

# Handgrip strength, and erectile dysfunction among men with metabolic syndrome attending an institutional primary care clinic in Malaysia: A cross-sectional study

Nik A. Nik Abdul Kadir<sup>1</sup>, Suraya Abdul-Razak<sup>1,2,3</sup>, Aqil M. Daher<sup>4,5</sup>,  
Nafiza Mat Nasir<sup>1</sup>

<sup>1</sup>Department of Primary Care Medicine, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh Campus, Sungai Buloh, Selangor, Malaysia, <sup>2</sup>Cardiovascular and Lungs Research Institute (CaVaLRI), Hospital Al-Sultan Abdullah UiTM, Sungai Buloh Campus, Sungai Buloh, Selangor, Malaysia, <sup>3</sup>Institute of Pathology, Laboratory and Forensic Medicine (I-PPerForM), Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia, <sup>4</sup>Department of Community Medicine, School of Medicine, International Medical University, Bukit Jalil, KL, Malaysia, <sup>5</sup>College of Health and Medical Techniques, AlMaqal University, Basrah, Iraq

## ABSTRACT

**Background:** Erectile dysfunction (ED) is an independent predictor for cardiovascular diseases (CVD). The prevalence increases with age, but little is known about the relationship between handgrip strength (HGS) and ED, especially among men with a high risk of CVD. This study aimed to determine the prevalence of ED among men aged  $\geq 40$  years with metabolic syndrome (MetS) and its association with HGS. **Materials and Methods:** A cross-sectional study at an institutional primary care clinic in Malaysia was conducted between June 2021 and October 2021. HGS and erectile function were assessed using a hand dynamometer and International Index of Erectile Function (IIEF-5) questionnaire, respectively. Multiple logistic regression analyses were performed to determine the association between sociodemographics, clinical characteristics, and HGS with ED. **Results:** A total of 334 participants were recruited. The prevalence of ED was 79% (95% confidence interval [CI]: 0.75-0.84). ED was associated with elderly aged  $\geq 60$  years (odds ratio [OR] 3.27, 95% CI: 1.60-6.69), low HGS (OR 15.34, 95% CI: 5.64-41.81) and high total cholesterol (OR 0.36, 95% CI: 0.16-0.78). **Conclusion:** In conclusion, age above 60 years and those with low HGS are at higher risk of ED. Thus, robust screening of ED among men with MetS and improving muscle strength and physical fitness may be warranted.

**Keywords:** Erectile dysfunction (ED), handgrip strength (HGS), Malaysia, metabolic syndrome (MetS), muscle strength, primary care

## Introduction

Erectile dysfunction (ED) is a global health problem that affects nearly half of men over the age of 40 years.<sup>[1-4]</sup> In Malaysia, more

**Address for correspondence:** Dr. Suraya Abdul-Razak, Department of Primary Care Medicine, Faculty of Medicine Universiti Teknologi MARA, Sungai Buloh Campus, 47100 Sungai Buloh Selangor, Malaysia.  
E-mail: suraya617@uitm.edu.my

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than two-thirds of men aged above 40 years have ED,<sup>[5]</sup> while the majority of elderly Malaysians aged above 65 years old had ED in 2014.<sup>[6]</sup> ED is known to be attributed to various pathological mechanisms such as vascular impairment, neurological, hormonal, and psychological components. The most prevalent cause of ED is vascular ED, which accounts for up to 70% of all cases.<sup>[7]</sup> Robust studies have proven that ED has a positive association with hypertension, dyslipidemia, diabetes mellitus,

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heart disease, smoking, excessive alcohol use, obesity, depression, and metabolic syndrome (MetS).<sup>[8]</sup> ED is also an independent predictor of occult coronary artery disease.<sup>[9]</sup>

Being physically active has been documented to reduce the risk of non-communicable diseases, improve quality of life,<sup>[10]</sup> reduces the likelihood of major cardiovascular diseases (CVD),<sup>[11]</sup> and is associated with better erectile function.<sup>[12]</sup> Most evidence suggests that aerobic exercises have beneficial effects on CVD risks and continue to be the most common exercise prescription.<sup>[10,11]</sup> However, resistance training exercises have different physiologic effects, which improve muscle strength and appear to have positive effects on chronic heart failure<sup>[13]</sup> and CVD risks such as dyslipidemia and central obesity.<sup>[14]</sup>

Muscle strength is expressed as musculoskeletal fitness, which is an integral part of physical fitness.<sup>[15]</sup> Musculoskeletal fitness is a complex concept that refers to the ability of a specific muscle group to generate force (i.e., muscular strength), to resist repeated contractions over time (i.e., muscular endurance), and to exert force per unit of time (i.e., muscular power).<sup>[15]</sup> Muscle strength can be measured in a variety of ways including isometric muscle strength, e.g., the handgrip strength (HGS), knee extension, and flexion.<sup>[16]</sup> Another component of physical fitness includes cardiorespiratory fitness, which also has been linked to the prevention of CVD and CVD risks.<sup>[17]</sup>

