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Original article

Reduced upper and lower limb muscle strengths without reduced skeletal muscle in elderly patients with heart failure

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Abstract

Objective: This study aimed to characterize the muscle strength and skeletal muscle mass of patients with heart failure by investigating hand-grip strength, five times sit-to-stand (5STS) results, and skeletal muscle mass index (SMI).
Materials and Methods: Muscle strength was assessed based on hand-grip strength and 5STS, while skeletal muscle mass was assessed using a bioelectrical impedance analyzer. Hierarchical logistic regression analysis was performed to explore the association between patients with heart failure and healthy elderly individuals.
Results: Hierarchical logistic regression analysis was performed to examine the muscle strength and skeletal muscle mass characteristics in patients with heart failure. Hand-grip strength and 5STS responses but not SMI outcomes differed significantly between the two groups. The results of the hierarchical logistic regression analysis revealed that the hand-grip strength and 5STS were significant predictors of heart failure. The odds ratios for hand-grip strength and 5STS were 1.44 and 0.53, respectively.
Conclusion: Our results suggested that upper and lower limb muscle strengths (handgrip strength and 5STS) in elderly patients with heart failure worsened significantly without a decrease in skeletal muscle mass.

Key words: heart failure, healthy, hand strength, skeletal, muscle

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Introduction

A previous study showed that patients with heart failure often present with skeletal muscle abnormalities[1]. Specifically, fiber-type switching from type I to type II[2], muscle weakness[3], muscle atrophy[4], and abnormal energy metabolism, including oxidative phosphorylation disorders[5], have been reported. These changes are associated with a decline in various physical functions and activities of daily living, which ultimately leads to a lower quality of life and worse life expectancy[6, 7]. In particular, muscle strength and skeletal muscle mass are associated with mortality, rehospitalization rates, and sarcopenia prevalence[8–10]. Therefore, the loss of muscle strength and skeletal muscle mass is a serious problem in patients with heart failure.

In patients with heart failure, the common evaluation paradigms for muscle strength are hand-grip strength and five times sit-to-stand (5STS), while that for skeletal muscle mass is the skeletal muscle mass index (SMI)[11]. A high-quality study identified low hand-grip strength as an independent predictor of increased mortality and hospitalization in patients with heart failure[9]. Meanwhile, worse 5STS outcomes were associated with worse nutritional status and physical function in patients with heart failure[10]. SMI is also used to assist in the diagnosis of sarcopenia, with cutoff values in men and women of 7.0 and 5.7 kg/m^2, respectively[8]. Low skeletal muscle mass was associated with a low 5-year survival rate[12]. Thus, hand-grip strength, 5STS, and SMI outcomes are representative indicators of muscle strength

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and skeletal muscle mass in patients with heart failure.

Hand-grip strength, 5STS, and SMI in patients with heart failure were reportedly significantly worse than those in healthy elderly individuals[13, 14]. However, these previous studies had problems in that the ages of patients with heart failure were low (early 60s), and adjustments for confounding factors were not performed. Regarding the age-specific prevalence of heart failure in Japan, the Acute Decompensated Heart Failure Syndromes study reported that 50% of patients with heart failure who required hospitalization were >75 years of age and approximately 20% were >85 years of age[15]. The prevalence of heart failure in the European Rotterdam Study[16] was 4% in the 65–74-years age group, 9.7% in the 75–84-years age range, and 17.4% in the >85-years age group. The National Health and Nutrition Examination Survey in the United States reported heart failure prevalence rates for men and women of 1.5% and 1.2% in the 40–59-years age group, 6.6% and 4.8% in the 60–79-years age group, and 10.6% and 13.5% in >85-years age group[17]. The incidence of heart failure increases with age; therefore, studies on elderly patients with heart failure are needed. In addition, muscle strength and skeletal muscle mass are generally better in young men and individuals with larger body sizes[18, 19]. Heart failure often develops in elderly women, and weight loss is frequently observed if symptoms of heart failure are stable[14]. Previous studies did not adjust for confounding factors such as age, sex, and body size; thus, muscle strength and skeletal muscle mass in patients with heart failure may have been underestimated. Multivariate analysis after adjusting for confounding factors between elderly patients with heart failure and healthy elderly individuals can more accurately characterize the function and mass of skeletal muscle in elderly patients with heart failure.

