THE ANATOLIAN JOURNAL OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

A Novel Approach to Assessing the Severity of Acute Stroke and Neurological Deficits in Patients with Acute Ischemic Stroke Using Myocardial Work Echocardiography

ORIGINAL INVESTIGATION

ABSTRACT

Background: We aimed to evaluate the feasibility and performance of myocardial work echocardiography in assessing the severity of acute stroke and neurological deficits in patients with acute ischemic stroke.

Methods: A total of 176 patients were examined by echocardiography within 24-48 hours of symptom onset with the measurement of global and regional myocardial work. The National Institutes of Health Stroke Scale score of each patient was documented.

Results: With the increase of the National Institutes of Health Stroke Scale score, myocardial constructive work or positive work decreased ($P < .05$), while myocardial wasted work or negative work increased ($P < .05$). Except for global constructive work, global positive work, and global systolic constructive work, other myocardial work parameters all correlated with the National Institutes of Health Stroke Scale score ($P < .05$). Moreover, global wasted work, global negative work and global systolic wasted work had the strongest correlation with the National Institutes of Health Stroke Scale score ($P < .001$).Among these parameters, the ratio of global positive work/global negative work had the largest area (0.969, 0.938-1.001) under receiver operating characteristic curve in discriminating if the National Institutes of Health Stroke Scale score >15 or not. The optimal cutoff value was 3.89, with a sensitivity of 100%, a specificity of 93.0%, a positive predictive value of 84.9%, a negative predictive value of 100%, and an accuracy of 95.7%.

Conclusion: Noninvasive myocardial work is highly competent in assessing the severity of acute stroke and neurological deficits, which can be used as a powerful supplement to the conventional scoring system.

Keywords: Stroke, neurological deficits, NIHSS score, myocardial damage, myocardial work echocardiography

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Received: February 21, 2022
Accepted: July 5, 2022
Available Online Date: July 20, 2022

Cite this article as: Zhang J, Wu X, Zheng X. A novel approach to assessing the severity of acute stroke and neurological deficits in patients with acute ischemic stroke using myocardial work echocardiography. *Anatol J Cardiol*. 2022;26(12):893-901.

DOI:10.5152/AnatolJCardiol.2022.1769

INTRODUCTION

It has been confirmed by clinical observation[1-5] and experimental[6] and histopathological study[7] that acute cerebral lesions can cause myocardial damage. Moreover, the risk of myocardial damage increases proportionally to the severity of acute stroke and neurological deficits.[8] In other words, the more severe the clinical presentation of the acute stroke is, the more serious the myocardial damage is.

Myocardial work echocardiography (MWE) is a novel approach to assessing left ventricular (LV) function using pressure–strain loops (PSL) that take into account deformation as well as LV afterload.[9-16] Our previous study has demonstrated that global work efficiency (GWE) was superior to global longitudinal strain (GLS) and left ventricular ejection fraction (LVEF) to predict stroke-induced myocardial damage in patients with acute stroke.

The National Institutes of Health Stroke Scale (NIHSS) score has been widely used in the clinic to quantify the patients' neurological deficits and outcomes after treatment and has been a valid instrument that provides a standardized evaluation of symptoms and signs of stroke.[17-20] However, the reliability of this rating scale is always subject to the subjective factors of the observer and the cooperation degree of patients. A more objective evaluation method is needed.

In the present study, the correlation between myocardial work and NIHSS, and the feasibility and performance of myocardial work in predicting the severity of acute stroke and neurological deficit were investigated.

METHODS

Study Population

This is a time-limited cross-sectional case–control study. This study was performed in our Stroke Medical Center between November 2020 and August 2021. The study protocol was approved by the Ethics Committee of our institution. Written informed consent was obtained from all participants prior to enrollment. A total of 193 patients aged between 42 and 97 years with acute ischemic stroke were consecutively enrolled regardless of thrombolytic or endovascular therapy. Acute ischemic stroke was diagnosed by neurologists based on detailed clinical assessment, neurological examination, and image modalities which included brain computed tomography or brain magnetic resonance imaging (MRI). The exclusion criteria were transient ischemic attack, cerebellar infarcts, acute hemorrhagic stroke, traumatic brain injury, structural heart diseases, aortic stenosis, major valvulopathies (e.g., severe mitral regurgitation), the presence of pacemaker/implantable cardioverter, heart failure with reduced ejection fraction, active infection without treatment, autoimmune diseases, malignancy, major surgery within 3 months, advanced liver cirrhosis, and end-stage renal disease on peritoneal dialysis or hemodialysis. Additionally, patients presenting with hemodynamic instability, post cardiopulmonary resuscitation, or indication for immediate surgical intervention were also excluded from the present study.

A control group of age- and gender-matched 50 subjects (not patients with stroke) with similar risk factors (diabetes, hypertension, hyperlipidemia, history of coronary heart disease, etc.) was recruited from departmental volunteers and advertisement responders. Controls were excluded if they had a history of neurological disorders or if they had contraindications to MRI scanning.