HGS is widely used as an alternative to muscular fitness and a reliable measurement using a dynamometer where a person applies maximal isometric handgrip force for a short duration.<sup>[18]</sup> Low HGS has been associated with higher all-cause cardiovascular and non-cardiovascular mortality,<sup>[18,19]</sup> and ED.<sup>[20]</sup> Data are scarce, but a higher HGS also predicted a lower risk of ED among elderly men aged above 50 years old<sup>[21]</sup> and improved erectile function by 16%.<sup>[21]</sup> Studies have shown higher HGS has been associated with younger age,<sup>[22]</sup> being male,<sup>[22]</sup> normal body mass index, being a non-smoker, or non-alcohol consumer,<sup>[23]</sup> and being physically active.<sup>[24]</sup>

Muscle mass and strength begin to decline in the fourth decade of life and accelerate around the age of 40 years and older. Given the necessity of maintaining muscle strength for optimal health, it is crucial to know whether muscle strength is associated with ED among men over the age of 40 years. Hence, this study aimed to determine the association between HGS and ED as well as the prevalence of ED in men with MetS and other associated factors, including sociodemographics and clinical factors.

## Materials and Methods

### Study design

A cross-sectional study was conducted between June 2021 and October 2021 at an institutional primary care specialist clinic located in Gombak District, Selangor, Malaysia. This clinic is located in an urban area near Kuala Lumpur, which covers an area of 839.1 km<sup>2</sup> with a dense total population of 629,971.<sup>[25]</sup> The services

include chronic diseases and acute care, adolescent clinic, and health screenings by a multi-disciplinary team consisting of family physicians, the registrar of family medicine postgraduate program, nurses, pharmacists, dieticians, and administrative staff. The clinic also served as a teaching clinic for the medical undergraduates.

### Participants and sampling

Adult male patients who had their follow-up between June 1, 2021, and October 30, 2021, were eligible to participate in the study. The inclusion criteria were men aged  $\geq 40$  years, diagnosed to have MetS by the Joint Interim Statement (JIS) criteria<sup>[26]</sup> [see Box 1], able to read and understand Malay or English language, and had blood tests (fasting plasma glucose, fasting serum lipid, and HbA1c) at least 6 months prior the conduct of the study. Sampling was performed via a computer-generated simple random sampling method.

The exclusion criteria were: (i) established diagnosis of psychiatry illness or were mentally challenged (e.g. depression and anxiety disorder); (ii) presence of residual weakness from stroke (e.g., unilateral weakness, pure motor stroke, and sensory-motor stroke); (iii) past history of surgical treatment for ED (e.g., penile prostheses); (iv) patients who received hormone therapy for ED (e.g., testosterone therapy); (v) patients who were on anti-hypertensives (e.g., thiazide diuretics and beta-blocker), antidepressants (e.g., selective serotonin reuptake inhibitors and tricyclics), antipsychotics (e.g., neuroleptics), and antiandrogens (e.g. GnRH analogs and antagonists); (vi) current injury or history of wrist and hand injury in the past 1 month; (vii) history of wrist and hand surgery in the past 3 months.

The sample size was calculated using a single proportion formula based on the objective of the study. According to Ab Rahman *et al.*,<sup>[5]</sup> the prevalence of ED among adult males aged 40-76 years old was 69.5%. Taking the alpha value of 0.05 with a CI of 95%, the minimum required sample was 304 patients. Considering a 15% non-response rate, the final sample was 350 participants.

### Study instruments

A four-part questionnaire was devised for data collection. The sociodemographics and medical history section was constructed to obtain information on participant's age, ethnicity, education

#### Box 1: Diagnostic criteria of metabolic syndrome (MetS) based on JIS 2009 criteria

MetS is diagnosed if three or more of the following five criteria were satisfied:

1. Waist circumference (WC) using South Asian cut-points: Male  $\geq 90$  cm or Female 80 cm
2. Systolic blood pressure (SBP)  $\geq 130$  mmHg and/or diastolic blood pressure (DBP) 85 mmHg or on treatment for hypertension
3. Fasting plasma glucose (FPG)  $\geq 5.6$  mmol/L or on treatment for elevated glucose;
4. Triglyceride (TG)  $\geq 1.7$  mmol/L or on treatment for TG
5. High Density Lipid-Cholesterol (HDL): Male  $< 1.0$  mmol/L or female  $< 1.3$  mmol/L (considered as low) or on treatment for HDL.

level, marital status, household income, smoking and alcohol status, and comorbid history. Clinical examinations such as weight, height, body mass index (BMI), waist circumference (WC), blood pressure (BP), and HGS were performed and documented. The blood profile results including fasting plasma glucose, fasting serum lipid, and HbA1c were obtained from the electronic medical record (EMR), and the International Index of Erectile-5 (IIEF-5) was used to measure ED.

HGS was determined using a Jamar dynamometer (Sammons Preston, Bolingbrook, IL, USA) according to a standardized protocol.<sup>[27]</sup> The arm was positioned vertically to the body with the elbow flexed to 90° while holding the dynamometer. The participant was instructed to squeeze the device as hard as possible for three seconds. The measurement was repeated thrice at 30-second intervals. In this study, the highest measurement obtained for the dominant hand was used.<sup>[22]</sup> The reference range of HGS was developed in a large epidemiological study in the United Kingdom in 2014 involving 60,803 respondents, including 49,964 male participants and 26,687 female participants from 12 general population studies in Great Britain, where centile curves were produced based on age for ages 4–90 years.<sup>[22]</sup> The result of HGS within each stratum was displayed in centile, stratified according to age and gender.