This study aimed to clarify the skeletal muscle mass and muscle strength characteristics in elderly patients with heart failure after adjusting for confounding factors.

Materials and Methods

Study participants and setting

This cross-sectional study was conducted in two hospitals and universities, using previously collected data. The study ethics were ensured by adopting an opt-out format and guaranteeing sufficient opportunities for the research participants and their proxies to refuse. This study complied with the principles of the Declaration of Helsinki and was approved by the Research Ethics Committees of Kure Kyosai Hospital (Hiroshima, Japan) [reference no. 2021-30], Saiseikai Kure Hospital (Hiroshima, Japan) [reference no. 155], and Hiroshima International University (Hiroshima, Japan) [reference no. 21-044]. Patients with heart failure hospitalized between February 2020 and August 2021 were recruited from the two hospitals, and data were collected by the hospital staff before discharge. The inclusion criteria for patients with heart failure included participants who a) were 65 years or older, b) could stand from a chair once without using their arms, and c) required urgent therapy and hospitalization owing to heart failure symptoms based on the Framingham criteria[20] as judged by cardiologists during the initial treatment. The exclusion criteria for patients with heart failure were those with pacemakers, who had experienced complications during hospitalization, and who had severe dementia (Hasegawa dementia rating scale-revised ≤9). Healthy elderly participants were recruited in commuting places, and data were collected by university staff members between November 2020 and March 2021. The inclusion criteria for healthy elderly individuals were a) age >65 years and b) ability to stand from a chair once without using their arms. The exclusion criterion for healthy elderly individuals was a previous medical history of cardiac diseases.

Basic and medical information

The basic and medical information included age, sex, body mass index (BMI), presence or absence of previous medical history (hypertension, diabetes, dyslipidemia, chronic renal dysfunction, stroke, and dementia), and the degrees of sarcopenia and frailty. Sarcopenia was defined using the diagnostic algorithm recommended by the 2019 Asian Working Group for Sarcopenia (AWGS), which assesses the presence of low muscle mass, muscle function, and physical function[21]. Frailty was evaluated using the Japanese version of the Cardiovascular Health Study index[22] and frailty index[23] for elderly patients with heart failure and healthy elderly individuals, respectively.

Muscle strength and skeletal muscle mass

Muscle strength was assessed using hand grip strength and 5STS, while skeletal muscle mass was assessed using a bioelectrical impedance analyzer. Hand-grip strength was measured in a standing position with the upper limb abducted by approximately 20° from the body using a digital hand-grip strength dynamometer (elderly patients with heart failure: TKK-5101, Takei Scientific Instruments, Tokyo, Japan, or 12B3X00030, Tsutsumi Works, Chiba, Japan; healthy elderly individuals: TKK-5401, Takei Scientific Instruments, Tokyo, Japan). Two measurements were performed on each side, with the maximum value (rounded to the nearest 0.1 kg) used for the analysis[24]. Standing from the chair and sitting were repeated five times as quickly as possible, with the time from the onset of the movement in the first standing position to the full standing position after the completion of five standing movements measured with a stopwatch as the 5STS outcome. The chair was 45 cm high, with a backrest. The same chair was used for all participants.

An In-Body Biospace device (Tokyo, Japan) was used according to the manufacturer's guidelines, as described previously[25]. Thirty impedance measurements were obtained using six different frequencies (1, 5, 50, 250, 500, and 1,000 kHz) at five body segments (right and left arms, trunk, and right and left legs). The measurements were conducted while the participants rested quietly in the supine position with their elbows extended and relaxed along their trunks. The skeletal muscle mass was measured. SMI (appendicular skeletal muscle mass/height^2, kg/m^2) was also measured as the sum of the lean soft tissue of the upper and lower limbs. Models S10 and 270 of In Body Biospace devices were used in elderly patients with heart failure, while model 470 was used in healthy elderly individuals. The high measurement accuracies have been confirmed for these devices[26].

