.00	-1.000 ^b	0.317 ^b
3cm	4.10±0.14	4.20±0.08	1.000 ^a	0.391 ^a
4cm	4.03±0.15	4.10±0.14	1.000 ^a	0.391 ^a
5cm	4.08±0.17	4.05±0.13	-0.264 ^a	0.809 ^a
^a Paired t-test; ^b Wilcoxon signed-rank test				

2.Ex Vivo Experiments Findings

The IMT for the handheld ultrasound was 0.60 ± 0.03 mm, and that for the HE was 0.57 ± 0.01 mm. The difference of IMT were not statistically significant ($P \geq 0.05$). The images were shown in Figure 3.

Volunteer Population

We examined 25 volunteers (2 males and 23 females) and repeated the scan after a week. Therefore, 47 ultrasound examinations were performed and 3 ultrasound examinations were lost. Loss of consented volunteers was due to withdrawn consent or time constraints. The volunteers ranged in age from 22 to 50 years, mean age was 35.20 ± 8.68 years.

3.Measurements of CCA using handheld and conventional ultrasound

To assess whether the carotid structure and hemodynamic parameters could be accurately carried out with the handheld ultrasound device, we compared the values of max IMT, mean IMT and hemodynamic parameters measurements from the handheld ultrasound with those from the conventional ultrasound. The comparisons of values between the handheld and conventional ultrasound were shown in Table 2. The mean value of mean IMT was increased in handheld ultrasound group when compared with the conventional ultrasound group ($0.50\pm0.07\text{mm}$ vs. $0.46\pm0.07\text{mm}$, <0.001). However, the measurements had a good ICC of 0.79 for the mean IMT [95% confidence interval (CI): 0.66, 0.88]. The detailed analysis was shown in Table 3.

Table 2
Changes and comparisons of conventional and handheld ultrasounds values ($\bar{x}\pm s$) (n=47)

Item	Conventional ultrasounds	Handheld ultrasounds	t/Z value	p value
Max IMT (mm)	0.54 ± 0.08	0.51 ± 0.07	-2.950 ^b	0.003 ^b
Mean IMT (mm)	0.46 ± 0.07	0.50 ± 0.07	-4.495 ^b	$<0.001^b$
PSV (cm/s)	78.31 ± 10.37	76.65 ± 12.52	0.868 ^a	0.390 ^a
EDV (cm/s)	25.2 ± 3.45	21.89 ± 4.54	4.402 ^b	$<0.001^b$
PI	1.34 ± 0.22	1.52 ± 0.30	-5.374 ^b	$<0.001^b$
RI	0.67 ± 0.05	0.71 ± 0.05	-5.377 ^b	$<0.001^b$
S/D	3.14 ± 0.47	3.61 ± 0.8	-5.519 ^b	$<0.001^b$
ACCEL (cm/s ²)	699.65 ± 218.64	622.85 ± 142.28	2.701 ^a	0.010 ^a
AT (s)	0.08 ± 0.02	0.09 ± 0.01	-4.148 ^b	$<0.001^b$
TAMEAN (cm/s)	24.7 ± 3.58	23.91 ± 4.36	1.186 ^a	0.242 ^a
HR (bpm)	72.87 ± 8.18	74.4 ± 8.82	-2.571 ^a	0.013 ^a
IMT: Intima-media thickness; PSV: Peak systolic velocity; EDV: End diastolic velocity; PI: Pulsatility index; RI: Resistive index; S/D: Systolic-diastolic ratio; ACCEL: Blood flow acceleration; AT: Acceleration time; TAMEAN: Time averaged mean velocity; HR: Heart rate				
^a Paired t-test; ^b Wilcoxon signed-rank test				

Table 3
ICC analysis for conventional ultrasounds vs handheld ultrasounds
(n=47)