The IIEF-5 questionnaire was bilingual in both English and Malay. Lim *et al.*<sup>[28]</sup> adapted and validated the Malay version of the IIEF-5 in 2003. The sensitivity and specificity of the IIEF-5 questionnaire were 85% and 75%, respectively, with a Cronbach alpha of 0.9.<sup>[28]</sup> The IIEF-5 consisted of five items, where each item was scored on a five six-scale, ranging from zero to five. The total score ranged from 1 to 25. The presence of ED was indicated by IIEF-5 scores that were equal or less than 21. The severity of ED was further categorized based on the IIEF-5 scores: severe (5-7), moderate (8-11), mild to moderate (12-16), mild (17-21), and no ED (22-25).

### Variable definition

The dependent variable for the study was the presence of ED as diagnosed using the IIEF-5 questionnaire. Age, ethnicity, marital status, household income, education level, smoking, alcohol intake, presence of comorbidity, waist circumference (WC), obesity, HSG, and blood profiles were the independent variables. Malay or non-Malay ethnicities were distinguished. Marital status was grouped as either married or single/divorced/widowed. Meanwhile, household income was divided into (i) high (T20) and middle income (M40) if  $\geq$  RM4,850/household; or (ii) low income (B40) if  $<$  RM4,850/household. These classifications were developed in 2019 according to the Household Income and Basic Amenities Survey Report, 2019.<sup>[29]</sup> While education level was categorized into: (i) secondary and below or (ii) tertiary. Secondary and below education level is defined as either having no formal education or has attended primary and/or secondary school from the age of seven years up to 17 years old. Meanwhile, tertiary education is defined as any education pursued beyond secondary school including universities and colleges. Regarding alcohol consumption,

alcohol drinker is defined as those who drank alcohol daily, weekly, or occasionally for the past 12 months in the past 1 year.<sup>[30]</sup> Non-drinker is defined as those who did not drink any alcohol in the past 1 year. For smoking status, participants were classified as ever smoked if they were currently smoking or an ex-smoker who had at least stopped smoking in the past 30 days. Whereas never smoked is defined as those who had never smoked in the past. Hypertension, diabetes mellitus (DM), and coronary artery disease, cerebrovascular accidents were present if these diagnoses were recorded in the EMR, or participants were on medication for these conditions. Dyslipidemia was identified via patient self-report of diagnosis of “high cholesterol,” cholesterol-lowering medication taken, or any elevation of fasting serum lipid or had been diagnosed in the EMR. The definition of elevation of fasting serum lipid were as follows: Total cholesterol (TC)  $>$ 5.2 mmol/L, high-density lipoprotein – cholesterol (HDL-C)  $<$ 1.0 mmol/L (males) or  $<$ 1.2 mmol/L (females), triglycerides (TG)  $>$ 1.7 mmol/L, and elevated low-density lipoprotein – cholesterol (LDL-C) levels.<sup>[31]</sup> The LDL-C levels will depend on the patient’s cardiovascular risk<sup>[31]</sup> [see Box 2].

Weight and height were measured using Secca 767 and were expressed as kilogram (kg) and centimeters (cm), respectively. WC was measured to the nearest 0.1 cm using non-stretchable measuring tape with the participants standing in a relaxed position and arms at the side. The measurement was taken at the midpoint between the lower rib margin (12<sup>th</sup> rib) and the iliac crest. The classification of weight by BMI is described in Table 1.<sup>[32]</sup>

### Sampling method, participant recruitment, and data collection procedure

This study employed a simple random sampling method. A list of all male patients who had their follow-ups at the

#### Box 2: Risk Stratification of Cardiovascular (CV) Risk and Target LDL-C Levels

1. Low CV risk  $<$ 3 mmol/L
    - FRS (Framingham Risk Score) 10- year CVD Risk  $<$ 10%
  2. Intermediate (Moderate) CV risk  $<$ 3mmol/L
    - FRS 10- year CVD Risk 10% - 20%
  3. High CV risk  $\leq$ 2.6 mmol/L
    - Diabetes without target organ damage
    - CKD with eGFR  $\geq$ 30-60 30ml/min<sup>-1</sup>/1.73 m<sup>2</sup> (stage 3)
    - FRS 10- year CVD Risk  $>$ 20%
  4. Very high CV risk  $<$ 1.8 mmol/L
    - Established CVD
    - Diabetes with proteinuria
    - chronic kidney disease with eGFR  $<$ 30ml/min -1/1.73 m<sup>2</sup> (stage 4)
- \*eGFR (estimated glomerular filtration rate)

Table 1: Classification of weight by BMI

Classification	BMI (kg/m <sup>2</sup> )
Underweight	$<$ 18.5
Normal range	18.5-22.9
Overweight	23.0–27.4
Obesity	$\geq$ 27.5

clinic between January 1, 2020, and December 31, 2020, was obtained from the IT Unit. All male patients classified as MetS based on the JIS criteria were randomly sampled using a computer-generated random sampling number. Their presence on the follow-up day was confirmed by phone call. On the patient's follow-up day, they were given the patient's information leaflet and consent form, and their eligibility according to the inclusion and exclusion criteria was performed. Eligible participants who consented were given a data collection form and were examined. Data were collected by a trained research assistant to guarantee a uniform data-gathering procedure. Figure 1 illustrates the flowchart for this study.