Statistical analysis

The propensity score was used to select matching pairs with adjusted confounding factors to compare outcomes between patients with heart failure and healthy elderly individuals. The propensity score was estimated using the probability obtained from logistic regression analysis with the patient characteristics as the independent variable and the assigned group as the dependent variable. Pairs with the same propensity score were extracted from among elderly patients with heart failure and healthy elderly individuals. To determine whether the adjustment for confounding factors was successful, background factors were compared statistically between the two groups, including only the extracted pairs. Hierarchical logistic regression analysis was performed to explore the association between patients with heart failure (scored as 1) and healthy elderly individuals (score 0). The independent variables included frailty, hand-grip strength, 5STS times, and SMI. First, age, sex, and BMI were forcibly input as confounding factors in Block 1. Thereafter, the other independent variables were input into Block 2 using a stepwise method. Factors associated with heart failure were extracted independently from the confounding factors (age, sex, and BMI). To account for multicollinearity, the threshold of the correlation coefficient between the independent factors was set to 0.8, and a high correlation with the dependent variable was selected. After logistic regression analysis, the receiver operating characteristic (ROC) curve[27] was calculated as a significant predictor to assess the cut-off point for heart failure characteristics. The area under the curve (AUC) could distinguish between nonpredictive (AUC <0.5), less predictive (0.5< AUC <0.7), moderately predictive (0.7< AUC <0.9), highly predictive (0.9< AUC <1.0), and perfect prediction (AUC=1)[28, 29]. All statistical analyses were performed using SPSS for Macintosh (version 28.0; IBM Corporation, Armonk, NY, USA), and the significance level was set at $P<0.05$.

Sample size

The study size was calculated using MedCalc statistical software (version 19.2; MedCalc Software bvba, Ostend, Belgium). Before plotting the area under the ROC (AUROC), the following values were established: statistical significance ($P<0.05$), alpha (0.05), statistical power (0.80), and an AUROC value to be included in the null hypothesis (0.5). The AUROC distinguished between non-predictive (AUROC <0.5), less predictive (0.5< AUROC <0.7), moderately predictive (0.7< AUROC <0.9), highly predictive (0.9< AUROC <1), and perfectly predictive (AUROC=1) outcomes[30]. In this study, an AUC value of 0.7 was set to indicate the superiority of statistical discrimination. The improvement ratios from frailty (positive/negative ratio) varied widely among previous studies[14]. Therefore, the positive/negative ratio used in this study was set at 1:1. Moreover, a large sample size was required to account for the possibility of stratified analysis. A total of 64 participants were required, including 32 elderly patients with heart failure and 32 healthy elderly individuals.

Results

Figure 1 shows the study flow diagram. Of the 108 elderly patients with heart failure, 28 were excluded from the analysis: 12 had pacemakers, 7 developed complications during admission, and 9 had severe dementia. Of the 87 healthy elderly individuals, 13 were excluded from the analysis due to heart disease. After propensity score matching, the analysis included 31 of 80 patients (38.8%) in the heart failure group and 31 of 74 (41.9%) individuals in the healthy group.

Table 1 presents the individual and patient characteristics of the two groups. Age, sex, BMI, and presence or absence of previous medical history (stroke) did not differ significantly between the two groups; however, previous medical history (other than stroke) and the degree of sarcopenia differed between the two groups. Similar results were obtained for analyses performed separately according to sex. Hand-grip strength and 5STS but not SMI differed significantly between the two groups. Similar results were obtained for analyses performed separately according to sex.

For the hierarchical logistic regression analysis in this study, the final independent variables were age, sex, BMI, presence or absence of previous medical history, SMI, hand-grip strength, and 5STS. The results revealed that hand-grip strength ($P<0.05$) and 5STS ($P<0.05$) were significant predictors of heart failure (Table 2). The odds ratios for hand-grip strength and 5STS were 1.44 and 0.53, respectively. The ROC analysis results revealed a cut-off hand-grip value of 15.4 kg, with a sensitivity and specificity of 0.97 and 0.48, respectively (Figure 2). The results of ROC analysis revealed a 5STS cut-off value was 10.1 s, with sensitivity and specificity of 0.87 and 0.87, respectively (Figure 3).