The NIHSS scores, the electrocardiogram (ECG) results, and the results of laboratory tests of all the subjects, such as blood creatine kinase (CK), creatine kinase isoenzyme MB (CK-MB), cardiac troponin-T (cTnT), and B-type natriuretic peptide (BNP), were simultaneously recorded.

Conventional Transthoracic Echocardiography

Comprehensive transthoracic echocardiography was performed in all patients within 24-48 hours of symptom onset using a commercially available machine equipped with an M5s 3.5-MHz transducer (Vivid E95, GE Healthcare, Horton, Norway). Images were stored on a dedicated workstation for subsequent analysis (EchoPAC, version 203 for PC, GE Healthcare, Horton, Norway). The echocardiographers were blinded to the clinical features of the subjects.

All patients were in stable hemodynamic condition at the time of each exam. Left atrial end-systolic anteroposterior diameter (D_{LA}), LV end-diastolic anteroposterior diameter (D_{LV}), right atrial end-systolic transverse diameter (D_{RA}), right ventricular end-diastolic anteroposterior diameter (D_{RV}), coronary sinus diameter (D_{CS}), right ventricular fractional area change (FAC_{RV}), Simpson's biplane-derived LVEF, and LV mass index (LVM index) were obtained by real-time 2D echo method. Tricuspid annular plane systolic excursion (TAPSE) was obtained by M-mode echo method. The peak early diastolic transmitral filling velocities (E) and the velocity time integral at coronary sinus mouth (VTI_{CS}) were obtained by Doppler echo method. The peak early diastolic lateral mitral annulus tissue velocities (E′) were obtained by the tissue Doppler echo method. Finally, the ratio of E/E′ and antegrade coronary sinus (Flow)[21] was calculated.

Two-Dimensional Speckle-Tracking Echocardiography

Dynamic 2-dimensional gray-scale images of the LV were acquired continuously at 3-chamber view, 4-chamber view, and 2-chamber view with 50-80 frames/sec. The images were transferred to the dedicated workstation with the stored digital raw-data format and analyzed using custom software (GE Medical Systems, Version 203, Horten, Norway). Endocardium and epicardium borders were traced with automated function imaging (AFI) for each of the 2 apical views, with adjustments if deemed necessary. Global longitudinal strain was determined as the average of peak longitudinal strain from the 17 myocardial segments. Meanwhile, peak strain dispersion (PSD) was presented to assess LV myocardial systolic dyssynchrony.

Myocardial Work Measurement

The measurement of myocardial work was executed offline on the commercially available GE software (EchoPAC version 203) with AFI function. Myocardial work and related indices were calculated from a combination of 2D LV GLS data acquired by speckle-tracking echocardiography (STE) and a noninvasively estimated LV pressure curve. Brachial blood pressure was measured 3 times by cuff manometer at rest, immediately before the echocardiographic examination. Peak systolic LV pressure was assumed to be equivalent to brachial blood pressure. The measurement steps are as follows: (1) get the bull's-eye plot of GLS in 17-segmental myocardium using STE, (2) click the "myocardial work" button, (3) input the brachial artery blood pressure value, (4) click the "Approve" button then a Bull's-eye plot showing 17-segmental longitudinal peak systolic strain, time to peak,

HIGHLIGHTS

- Myocardial work parameters correlated well with the National Institutes of Health Stroke Scale (NIHSS) score in patients with acute ischemic stroke.
- The ratio of global positive work and global negative work had a powerful performance on discriminating if NIHSS score >15 or not.
- Noninvasive myocardial work can serve as a powerful supplement to the conventional scoring system.

myocardial work index, and myocardial work efficiency is generated automatically, and (5) click the "Export" button, and the following indices of myocardial work are automatically generated and presented in an Excel table (Figure 1).

a. Global work index (GWI, mm Hg %): total work within the area of the LV PSL calculated from mitral valve closure to mitral valve opening.[9,22-28]
b. Global constructive work (GCW, mm Hg %): work performed by LV segmental shortening during systole and lengthening during isovolumic relaxation (IVR), which contributes to the LV ejection.[9,22-28]
c. Global wasted work (GWW, mm Hg %): work performed by LV myocardial lengthening during systole and shortening during IVR, which does not contribute to LV ejection (represented energy loss).[9,22-28]
d. Global work efficiency (GWE, %): stemmed from the ratio of constructive and wasted work as GCW/(GCW + GWW) × 100%.[9,22-28]
e. Global positive work (GPW, mm Hg %): myocardial work during shortening in systole and IVR (work during systole and IVR is treated the same).
f. Global negative work (GNW, mm Hg %): myocardial work during lengthening in systole and IVR (work during systole and IVR is treated the same).
g. Global systolic constructive work (GSCW, mm Hg %): myocardial work during shortening in systole (IVR not included).
h. Global systolic wasted work (GSWW, mm Hg %): myocardial work during lengthening in systole (IVR not included).