### Data entry and statistical analysis

The IBM® Statistical Package for Social Sciences (SPSS) version 27 software (IBM Corp., Armonk, NY, USA) was used

for data entry and statistical analysis. The sociodemographic characteristics, clinical profiles, and prevalence of ED among men with MetS were described using descriptive analysis. The continuous data were described either in terms of mean with standard deviations (SD) or median with interquartile ranges (IQR) based on normality of distribution. The categorical data was described using frequencies and percentages. To identify the factors associated with ED, inferential analysis was used. Odds ratios (OR) and their 95% CI were calculated using simple logistic regression (SLogR) and multiple logistic regression (MLogR). Variables with a *P* value that was  $<0.25$  from the SLogR were subsequently included in the MLogR. The MLogR was performed using the forward selection likelihood ratio method. Model fitness was checked using the Hosmer – Lemeshow goodness-of-fit test. Interactions, multicollinearity, and assumptions were also checked. Statistical significance was taken at a *P*-value that was  $<0.05$ .

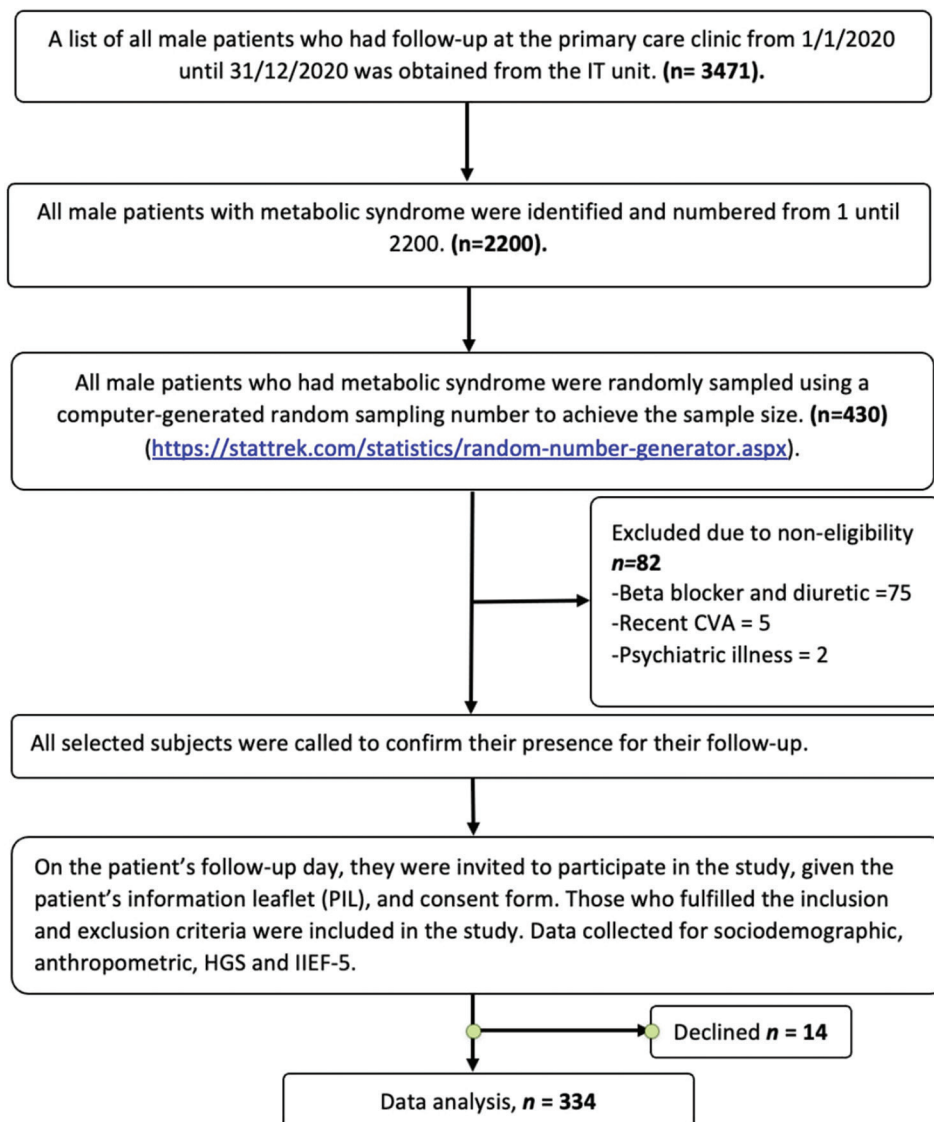


Figure 1: Flowchart of study

**Table 2: Sociodemographics and clinical characteristics of the participants (n=334)**

Characteristics	n=334
Age, mean ( $\pm$ SD) years	58.87 ( $\pm$ 8.84)
Age groups (years) (n, %)	
Young ( $\geq$ 40 to <60)	153 (45.80)
Elderly ( $\geq$ 60)	181 (54.20)
Marital status (n, %)	
Married	330 (98.80)
Single/divorcee/widower	4 (1.20)
Ethnicity (n, %)	
Malay	318 (95.20)
Others	16 (4.80)
Education level (n, %)	
Secondary or below	113 (33.80)
Tertiary	221 (66.20)
Household income (RM) (n, %)	
B40 (<RM 4850/household)	158 (47.30)
M40 and T20 ( $\geq$ RM 4850 to >RM10,959/household)	176 (52.70)
Smoking status (n, %)	
Non-smoker	175 (52.40)
Former smoker	101 (30.20)
Active smoker	58 (17.40)
Alcohol consumption (n, %)	
No	320 (95.80)
Yes	14 (4.20)
Hypertension (n, %)	
No	78 (23.40)
Yes	256 (76.60)
Diabetes mellitus (n, %)	
No	175 (52.40)
Yes	159 (47.6)
Dyslipidemia (n, %)	
No	7 (2.10)
Yes	327 (97.90)
Coronary artery disease (n, %)	
No	282 (84.40)
Yes	52 (15.60)
Cerebrovascular accident (n, %)	
No	316 (94.60)
Yes	18 (5.40)
BMI (kg/m <sup>2</sup> ) (n, %)	
Normal ( $\geq$ 18.5 to <23)	28 (8.40)
Overweight ( $\geq$ 23 to <27.5)	128 (38.30)
Obesity ( $\geq$ 27.5)	178 (53.30)
Waist circumference (n, %)	
Normal (WC <90 cm)	151 (45.20)
Abnormal (WC $\geq$ 90 cm)	183 (54.80)
SBP (n, %)	
Normal (SBP <140 mmHg)	182 (54.50)
Abnormal (SBP $\geq$ 140 mmHg)	152 (45.50)
DBP (n, %)	
Normal (DBP <90 mmHg)	285 (85.30)
Abnormal (DBP $\geq$ 90 mmHg)	49 (14.70)