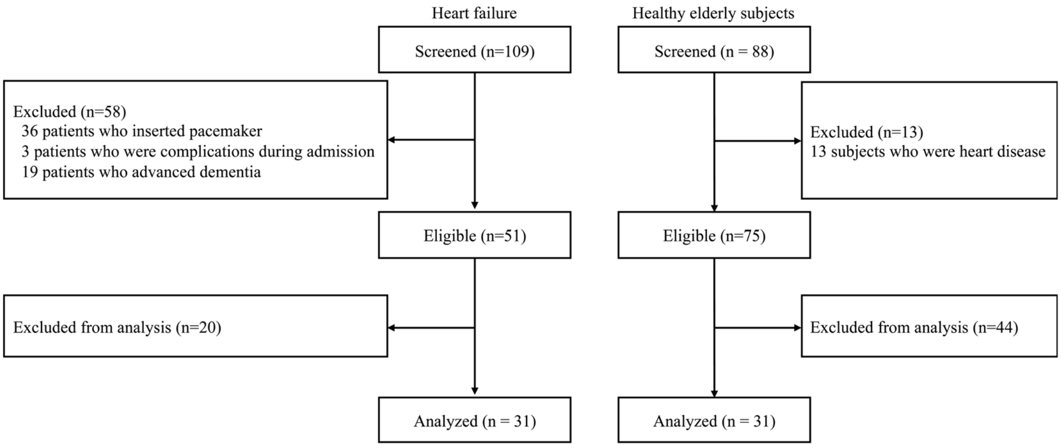

Figure 1 Flow diagram for elderly patients with heart failure and healthy elderly subjects.

Table 1 Subject and patient characteristics

Variable	Category	ALL (n=62)			Male (n=18)			Female (n=44)		
		Healthy elderly subjects (n=31)	Heart failure patients (n=31)	*P* value	Healthy elderly subjects (n=8)	Heart failure patients (n=10)	*P* value	Healthy elderly subjects (n=23)	Heart failure patients (n=21)	*P* value
Age (years)		82.7 ± 5.7	83.0 ± 6.4	0.66‡	82.5 ± 5.3	82.4 ± 7.3	0.97*	82.7 ± 6.0	83.4 ± 6.1	0.68‡
Sex	Male / Female	8 / 23	10 / 21	0.78†						
BMI (kg/m^2)		21.4 ± 2.8	22.6 ± 4.4	0.24‡	22.6 ± 1.6	24.3 ± 6.0	0.57‡	21.0 ± 3.0	22.0 ± 3.4	0.46*
Medical history										
Hypertentsion	Presence / Absence	16 / 15	29 / 2	0.00†	5 / 3	10 / 0	0.07†	11 / 12	19 / 2	0.00†
Diabetes mellitus	Presence / Absence	3 /28	15/16	0.00†	1 / 7	5 / 5	0.15†	2 / 21	10 / 11	0.01†
Hyperlipidaemia	Presence / Absence	2 / 29	12 / 19	0.01†	1 / 7	2 / 8	1.00†	1 / 22	10 / 11	0.00†
Chronic renal failure	Presence / Absence	1 / 30	11 / 20	0.00†	0 /8	5 / 5	0.04†	1 / 22	6 / 15	0.04†
Stroke	Presence / Absence	2 / 29	7 / 24	0.15†	2 / 6	1 / 9	0.56†	0 / 23	6 / 15	0.01†
Dementia	Presence / Absence	0 / 31	8 / 23	0.01†	0 / 8	4 / 6	0.09†	0 / 23	4 / 17	0.04†
Sarcopenia	Severe sarcopenia / Sarcopenia / non sarcopenia	1 / 9 / 21	12 / 7 / 12	0.00†	0 / 2 / 6	5 / 3 / 2	0.04†	1 / 7 / 15	7 / 4 / 10	0.02†
Frailty	Frailty / pre frailty / non frailty	7 / 13 /11	18 / 13 /0	0.00†	2 / 3 / 3	6 / 4 / 0	0.00†	5 / 10 / 8	12 / 9 / 0	0.08†
SMI		5.9 ± 0.8	5.7 ± 1.1	0.33*	6.8 ± 0.5	6.2 ± 0.9	0.13*	5.6 ± 0.7	5.4 ± 1.1	0.49*
Hand-grip strength (kg)		23.7 ± 7.4	16.6 ± 5.6	0.00‡	33.3 ± 6.2	22.2 ± 4.0	0.00*	20.0 ± 4.3	13.9 ± 4.0	0.00*
5STS (second)		8.2 ± 3.1	18.0 ± 8.9	0.00‡	7.7 ± 1.9	17.5 ± 9.2	0.00‡	8.4 ± 3.4	19.0 ± 9.0	0.00‡

* Average and standard deviation, ( ) %, * Independence t-test, † χ^2 test, ‡ Manne Whitney U test. BMI: Body Mass Index; SMI: Skeletal muscle mass index; 5STS: Five times sit-to-stand.