Finally, click the "Advanced" button. Pressure–strain loops curve corresponding to LV segmental, and global myocardial work index and myocardial work efficiency are generated automatically. The ratio of GCW/GWW, GPW/GNW, and GSCW/GSWW is calculated.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation. Kolmogorov–Smirnov test and P-P plots were used to test the conformity of the conditional variables to the normal distribution. In the comparisons of the 2 groups, normally distributed continuous data were tested with the independent samples Student's *t*-test and non-normally distributed continuous variables with the Mann–Whitney *U* test. Categorical variables were tested with Pearson's chi-square test. In the comparisons of 3 or more groups, 1-way analysis of variance was used for groups with normal distribution and Kruskal–Wallis *H* test for groups that were not normally distributed. Multiple comparisons test was used for the simultaneous pairwise multiple comparisons of the groups. For the nonparametric post hoc tests, Bonferroni test was applied in which Kruskal–Wallis *H* test has been used. The Pearson's correlation analysis was used for determining the significance of correlations between myocardial work values and NIHSS score. A receiver operating characteristic curve (ROC) analysis of myocardial work was used to differentiate if NIHSS >15 or not and to determine the optimal cutoff points and validity parameters. Bland and Altman was used to measure the inter/intraobserver variability. All tests were 2-sided, and P-values < .05 were considered to indicate statistical significance. All statistical analyses were processed using a statistical software program (SPSS Version 19.0, IBM, Chicago, Ill, USA).

RESULTS

Clinical and Laboratory Characteristics

Seventeen of the 193 patients with stroke were excluded due to poor 2D echo imaging quality, and 176 patients were eventually included in the study. Eighty-five of them had acute ECG abnormalities, including unspecified ST-T changes, ST-segment elevation, ST-segment depression, QT prolongation, T inversion, abnormal T wave morphology, bundle branch block, and pathological Q waves, 17 of them had atrial fibrillation, and the remaining 74 patients had normal sinus rhythm. According to the NIHSS score, they were divided into 4 groups: group 1 (n=54), normal or near normal, 0-1 points (normal neurological examination); group 2 (n=45), mild or minor stroke, 2-4 points (mild or minor facial palsy, mild or minor abnormality of eye movements, visual field, motor arm, motor leg, limb ataxia, mild or minor abnormality of sensory, language, speech, extinction, and inattention); group 3 (n=36), moderate stroke, 5-15 points (moderate abnormality mentioned above accompanied by mild disturbance of consciousness); and group 4 (n=41), moderate-severe stroke, 16-42 points (moderate-severe abnormality mentioned above accompanied by moderate-severe disturbance of consciousness and even unresponsiveness coma). The mean NIHSS score for the whole patient group was 9.8.

As shown in Table 1, there were no differences in terms of age, gender, body surface area, heart rate, and blood pressure between the control group and patients with ischemic stroke(P > .05). Comorbidities such as diabetes mellitus and hypercholesterolemia and medications such as β-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, statins, and calcium channel blockers were more common among patients with ischemic stroke (P <.05). The prevalence of coronary heart disease was similar between the patients with ischemic stroke and the control group. There was a significant increase in hs-cTnT, CK, CK-MB, and BNP in patients with ischemic stroke compared to the control group (P < .05).

Conventional Echocardiographic Parameters

The conventional echocardiographic characteristics of entire cohort are presented in Table 2. Compared with control group, the atria was larger in patients with ischemic stroke (P < .05), but there was little change in ventricular size and LVM index (P > .05). In patients with ischemic stroke, there was no significant change in cardiac size between each other (P >.05). With the increase of NIHSS, patients had more impaired cardiac systolic function (represented by lower LVEF and FAC_{RV}), more impaired cardiac diastolic function (represented by higher E/E'), and more reduced myocardial perfusion (represented by slightly lower Dcs, VTI, and Flow) (P <.05). Tricuspid annular plane systolic excursion was still within the normal range (P > .05).