FBS (n, %)	
Normal (FBS <7.0 mmol/L)	244 (73.10)
Abnormal (FBS $\geq$ 7.0 mmol/L)	90 (26.90)
HbA1c (n=167, %)	
Normal (HbA1c <6.5 mmol/L)	61 (36.50)

*Contd...*

Table 2: Contd...

Characteristics	n=334
Abnormal (HbA1c $\geq 6.5$ mmol/L)	106 (63.50)
Total cholesterol (n, %)	
Normal (Total cholesterol $< 5.2$ mmol/L)	258 (77.20)
Abnormal (Total cholesterol $\geq 5.2$ mmol/L)	76 (22.80)
Triglyceride (n, %)	
Normal (Triglyceride $\leq 1.7$ mmol/L)	236 (70.70)
Abnormal (Triglyceride $> 1.7$ mmol/L)	98 (29.30)
LDL based on CV risk (n, %)	
Normal (very high risk: LDL $< 1.8$ mmol/L, high risk: LDL $\leq 2.6$ mmol/L, moderate risk, and low risk LDL $< 3$ mmol/L)	180 (53.90)
Abnormal (very high risk: LDL $\geq 1.8$ mmol/L, high risk: LDL $< 2.6$ mmol/L, moderate risk, and low risk LDL $\geq 3$ mmol/L)	154 (46.1%)
HDL (n, %)	
Normal (HDL $> 1.0$ mmol/L)	252 (75.40)
Abnormal (HDL $\leq 1.0$ mmol/L)	82 (24.60)
Handgrip strength centile (kg)	
$\geq 50^{\text{th}}$	0 (0.00)
$\geq 25^{\text{th}} - < 50^{\text{th}}$	32 (9.58)
$\geq 10^{\text{th}} - < 25^{\text{th}}$	80 (23.95)
$< 10^{\text{th}}$	222 (66.47)

## Ethical consideration

This research was reviewed and approved by the University Teknologi Mara (UiTM) Research Ethics Committee (REC/01/2021/FB 03) prior to data collection, and the data collection process was performed in accordance with the Helsinki Declaration.

## Results

### Sociodemographic and clinical characteristics

The sociodemographic and clinical characteristics are shown in Table 2. The mean age was 58.8 ( $\pm 8.84$ ) years old. The majority were Malays (95.2%) and married (98.8%). More than half of the participants were non-smokers (52.4%), and most did not consume alcohol (95.8%). A majority had been diagnosed with hypertension and dyslipidemia, which were 76.6% and 97.9%, respectively, while slightly more than half had diabetes (52.4%).

### Prevalence and severity of ED

The overall prevalence of ED was 79.6% (95% confidence interval [CI]: 0.75–0.84). A total of 266 participants had ED in various severities, of which 45.8% of them had mild ED, more than a third of them had mild to moderate ED, 11.3% of them had moderate ED, and another 11.3% of them had severe ED [see Table 3].

### Factors associated with ED

In univariate binary logistic regression, the significant factors of ED were as follows: elderly, tertiary education, income classification (middle and high income), active smoking hypertensive, obesity, abnormal BP, abnormal fasting serum lipid, and HGS [see Table 4]. DM, coronary artery disease, and dyslipidemia did not show significant results. All variables with  $P < 0.25$  in the univariate analysis were included in the MLogR.