Discussion

Hand-grip strength and 5STS were significantly worse in elderly patients with heart failure compared to those in healthy elderly individuals. Furthermore, handgrip strength and 5STS were identified as significant associating factors for elderly patients with heart failure, independent of age, sex, and BMI. These results indicated that muscle weakness occurred in both the upper and lower limbs of patients with heart failure. It is well known that skeletal muscle abnormalities occur in patients with heart failure, among which muscle atrophy is one of the most common[31, 32]. Because the physiological cross-sectional area of the muscle is proportional to its contractile tension[33], muscle atrophy is directly related to muscle weakness. However, in this study, SMI as a measure of skeletal muscle mass did not differ significant-

Table 2 Hierarchical logistic regression analysis

Variable	Partical regeression coefficient	Odds ratio	95% confidence interval		P value
			lower limit	upper limit	
Age	–0.22	0.81	0.64	1.00	0.06
Sex	–5.8	0.00	0.00	0.27	0.01
BMI	0.35	1.42	1.00	2.00	0.05
Hand-grip strength	0.36	1.44	1.00	2.00	0.04
5STS	–0.63	0.53	0.34	0.85	0.01
Constant	22.95				0.06

χ^2 test: P<0.05, Discrimination rate=88.7%. BMI: Body Mass Index; 5STS: Five times sit-to-stand.

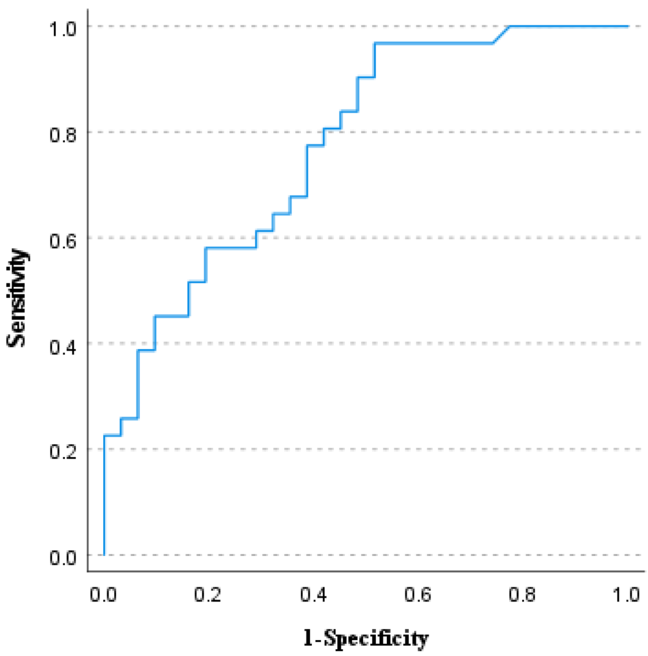

Figure 2 Analysis of the receiver operating characteristic analysis results revealed a hand-grip cut-off value of 15.4 kg, with a sensitivity and specificity of 0.97 and 0.48, respectively.