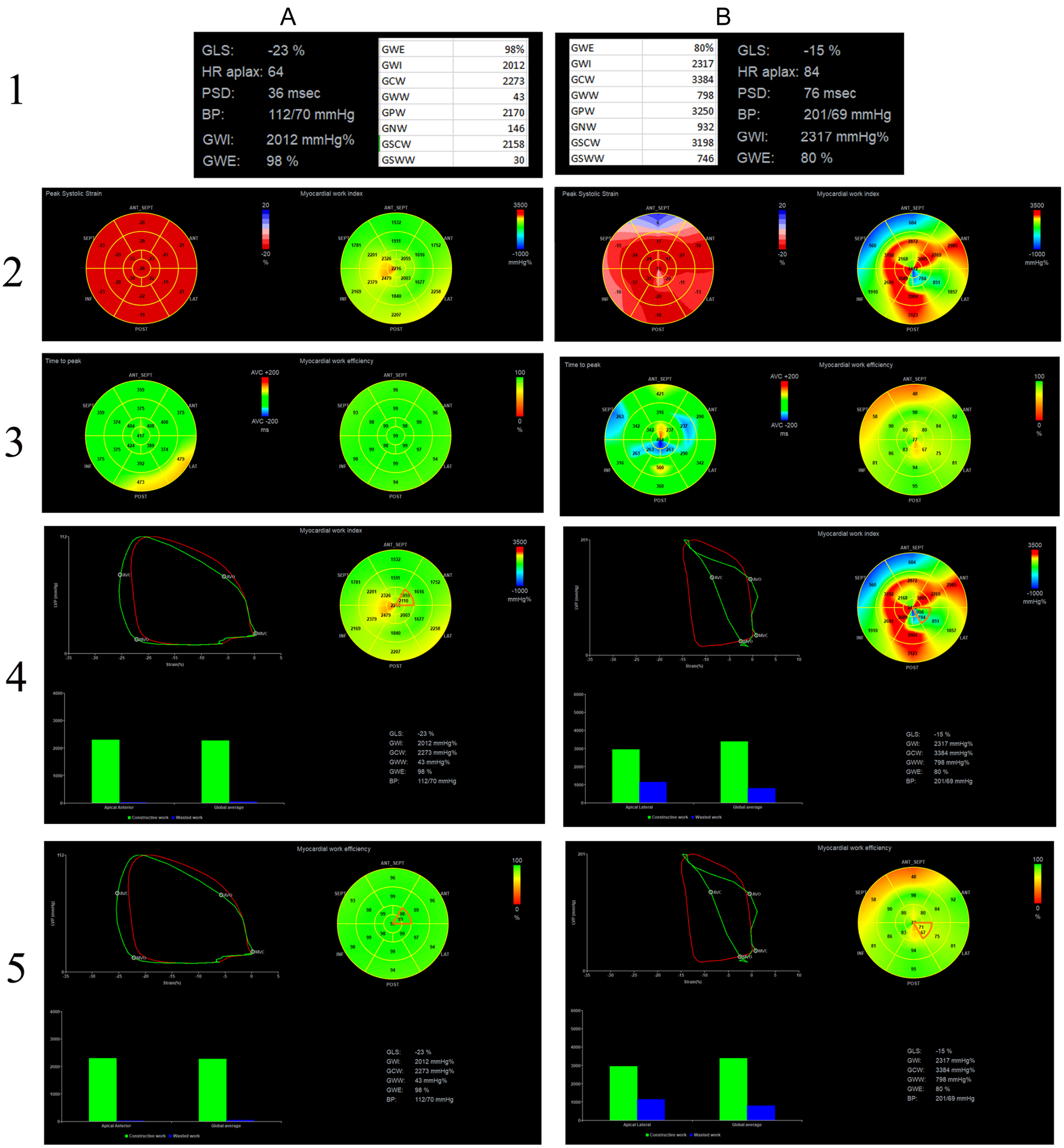

Figure 1. Myocardial work and related indices in a subject of control group (A) and a patient with a NIHSS score of 28 (B). A1 and B1, the value of myocardial work and related indices; A2 and B2, bull's-eye plots showing left ventricular 17-segment longitudinal peak systolic strain and myocardial work index; A3 and B3, bull's-eye plots showing time to peak and myocardial work efficiency; A4 and B4, pressure–strain loops curve corresponding to left ventricular segmental and global myocardial work index (GWI); A5 and B5, pressure–strain loops curve corresponding to left ventricular segmental and global myocardial work efficiency (GWE). GCW, global constructive work; GLS, global longitudinal strain; GNW, global negative work; GPW, global positive work; GSCW, global systolic constructive work; GSWW, global systolic wasted work; GWE, global work efficiency; GWI, global work index; GWW, global wasted work; PSD, peak strain dispersion.

Table 1. Clinical and Laboratory Characteristics of the Control Group and Patients with Ischemic Stroke