Item	ICC (95% CI)	<i>p</i> value
Max intima-media thickness (mm)	0.73 (0.56-0.84)	<0.001
Mean intima-media thickness (mm)	0.79 (0.66-0.88)	<0.001
Peak systolic velocity (cm/s)	0.52 (0.13-0.73)	0.008
End diastolic velocity (cm/s)	0.58 (0.25-0.77)	0.002
Pulsatility index	0.80 (0.65-0.89)	<0.001
Resistive index	0.84 (0.72-0.91)	<0.001
Systolic-diastolic ratio	0.70 (0.47-0.84)	<0.001
Blood flow acceleration (cm/s ²)	0.61 (0.31-0.78)	0.001
Acceleration time (s)	0.29 (-0.28-0.60)	0.129
Time averaged mean velocity (cm/s)	0.51 (0.13-0.73)	0.008
Heart rate (bpm)	0.94 (0.89-0.97)	<0.001

4. Agreement and reproducibility of the handheld ultrasound

To determine the reproducibility of mean IMT using a handheld ultrasound, the operator performed scans and measurements on the volunteers after a week. Bland-Altman analysis showed that the mean and standard deviation of the difference in the mean IMT measurements of handheld ultrasounds before and after were (0.015 ± 0.057), and the mean and standard deviation of the difference in the mean IMT measurements of conventional ultrasounds before and after were (-0.004 ± 0.046). The two measurements showed a consistent trend between the differential and mean values (Fig. 4a and c).

The repeatability test showed the handheld ultrasounds measurements of mean IMT before and after were correlated ($r = 0.680$, $P < 0.01$), and the linear regression equation was $y = 0.117 + 0.739x$. The conventional ultrasounds measurements of mean IMT before and after were highly correlated ($r = 0.789$, $P < 0.01$), and the linear regression equation was $y = 0.040 + 0.922x$. These values correspond to good reproducibility for this handheld ultrasound. The detailed analysis was shown in Figure 4b and d.

Discussion

This observational study assessed the diagnostic feasibility of carotid artery structure and hemodynamic parameters using a handheld ultrasound. The main finding of this study was: The handheld ultrasound scans that focused on the basic assessment of carotid and hemodynamic parameters showed a moderate to good correlation with conventional ultrasound images.

AS is a chronic inflammatory disease caused by a variety of etiologies and risk factors, which can affect many blood vessels in the whole body. The development of progressive vascular AS is the cause of most cardiovascular diseases (CVD) [7]. In the early stage of carotid atherosclerosis, a small amount of lipid will deposit on the intima, increasing CIMT. Previous studies have shown that the CIMT is an important indicator of arteriosclerosis and independent predictors of cardiovascular events [8]. Usually, the ultrasound scan is the most widely used method for CCA with its simplicity, non-invasion and excellent reproducibility, and utilized to evaluate the artery hemodynamic status and the measurement of the CIMT.

Handheld ultrasound is a small portable device and is a rapidly evolving technology with significant challenges and opportunities. At present, it is mainly used in the preliminary screening of diseases in an emergency, operating room and community chronic disease management [9]. The examination items include various examinations of the heart, carotid artery, liver, kidney, thyroid and other organs. It has gradually become one of the important examination instruments for volunteers with cardiovascular diseases [10, 11].

Of course, concerns about the limited size of handheld ultrasound devices degrades the imaging quality, which reduces the diagnostic reliability have been raised [12, 13]. In addition, operator dependence, including high inter-and intra-operator variability, is crucial in using a handheld ultrasound device [14, 15]. In our study, the results showed the differences in CIMT and hemodynamic parameters value between handheld ultrasound and conventional ultrasound. The reasons for these errors in our study may relate to the differences in quality between the handheld and conventional ultrasound images and the lower blood flow sensitivity compared to conventional ultrasound. The variability of Doppler-derived carotid hemodynamic measures has many sources, such as a small diversity in the insonation angle may result in a large velocity diversity [16, 17]. In addition, ultrasound protocols to measure CIMT may vary in the selections of the carotid segments, angles, and walls of the carotid artery measured [18]; this partially increase random differences in making outline and measurement of CIMT. However, in this study, the results showed the good agreement for the measurements between the handheld ultrasound and conventional ultrasound imaging studies. Although the values in this study between handheld ultrasound and conventional ultrasound are significant difference, our results suggested that the differences of values could be accepted within the clinical range.