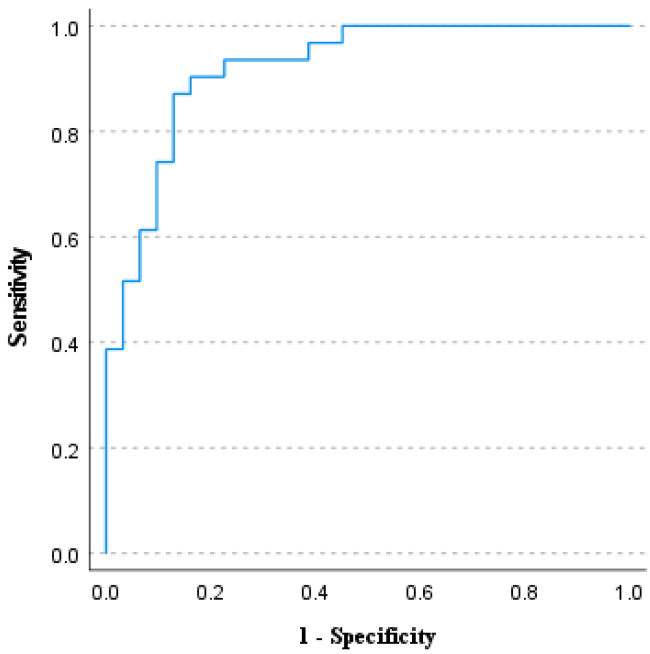

Figure 3 Analysis of the receiver operating characteristic analysis results revealed a 5STS cut-off value of 10.1 s, with a sensitivity and specificity of 0.87 and 0.87, respectively.

ly between elderly patients with heart failure and healthy elderly individuals. Therefore, muscle weakness in elderly patients with heart failure cannot be explained by muscle atrophy. Alternatively, differences in muscle strength between elderly patients with heart failure and healthy elderly individuals may be explained by changes in neuromuscular activity or qualitative changes in muscles, such as intramuscular fat content, or both. Muscle quality is associated with muscle strength in patients with heart failure[34)]. However, the present study did not investigate these possibilities; thus, additional studies are required.

As mentioned above, SMI did not differ between elderly patients with heart failure and healthy elderly individuals in the present study. Conversely, a decrease in skeletal muscle mass has been reported in patients with heart failure. For example, Fluster *et al.*[35)] reported an approximately 20% decrease in skeletal muscle mass in patients with heart failure compared to healthy individuals. Tsuji *et al.*[14)] also reported significantly lower SMI values in patients with heart failure compared to healthy elderly individuals. The discrepancies between our study and previous studies may be explained by differences in study participants. In general, skeletal muscle mass decreases at a rate of 1%–2% per year after the age of 50 years, and the skeletal muscle mass at 70 years of age is usually 25%–30% lower than that in individuals in their 20s[36)]. This age-related loss of muscle mass is referred to as sarcopenia. Sarcopenia is present in 10% of elderly individuals aged 60–70 years[37, 38)]. In our study, the mean age of the healthy elderly individuals was 82.7 ± 5.7 years, higher than that in a previous study (70.4 ± 9.3 years)[14)]. In addition, the prevalence of sarcopenia in our healthy elderly individuals was high (32.2%, 10 of 31). Accordingly, the SMI values in healthy elderly individuals in our study (5.9 ± 0.8) were considerably lower than those reported previously (9.2 ± 1.1)[14]. These differences in healthy elderly individuals may be one explanation for the lack of differences in SMI between healthy elderly individuals and elderly patients with heart failure. The present study also selected participants using propensity score matching to adjust for confounding factors, including age, sex, and BMI. A previous study by Tsuji *et al.*[14] did not perform such matching, and the BMI values of healthy individuals were significantly higher than those of patients with heart failure. In general, BMI is related to SMI[39]. Therefore, the possibility that skeletal muscle mass in healthy individuals was overestimated because of a higher BMI could not be ruled out. The results of our study suggest that SMI in elderly patients with heart failure did not differ from that in healthy elderly individuals when the BMI was similar.

A limitation of this study was the severity of heart failure. This study included patients with heart failure who required admission to an acute-care hospital. Therefore, the patients with heart failure in this study had lower cardiac function compared to that in outpatients with heart failure. Decreased cardiac function may also be associated with impaired muscle function. Therefore, caution is needed when generalizing our results to patients with milder heart failure, such as those with a New York Heart Association functional score of 1. Additional investigations are needed, including studies on various stages of heart failure.

Conclusion

Hand-grip strength and 5STS in elderly patients with heart failure were significantly worse than those in healthy elderly individuals, even though the SMI values in the two groups did not differ. Our results suggest that upper and lower limb muscle strengths, such as hand-grip strength and 5STS in patients with heart failure, significantly worsened without concomitant decreases in skeletal muscle mass.

Author contributions: All authors contributed to the study conception and design. Material preparation and analysis were performed by TU and AK. The first manuscript draft was written by TU and all authors commented on the previous versions of the manuscript. NK supervised and reviewed the manuscript. Data were collected by TY, NK, WK, and DK. All the authors have read and approved the final manuscript.

Conflict of interest: The authors declare that there are no conflicts of interest.

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