Variables	Control Group (n = 50)	Patient with Ischemic Stroke (n = 176)	*P*
Age (years)	68.9 ± 15.3	71.3 ± 17.8	**.792**
Male (%)	32 (64)	106 (60)	**.763**
BSA (m^2)	1.98 ± 0.31	2.11 ± 0.32	**.568**
Heart rate (beats/min)	68.9 ± 11.3	64.6 ± 11.9	**.437**
Systolic BP (mm Hg)	147.6 ± 13.9	148.5 ± 31.5	**.841**
Diastolic BP (mmHg)	89.4 ± 8.9	86.2 ± 12.9	**.726**
Hypertension (%)	31 (62)	108 (61.3)	**.634**
Diabetes mellitus (%)	7 (14)	53 (30)	**.037**
Hypercholesterolemia (%)	24 (48)	110 (63)	**.023**
Coronary heart disease (%)	6 (12)	23 (13)	**.881**
β-blockers (%)	2 (4)	37 (21)	**.016**
Calcium channel blockers (%)	3 (6)	52 (29)	**.017**
ACE inhibitors (%)	4 (8)	49 (28)	**.026**
Statins (%)	16 (32)	114 (65)	**.032**
ARBs (%)	3 (6)	41 (23)	**.019**
CK, u/L	69.36 ± 25.54	122.79 ± 98.03	**.011**
CK-MB, u/L	9.97 ± 4.21	15.72 ± 8.39	**.009**
CK-MB, ng/mL	1.36 ± 0.98	4.49 ± 2.15	**.017**
BNP, pg/mL	78.53 ± 14.28	227.63 ± 181.66	**<.001**
hs-cTnT, ng/L	6.3 8 ± 2.69	23.18 ± 12.45	**<.001**

Data are expressed as mean ± SD or as number (percentage).
ACE, angiotensin-converting enzyme, ARB, angiotensin II receptor blockers; BNP, B-type natriuretic peptide; BSA, body surface area; CK, blood creatine kinas; CK-MB, creatine kinase isoenzyme MB, cTnT, cardiac troponin-T.
P < .05 were considered to indicate statistical significance.

Left Ventricular Systolic Deformation and Myocardial Work

As shown in Table 3, with the increase of NIHSS, myocardial constructive work or positive work decreased (*P* < .05), such as GWI, GCW, GPW and GSCW, while myocardial wasted work or negative work increased (*P* < .05), such as GWW, GNW, and GSWW and therefore, GWE, the ratio of GCW/GWW, GPW/GNW, and GSCW/GSWW decreased (*P* < .05). In addition, with the increase of NIHSS, PSD was prolonged and GLS was decreased (*P* < .05).

Correlation Analysis Between National Institutes of Health Stroke Scale Score and Echocardiographic Parameters

As shown in Table 4, echocardiographic parameters including LVEF, GLS, PSD, GWE, GWI, GWW, the ratio of GCW/GWW,GNW, the ratio of GPW/GNW,GSWW, and the ratio of GSWW/GSCW all correlated with the NIHSS score (*P* < .05). Moreover, myocardial wasted work or negative work, such as GWW, GNW, and GSWW, had the strongest correlation with the NIHSS score (*P* < .001).However, there was no statistically significant correlations between the NIHSS score and GCW, GPW, and GSCW (*P* > .05).

Receiver Operating Characteristic Curve Analysis

As shown in Table 5, the ratio of GPW/GNW had the largest area (0.969, 0.938-1.001) under ROC in discriminating if NIHSS >15 or not. Next was the ratio of GSWW/GSCW (0.919, 0.853-0.986), and GPW had the smallest area (0.714, 0.531-0.898). The optimal cutoff value of the ratio of GPW/GNW was 3.89, with a sensitivity of 100%, a specificity of 93.0%, a positive predictive value of 84.9%, a negative predictive value of 100%, and an accuracy of 95.7%.

Inter/Intra Observer Variability

Interobserver and intraobserver agreement for the measurement of myocardial work was very good: intraclass correlation coefficients were all > 0.93 for interobserver and intraobserver variability.

Table 2. Conventional Echocardiographic Characteristics of the Control Group and Patients with Ischemic Stroke According to the NIHSS Score

Variables	Control Group (n = 50)	0-1 (n = 54)	2-4 (n = 45)	5-15 (n = 36)	16-40 (n = 41)
D_{RV}, mm	20.75 ± 1.71	19.72 ± 2.54	18.29 ± 3.21	20.55 ± 4.87	20.16 ± 5.83
D_{RA}, mm	27.52 ± 3.87	34.85 ± 5.96*	35.08 ± 5.88*	35.58 ± 6.23*	36.66 ± 8.53*
D_{LV}, mm	42.03 ± 6.05	38.24 ± 5.73	39.65 ± 5.66	37.85 ± 8.56	38.69 ± 11.37
D_{LA}, mm	26.75 ± 4.19	36.8 ± 6.23*	37.52 ± 6.98*	36.94 ± 6.77*	37.23 ± 9.34*
LVEF, %	59.10 ± 4.27	57.74 ± 5.81	56.02 ± 6.05	50.38 ± 11.46*	49.22 ± 6.71*
LVM index, g/m^2	69.25 ± 4.42	74.85 ± 21.96	78.22 ± 25.34	76.39 ± 24.67	77.26 ± 23.78
E/E′	4.87 ± 1.28	9.17 ± 4.51	8.12 ± 4.20	10.56 ± 1.09	9.25 ± 1.95
TAPSE, mm	22.25 ± 4.39	20.92 ± 4.09	21.88 ± 3.63	17.53 ± 2.99	19.62 ± 9.82
FAC_{RV}, %	49.57 ± 3.09	50.08 ± 9.08	53.07 ± 4.99	42.58 ± 14.83*	44.22 ± 7.74*
Dcs, mm	5.12 ± 1.03	4.81 ± 1.06	5.02 ± 1.82	4.71 ± 2.43	4.05 ± 1.08*
VTI, cm	13.22 ± 4.67	12.86 ± 2.84	12.61 ± 2.40	12.03 ± 3.21*	11.44 ± 0.81*
Flow, mL/min	211.94 ± 127.60	157.08 ± 110.25	163.22 ± 120.46	135.86 ± 67.43	124.13 ± 55.14*