Table 3: Severity of ED among men with ED (n=266)

Severity of ED	Proportion (n, %)
Mild (score $\geq 17 - \leq 21$ )	122 (45.80)
Mild to moderate (score $\geq 12 - < 17$ )	84 (31.60)
Moderate (score $\geq 8 - < 12$ )	30 (11.30)
Severe (score $\geq 1 - < 8$ )	30 (11.30)

MlogR analysis was undertaken to assess the relationship between the sociodemographic characteristics and comorbid predictors and ED. The model consisted of 13 independent variables: elderly, education level, income classification, smoking status, hypertension, obesity, elevated systolic BP and diastolic BP, total cholesterol, triglyceride, LDL, HDL, and HGS. Following the stepwise regression, the full model containing the three remaining factors was statistically significant, as shown in Table 5. The model explained the variance of ED between 31% (Cox and Snell R2) and 48.8% (Nagelkerke R2), as well as correctly classified 88.6% of cases. Three independent factors were identified: elderly ( $\geq 60$ ), HGS  $< 10^{\text{th}}$  centile and total cholesterol.

## Discussion

### Prevalence of ED

We found that the prevalence of ED among MetS was high, with 79.6% (95% CI: 0.75–0.84) among men with MetS aged above 40 years old. Our result is consistent with a study in Egypt, which reported that the prevalence of ED was 79.4% in men aged between 30 and 75 years old who had MetS.<sup>[33]</sup> Previous studies also showed a similar prevalence as in this study, with more than 70% of men with MetS having ED.<sup>[34,35]</sup> The prevalence of ED among MetS was not surprising to be higher compared to the general populations in Asian and Western studies.<sup>[1,3,5,36-39]</sup> This study supports the strong pathogenicity of MetS in ED.<sup>[35,40]</sup>

**Table 4: Factors associated with ED among men with metabolic syndrome from simple logistic regression analysis**

Variables	Wald (df)	Crude OR (95% CI)	P
Age group (years)			
Young ( $\geq 40$ to $< 60$ )		1	ref
Elderly ( $\geq 60$ )	23.00 (1)	4.26 (2.36,7.70)	$< 0.001^*$
Marital status			
Unmarried/divorcee/widower		1	ref
Married	0.00 (1)	0.000 (0.00)	0.999
Ethnicity			
Malay		1	ref
Others	0.23 (1)	0.76 (0.24,2.42)	0.638
Education level			
Low education (no formal education/primary/secondary)		1	ref
High education	2.93 (1)	0.59 (0.32-1.08)	0.087*
Household income (Ringgit Malaysia [RM])			
Low income ( $< RM4850$ /household)		1	ref
Middle and high income ( $\geq RM4850$ to $> RM10,959$ /household)	4.86 (1)	0.54 (0.31-0.93)	0.028*
Smoking status			
Non-smoker		1	ref
Former smoker	0.01 (1)	0.97 (0.52-1.81)	0.914
Active smoker	3.13 (1)	0.54 (0.27 -1.07)	0.077*
Alcohol consumption			
No		1	ref
Yes	0.01 (1)	0.94 (0.25-3.45)	0.919
Hypertension			
No		1	ref
Yes	2.08 (1)	1.59 (0.85-3.01)	0.150*
Diabetes mellitus			
No		1	ref
Yes	0.18 (1)	1.12 (0.66-1.92)	0.668
Dyslipidemia			
No		1	ref
Yes	0.16 (1)	0.65 (0.08-5.46)	0.689
Coronary artery disease			
No		1	ref
Yes	0.35 (1)	1.26 (0.58-2.74)	0.553
Cerebrovascular accident			
No		1	ref
Yes	0.16 (1)	1.30 (0.36-4.61)	0.690
BMI ( $\text{kg}/\text{m}^2$ )			
Normal ( $\geq 18.5$ to $< 23$ )		1	ref
Overweight ( $\geq 23$ to $< 27.5$ )	3.07 (1)	0.26 (0.06-1.17)	0.080*
Obesity ( $\geq 27.5$ )	2.63 (1)	0.29 (0.07-1.30)	0.105*
Waist circumference (cm)			
Normal (WC $< 90$ )		1	ref
Abnormal (WC $\geq 90$ )	0.12 (1)	1.10 (0.64-1.87)	0.731
SBP (mmHg)			
Normal (SBP $< 140$ )		1	ref
Abnormal (SBP $\geq 140$ )	5.83 (1)	2.00 (1.14- 3.51)	0.016*
DBP (mmHg)			
Normal (DBP $< 90$ )		1	Ref
Abnormal (DBP $\geq 90$ )	3.63 (1)	0.52 (0.26-1.02)	0.057*
FBS (mmol/L)			
Normal (FBS $< 7.0$ )		1	ref
Abnormal (FBS $\geq 7.0$ )	0.01 (1)	1.03 (0.56-1.88)	0.921
HbA1c (mmol/L)			
Normal (HbA1c $< 6.5$ )		1	ref
Abnormal (HbA1c $\geq 6.5$ )	0.30 (1)	0.79 (0.35-1.82)	0.585

Contd...

Table 4: Contd...