Our findings of handheld ultrasound are consistent with those in previously published studies. Jang et al. noted excellent agreement and repeatability between wireless handheld ultrasound and standard ultrasound in max-CIMT measurement [19]. Prinz et al. found that handheld echocardiographic devices showed a moderate to perfect correlation with standard echocardiography [20]. Notably, in our study, the

reproducibility and consistency in assessing mean IMT using a handheld ultrasound device are good. These results suggested that the handheld ultrasound is effective as a screening tool for the identification of carotid artery structure and hemodynamic parameters disorders in clinical practice. Certainly, the differences could be reduced and reversed by successful image acquisition and assessment with improved intelligent analysis metabolism. Thus, this puts forward higher requirements in accuracy and sensitivity for handheld ultrasound equipment.

However, this technique can provide a more helpful tool for screening in carotid artery disease or imaging biomarkers for CVD and cardiovascular risk. The use of handheld ultrasound can realize the preliminary judgment of ultrasonic image abnormalities in settings such as the primary care office or the emergency department, which may provide more cost-effective and time-efficient than traditional ultrasound. It is believed that with the development of science and technology, the detection of the carotid artery by handheld ultrasound will be more convenient, objective and accurate.

Limitations

In this study, we only scanned the carotid structure and hemodynamic parameters with high-frequency linear probes using handheld ultrasound; therefore, we cannot comment on the use of handheld ultrasound in other superficial organs' examinations with linear probes, such as thyroid, breast, or with other types of probes. In addition, experiments in vitro and volunteers under more complicated conditions, such as CCA plaques were not tested. These image quality and parameters comparison with conventional ultrasound should be examined in the future.

Conclusions

Concerning primary assessment of carotid, the images obtained using handheld ultrasonic devices showed a moderate to good correlation with a conventional ultrasound system. The handheld ultrasound device can be used as a screening and follow-up tool to determine or exclude carotid artery abnormalities before the application of conventional ultrasound, and has the potential to be widely used as a diagnostic tool for carotid artery structure and hemodynamics examination, and it will bring more convenience to clinical work and better serve volunteers.

Abbreviations

CIMT: carotid intima-media thickness

Declarations

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We thank all of the patients involved in this study.

Authors' contributions

ZJL conceived the study and revised the manuscript. JXC designed and performed the experiments. LJ performed the data analyses and drafted the manuscript. CQS and LYT are involved in ultrasound examination and diagnosis. LFD analyzed and interpreted data. All authors read and approved the final manuscript.

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Ethics approval and consent to participate

This study protocol was approved by the medical ethics committee of Shanghai General Hospital (2019KY009-4) and registered on the official website of China Clinical Trial Registration Center (ChiCTR2000035937).

Consent for publication

Written informed consent was obtained from all the patients for publication of this manuscript and any accompanying images.

Availability of data and materials

The datasets used in the manuscript are available from the corresponding author upon reasonable request.

Competing interests:

The authors declare that there is no conflict of interest with any financial organization or corporation or individual that can inappropriately influence this work.

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Figures

Figure 1

An ex vivo carotid (a), the data acquisition method using handheld ultrasound scanner (b), and pathological examination (c).

Figure 2

The handheld ultrasound image system, showing the measurement of CIMT and hemodynamic indexes with linear probe by the handheld ultrasound

Figure 3

IMT of pig carotid detected by handheld ultrasound (a) and hematoxylin and eosin (b). scale bar shows 400 μ m ($\times 40$).

Figure 4

Repeatability was analyzed by Bland–Altman Plots (a and c) and linear correlation analysis (b and d). The results showed a consistent trend in the difference value and the mean value of IMT before and after.