Data are expressed as mean ± SD. * *P* < .05, vs. the control group.
D_{CS}, coronary sinus diameter; D_{LA}, left atrial end-systolic anteroposterior diameter; D_{LV}, left ventricular end-diastolic anteroposterior diameter; D_{RA}, right atrial end-systolic transverse diameter; D_{RV}, right ventricular end-diastolic anteroposterior diameter; FAC_{RV}, right ventricular fractional area change; LVM index, left ventricular mass index; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion; VTI_{CS}, velocity time integral at coronary sinus mouth.
P < .05 were considered to indicate statistical significance.

Table 3. Myocardial Work Characteristics of the Control Group and Patients with Ischemic Stroke

Variables	Control (n = 50)	0-1 (n = 54)	2-4 (n = 45)	5-15 (n = 36)	16-40 (n = 41)
GLS, %	-19.35 ± 2.96	-16.67 ± 2.68	-16.27 ± 1.55	$-11.79 \pm 9.07^{*\#\S}$	$-11.78 \pm 2.31^{*\#\S}$
PSD, ms	40.14 ± 13.47	$60.18 \pm 14.50^{*}$	$66.44 \pm 14.05^{*}$	$86.23 \pm 24.74^{**\#\S}$	$86.68 \pm 24.62^{**\S\#}$
GWE, %	96.00 ± 3.37	92.69 ± 2.44	91.00 ± 3.38	$84.34 \pm 7.68^{*\#\S}$	$75.94 \pm 7.95^{**\#\S}$
GWI, mm Hg %	1832.32 ± 201.08	$1654.42 \pm 276.61^{*}$	$1754.7 \pm 253.55^{*}$	$1519.93 \pm 449.81^{*\#\S}$	$1111.62 \pm 673.64^{**\#\S\S\triangle}$
GCW, mm Hg %	2087.59 ± 194.97	2007.82 ± 308.47	2136.00 ± 293.55	$1929.47 \pm 473.49^{*\S}$	$1805.95 \pm 894.10^{*\#\S}$
GWW, mm Hg %	79.00 ± 69.51	$136.48 \pm 70.92^{**}$	$181.19 \pm 93.48^{**\#}$	$324.82 \pm 209.44^{**\#\#\S\S}$	$550.06 \pm 254.53^{**\#\#\S\S\triangle}$
GCW/GWW	33.32 ± 20.97	$14.53 \pm 9.10^{**}$	$11.76 \pm 5.84^{**\#}$	$5.59 \pm 2.15^{**\#\#\S\S}$	$3.12 \pm 1.38^{**\#\#\S\S\triangle\triangle}$
GPW, mm Hg %	1960.70 ± 209.50	1898.33 ± 294.87	2044.50 ± 278.48	$1894.45 \pm 446.58^{*}$	$1741.73 \pm 865.15^{*\#\S\triangle}$
GNW, mm Hg %	181.337 ± 3.66	$244.26 \pm 81.92^{*}$	$272.5 \pm 94.09^{*}$	$359.64 \pm 174.11^{**\#\S}$	$614.71 \pm 240.05^{**\#\#\S\S\triangle\triangle}$
GPW/GNW	11.83 ± 3.95	$7.66 \pm 4.33^{*}$	$7.49 \pm 5.01^{*}$	$5.12 \pm 2.69^{**\#\S}$	$2.71 \pm 1.13^{**\#\#\S\S\triangle\triangle}$
GSCW, mm Hg %	1927.03 ± 223.43	1866.72 ± 295.51	1996.71 ± 272.44	$1827.25 \pm 444.21^{*}$	$1671.42 \pm 872.30^{*\#\S\triangle}$
GSWW, mm Hg %	58.01 ± 23.64	$104.74 \pm 65.33^{**}$	$133.54 \pm 70.61^{**\#}$	$257.46 \pm 189.37^{**\#\#\S\S}$	$479.83 \pm 246.95^{**\#\#\S\S\triangle}$
GSCW/GSWW	34.64 ± 16.27	$17.76 \pm 9.27^{**}$	$14.88 \pm 6.75^{**\#}$	$6.75 \pm 4.35^{**\#\S\#\S}$	$3.45 \pm 1.93^{**\#\#\S\S\triangle\triangle}$

Data are expressed as mean ± SD. $^{*}P < .05$, $^{**}P < .01$ vs. the control group; $^{\#}P < .05$, $^{\#\#}P < .01$ vs. the group of NIHSS = 0-1; $^{\S}P < .05$, $^{\S\S}P < .01$ vs. the group of NIHSS = 2-4; $^{\triangle}P < .05$, $^{\triangle\triangle}P < .01$ vs. the group of NIHSS = 5-15.
GCW, global constructive work; GLS, global longitudinal strain; GNW, global negative work; GPW, global positive work; GSCW, global systolic constructive work; GSWW, global systolic wasted work; GWE, global work efficiency; GWI, global work index; GWW, global wasted work; LVEF, left ventricular ejection fraction; PSD, peak strain dispersion.