Variables	Wald (df)	Crude OR (95% CI)	P
Total cholesterol (mmol/L)			
Normal (total cholesterol <5.2)		1	ref
Abnormal (total cholesterol ≥5.2)	11.14 (1)	0.37 (0.21-0.67)	<0.001*
Triglyceride (mmol/L)			
Normal (triglyceride ≤1.7)		1	ref
Abnormal (triglyceride >1.7)	4.36 (1)	0.55 (0.37-0.97)	0.037*
LDL based on CV risk (mmol/L)			
Normal (very high risk: LDL <1.8, high risk: LDL ≤2.6, moderate risk, and low risk LDL <3)		1	ref
Abnormal (very high risk: LDL ≥1.8, high risk: LDL <2.6, moderate risk, and low risk LDL ≥3)	2.35 (1)	0.66 (0.39-1.12)	0.125*
HDL (mmol/L)			
Normal (HDL >1.0)		1	ref
Abnormal (HDL ≤1.0)	3.90 (1)	0.56 (0.31-1.00)	0.048*
Handgrip strength centile (kg)			
≥25 <sup>th</sup> to <50 <sup>th</sup>		1	ref
≥10 <sup>th</sup> to <25 <sup>th</sup>	1.15 (1)	0.64 (0.28-1.45)	0.283
<10 <sup>th</sup>	33.90 (1)	16.49 (6.42-42.36)	<0.001

\*P&lt;0.25 is statistically significant

Table 5: Factors associated with ED among men with metabolic syndrome from multiple logistic regression

Variables	Crude OR <sup>a</sup> (95% CI)	Adjusted OR <sup>b</sup> (95% CI)	Wald statistic <sup>b</sup> (df)	P <sup>b</sup>
Age group				
Young (≥40-<60)	1	1		
Elderly (≥60)	4.26 (2.36-7.70)	3.27 (1.60-6.69)	10.52 (1)	0.001
Total cholesterol				
Normal (total cholesterol <5.2 mmol/L)	1	1		
Abnormal (total cholesterol ≥5.2 mmol/L)	0.374 (0.21-0.67)	0.36 (0.16-0.78)	6.68 (1)	0.010
Handgrip strength centile				
≥25 <sup>th</sup> to <50 <sup>th</sup>	1	1		
≥10 <sup>th</sup> to <25 <sup>th</sup>	0.64 (0.28-1.45)	0.57 (0.23-1.39)	1.54 (1)	0.215
<10 <sup>th</sup>	16.49 (6.42-42.36)	15.35 (5.64-41.81)	28.54 (1)	<0.001

<sup>a</sup>Simple logistic regression; <sup>b</sup>Multiple logistic regression. The Hosmer–Lemeshow goodness-of-fit test showed the final model was fit (P=0.915) and area under the receiver operating characteristic (ROC) curve (88.6%). There were no interactions or multicollinearity

The relationship between MetS and ED was first described by Gündüz *et al.* in 2004,<sup>[41]</sup> and there were consistent findings in the literature that reported that MetS was strongly associated with ED.<sup>[34,35,42-44]</sup> A meta-analysis revealed that patients with MetS had a 2.6-fold increased risk of having ED.<sup>[44]</sup>

The reason for this is generally attributed to a constellation of interrelated cardiac risk factors consisting of insulin resistance, abdominal obesity, atherogenic dyslipidemia, and systemic inflammation that can cause ED.<sup>[45]</sup> MetS can result in endothelial dysfunction, which has been implicated in atherosclerosis leading to ED. In a study conducted by Thompson *et al.*,<sup>[45]</sup> a strong association was indicated between elevated biomarkers of inflammation and endothelial dysfunction with increased odds of prediabetes, diabetes, and MetS among adults in China.<sup>[45]</sup> Endothelial dysfunction leads to a decrease in vascular nitric oxide levels, which results in impaired vasodilation and the increase in free radical concentration also leads to atherosclerotic damage.

## HGS and ED

Our study supports the inverse relation between HGS and the risk of developing ED. We found lower HGS centile had a

higher risk of ED, with HGS of <10<sup>th</sup> centile having the risk of ED more than 15-fold. HGS is a simple, convenient, and inexpensive measurement method to assess the overall strength of an individual apart from being a potential indicator of health conditions.<sup>[18]</sup> HGS refers to the greatest force or tension exerted by the hand and forearm muscles using a dynamometer. Measurement of HGS can be used to assess overall strength as its well correlated with muscle strength measurement from arm, trunk, and leg. HGS can be influenced by age, gender, BMI, hand dominance, smoking status, alcohol consumption, and nutritional status.<sup>[23]</sup>

Several studies have found a link between HGS and type 2 diabetes, cardiovascular disease, and other metabolic diseases.<sup>[46]</sup> According to Lee *et al.*,<sup>[46]</sup> HGS is significantly associated with cardiometabolic risk, and the association is stronger than when dominant HGS is used. Leong *et al.*<sup>[19]</sup> reported in a prospective epidemiologic study that HGS a risk marker for incident cardiovascular disease in some countries and populations. There are several possible explanations for the link between HGS and these diseases. Changes in muscle composition caused by aging, particularly lipid accumulation



in skeletal muscle fibers, contribute to poor muscle mass and strength. The skeletal muscle, also known as the primary protein site, accounts for 85% of glucose metabolism via the adiponectin receptors.<sup>[46]</sup> Adiponectin is a protein hormone and adipokine that regulates fatty acid metabolism and glucose levels. The interaction of this adiponectin with its receptor could have antihyperglycemic, anti-atherogenic, and anti-inflammatory effects, potentially slowing the progression of CVD.<sup>[46]</sup> It was discovered that positive effects of muscular strength and muscle mass include maintenance or increase in resting metabolic rate; the prevention of age-associated fat gains; the reduction of visceral adipose tissue; improvements in blood glucose levels, basal insulin levels, insulin response, and insulin sensitivity; improvements in resting BP, and decreases in HbA1c in diabetics patient.<sup>[47]</sup> These modifiable risk factors also link to ED, which subsequently will improve ED.