DISCUSSION

To our knowledge, this is the first report on the feasibility and performance of myocardial work in predicting the severity of acute stroke and neurological deficit. In patients with acute ischemic stroke, myocardial constructive works or positive works are reduced, while myocardial wasted works or negative works are increased, and therefore, their ratios are reduced. Our study demonstrates that noninvasive myocardial work has powerful performance in discriminating if NIHSS >15 or not. These findings are of great significance for the evaluation of neurological deficits and the follow-up of treatment results in stroke patients.

Table 4. Correlation Analysis Between NIHSS and Echocardiographic Parameters

Variables	Correlation Coefficient (*r*)	*P*
LVEF	−0.29	.001
GLS	0.25	.014
PSD	0.40	**<.001**
GWE	−0.68	**<.001**
GWI	0.32	.001
GCW	−0.02	.874
GWW	0.71	**<.001**
GCW/GWW	−0.57	**<.001**
GPW	0.01	.947
GNW	0.73	**<.001**
GPW/GNW	−0.63	**<.001**
GSCW	−0.01	.886
GSWW	0.73	**<.001**
GSWW/GSCW	−0.56	**<.001**

GCW, global constructive work; GLS, global longitudinal strain; GNW, global negative work; GPW, global positive work; GSCW, global systolic constructive work; GSWW, global systolic wasted work; GWE, global work efficiency; GWI, global work index; GWW, global wasted work; LVEF, left ventricular ejection fraction; PSD, peak strain dispersion.

The NIHSS score extends from 0 points (normal neurological examination) to 42 points (unresponsiveness coma), which is composed of 15 items: level of consciousness, horizontal eye movements, visual field test, facial palsy, motor arm, motor leg, limb ataxia, sensory, language, speech, extinction, and inattention.[29] This scoring system requires professional training, and there are inevitably some deviations among different observers and different units. However, MWE provides a simple, objective, and consistent approach.

The previous study has emphasized that cerebrovascular disease and cardiovascular disease are "two sides of the same coin," not only sharing common risk factors but also being mediated by common damage-associated mechanisms.[30,31] A series of pathophysiological processes lead to the clinical cardiovascular outcomes that occur after stroke, which include systemic [inflammation, central autonomic dysregulation, catecholamine release (adrenal gland and bone marrow), and cell death signals release] and local injury mechanisms [inflammation, sympathetic nerve sprouting (massive; catecholamine release), structural myocardial changes (necrosis, hemorrhage, and fibrosis), and vascular wall abnormalities (endothelial dysfunction, atherogenesis, and plaque rupture)].[1] These direct or indirect damages mentioned above result in alterations in metabolism, perfusion, structure, and function of myocardium. In theory, to evaluate the severity of myocardial damage can indirectly reflect the neurological impairments.

Myocardial work, derived from estimated LV PSLs, is a novel parameter in assessing quantitatively LV systolic function

Table 5. Comparison of the Performances of Echocardiographic Parameters on Differentiating if NIHSS >15 or Not Using ROC Analysis

Variables	AUC	Sensitivity (%)	Specificity (%)	Youden's Index	Cutoff Value (s)
LVEF	0.772 (0.641-0.904)	77.8	83.1	0.609	50.50
GLS	0.838 (0.751-0.925)	77.8	83.1	0.609	12.43
PSD	0.776 (0.516-0.836)	74.4	79.3	0.537	76.92
GWE	0.898 (0.821-0.975)	83.3	87.3	0.706	80.50
GWI	0.778 (0.586-0.970)	77.8	100	0.778	961.5
GCW	0.721 (0.537-0.905)	61.1	94.4	0.555	1489.00
GWW	0.814 (0.677-0.950)	83.3	88.7	0.720	357.14
GCW/GWW	0.905 (0.826-0.984)	83.3	93.0	0.763	4.33
GPW	0.714 (0.531-0.898)	77.8	80.3	0.581	1697.50
GNW	0.910 (0.846-0.974)	83.3	88.7	0.720	400.00
GPW/GNW	0.969 (0.938-1.001)	100.0	93.0	0.930	3.89
GSCW	0.732 (0.547-0.917)	77.8	78.9	0.567	1649.50
GSWW	0.836 (0.706-0.965)	83.3	88.7	0.720	270.27
GSCW/GSWW	0.919 (0.853-0.986)	83.3	93.0	0.763	4.97