Furthermore, a few studies reported the association of HGS with ED. Chung *et al.*,<sup>[20]</sup> who revealed that greater hand strength had a lower risk of having moderate to severe ED with OR 0.82, 95% CI: 0.74–0.90, and Kumagai *et al.*<sup>[21]</sup> reported that with 1 kilogram of handgrip increment, the IIEF5 will improve by 16%. Nevertheless, Park *et al.*<sup>[48]</sup> (2020) found that HGS was not significantly associated with severe ED with OR 0.76, 95%; CI: 0.30 to 1.91, which should be confirmed in future studies. The biological mechanism linking HGS and ED is still controversial. Skeletal muscle is thought to produce and release cytokines (myokines) that protect against CVDs.<sup>[49]</sup> Thus, more research is needed to determine the relationship between muscular strength and ED.

### ED and other associated factors

This study supports elderly aged 60 years old and above is an independent factor for ED which further confirms that the prevalence of ED is rising with advancing age.<sup>[1-3,36,50]</sup> The concomitant presence of comorbid illnesses and increase use of medications as aging occurs are plausible causes. With advancing age, the physiological changes of atherosclerosis in blood vessels may compromise the blood flow to the penile organs and thus increasing the risk of ED. Another possible explanation is that the aging process decreases the functions of various organs, including the skeletal muscle which is known as sarcopenia. Sarcopenia can be associated with low testosterone level due to the decrease of anabolism of the skeletal muscle. Sarcopenia was associated with severe ED with OR 1.89, (95% CI: 0.18 to 3.03) among elderly men in Korea.<sup>[48]</sup>

Elevated total cholesterol was shown to have a decreased risk of ED with OR 0.374, 95% CI: 0.21-0.67. This finding is unexpected and is contrary to the findings in most literatures.<sup>[51,52]</sup> It is difficult to explain this result, but it may be related to the participants of this study, who a majority had dyslipidemia; thus, they may be prescribed common anti-lowering cholesterol drugs such as statin. Therefore, it is possible that statin can reduce the risk

of ED as reported by a few meta-analyses.<sup>[53-56]</sup> Unfortunately, information about statin was not collected in this study. Besides, more than half of the participants who had abnormal total cholesterol were of younger age groups.

Many literatures reported the strong relationship between diabetes, cardiovascular diseases, and ED.<sup>[9,57,58]</sup> However, our findings did not support the association of diabetes, the presence of CVD and ED. Recent studies in Nepal and India showed a longer duration of DM and poor glycaemic control with HbA1c  $\geq 7\%$  had a higher risk of ED.<sup>[57,58]</sup> Nisahan *et al.*<sup>[59]</sup> also found that the duration of DM, and the presence of microvascular complications were associated with ED. However, few studies also did not find an association of glycaemic control with ED,<sup>[59,60]</sup> which corresponds with our study. Thus, serial HbA1c levels over time could be a useful tool in assessing long-term glycaemic control, with a better correlation than a single HbA1c value. Our inconsistent findings may be due to the limited information on the duration of diabetes and the presence of diabetes complications that predict ED.

Endothelial dysfunction has been linked to both CVD and ED, and it plays a significant role in the progression of atherosclerosis. However, our study did not show the association between CVD and ED like other studies.<sup>[2,59]</sup> This may be due to our study participants who were on beta-blocker and diuretics were excluded. Our study participants also had better control of CVD risk factors such as BP and lipid control.

### Clinical implication and recommendations

The current study discovered that ED was very common in men with MetS. The presence of ED to predict atherosclerotic involvement of coronary arteries within 2–5 years emphasizes the importance of ED screening among men above 40 years of age with MetS. ED is a critical men's health issue that must be included in all risk screening programs in primary care settings for early identification of risk factors and early cardiology intervention. In addition, raising public awareness about the importance of early detection of ED, particularly among men MetS, should be performed.

Our study found that lower HGS had a higher risk of ED, and as a result, HGS may be used to identify people who are at risk of developing ED and that increasing muscle strength might be a possible intervention for ED. Focused muscle strengthening exercise or resistance training intervention may improve outcomes, but further study is needed to investigate the effectiveness of resistance training in improving ED. Furthermore, future research directed to develop resistance training exercise prescriptions for men at risk of ED may be beneficial for clinicians and fitness professionals. Nevertheless, pharmacotherapy is the most effective treatment for ED in the short term, but muscle-strengthening exercises may be necessary for the improvement of ED.

## Strength and limitations

To the best of our knowledge, this is the first study to find the association between HGS and ED among men with MetS. The use of probability sampling also reduced sampling bias. However, there were several limitations. The findings of this study may not be generalizable to other primary care clinics in other settings as most of the participants were predominantly of Malay race. We also had limited information regarding diabetes duration and its complications that may contribute to ED. Furthermore, the HGS centile's reference was based on a study performed in United Kingdom, and the values might be different due to geographic and ethnic variation.

## Conclusions

In conclusion, most men aged above 40 years with MetS had ED. A lower HGS predicted higher risk of ED, suggesting that reduced muscle strength may contribute to ED. Further studies are needed to determine whether intervention using resistance training exercises to improve muscle strength can improve ED.

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## Conflicts of interest

There are no conflicts of interest.

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