AUC, area under receiver operating characteristic curve; GCW, global constructive work; GLS, global longitudinal strain; GNW, global negative work; GPW, global positive work; GSCW, global systolic constructive work; GSWW, global systolic wasted work; GWE, global work efficiency; GWI, global work index; GWW, global wasted work; LVEF, left ventricular ejection fraction; PSD, peak strain dispersion; NIHSS, the National Institutes of Health Stroke Scale; ROC, receiver operating characteristic curve.

by integrating noninvasive systolic blood pressure into longitudinal strain acquired with STE.[9] It is less load-dependent and is thought to be significantly superior to GLS or LVEF to detect myocardial damage. In our study, with the NIHSS score increase, myocardial constructive works (GCW and GSCW) or positive works (GPW) that contribute to LV ejection were all reduced. The reductions in myocardial work reflect the presence of damaged myocardial fibers,[7] impaired cardiac function, LV dyssynchrony, and myocardial ischemia and potentially reflect the pathologic adaptation of reduced metabolism demand and oxygen consumption in the myocytes due to acute ischemic stroke[24]. At the same time, with the NIHSS score increase, myocardial wasted works (GWW and GSWW) or negative works (GNW) were significantly increased in the patients with stroke. They represented energy loss, and none of them contributed to LV ejection. These changes once again reflect the myocardial damage caused by acute ischemic stroke through the common damage-associated mechanisms mentioned above. However, in the present study, GCW, GPW, and GSCW had no statistically significant correlation with the NIHSS score. This might be due to the systemic and local catecholamine release during the acute phase of ischemic stroke resulting in a compensatory enhancement of GCW, GPW, and GSCW. They only had a mild reduction with the increase in the NIHSS score. In addition, it might also be related to the small sample size of our study.

In our study, all patients were consecutively enrolled. They suffered from ischemic stroke for the first time, and 30% of them had a history of diabetes mellitus, which was consistent with the study of Khoury et al[32] in which the history of diabetes mellitus among first ischemic strokes was reported for 493/1709 (28%) in 1993/1994, 522/1778 (29%) in 1999, and 544/1680 (33%) in 2005. We believe that diabetes mellitus is a common factor affecting myocardial work and NIHSS simultaneously because patients with diabetes mellitus are prone to complications such as coronary heart disease and stroke. Moreover, the previous study had reported that in diabetic patients, with the increase in HbA1c levels, more number of cases were found to have a severe stroke, and it was statically significant as per the NIHSS score.[33] In our study, the correlation between myocardial work indices and NIHSS scores was only investigated in patients with ischemic stroke, which was not related to the control group.

Study Limitations

Our study was inevitably affected by several factors. First, patients with severe stroke were always delirious, could not cooperate with echo examination, and needed endotracheal intubation, mechanical ventilation, ECG monitoring, and other equipment, which made it difficult to obtain standard echo images. We had tried our best to overcome these factors. Second, arrhythmias, especially AF, inhibited accurate and reliable assessment of GLS by STE and resulted in an inaccurate calculation of myocardial work in such patients. Third, we did not explore the relationship between the subitems of NIHSS score and myocardial work, such as level of consciousness and ataxia scores, and so on. Further research on this aspect are needed. Finally, a higher prevalence of diabetes mellitus in the ischemic stroke group may affect myocardial work indices. Although there are some explanations in the literature, further studies are needed.

CONCLUSION

In this study, we investigated the correlation between myocardial work and NIHSS score, and the feasibility and performance of myocardial work in predicting the severity of acute stroke and neurological deficits. Our data demonstrate that myocardial work parameters correlated well with the NIHSS score, and using noninvasive myocardial work parameters to evaluate the severity of acute stroke and neurological deficits in stroke patients is a novel and useful method, which can be used as a powerful supplement to the conventional scoring system.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Yangpu Hospital, School of Medicine, Tongji University (approval no: LL-2021-SCI-006).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Z.X.Z., Z.J.; Design – Z.X.Z.; Supervision – Z.X.Z.; Funding – Z.X.Z.; Materials – Z.X.Z., Z.J., W.X.C.; Data Collection and/or Processing – Z.J., W.X.C, Z.X.Z.; Analysis and/or Interpretation – Z.X.Z., Z.J.; Literature Review – Z.X.Z., Z.J., W. X.C.; Writing – Z.J., W.X.C., Z.X.Z.; Critical Review – Z.X.Z.

Acknowledgments: The authors gratefully acknowledge the technical assistance of Yan Zhu,Ya-Peng Li, Hong-Ye Wang, Lei Zhang and Dan Huang from the Department of Ultrasound, Yangpu Hospital, School of Medicine, Tongji University, Shanghai, P.R. China.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: This study received no funding.

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