

Factors associated with six-minute walk distance among Indonesian Hajj Pilgrims

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ABSTRACT

The Hajj pilgrimage is a physically demanding religious rite that is associated with the health status of pilgrims. Several factors are associated with functional limitations. We aimed to determine the relationship between clinical data and six-minute walk test (6-MWT) findings. The 6-MWT is a measure of functional capacity that is routinely applied to Indonesian pilgrim candidates before they embark on the Hajj. This cross-sectional study analysed Indonesian Hajj pilgrimage data obtained from 2,933 participants before their departure for the Hajj in 2022. The data included participants' characteristics, laboratory results, and six-minute walk findings. The resulting aggregates were analysed using Pearson correlations. Serum creatinine significantly correlated with 6-MWT findings ($r = 0.003$; $p < 0.05$). Low-density lipoprotein-cholesterol (LDL-C) values and platelet counts were significantly associated with 6-MWT results ($r = 0.101$ and 0.038 , respectively; $p < 0.05$). Serum creatinine, LDL-C, and platelet values were associated with increased 6-MWT, indicating a correlation with functional capacity among Hajj pilgrims.

Key words:

Hajj pilgrim; six-minute walk test; functional capacity

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INTRODUCTION

The Hajj is a physically demanding religious rite that requires sufficient physical fitness among pilgrims. The series of pilgrimages involves seven laps around the Kaaba, with the closest distance being 1.4 km from it for Tawaf. Sa'i involves jogging back and forth seven times between the Safa and Marwa hills, which are 2.8 km apart. Wukuf in Arafat and Jumrah (throwing pebbles) in the Jamarat area cover a distance of 14,273 km². Pilgrims have to endure extreme temperatures and densely populated conditions.^{1,2}

The Islamic fiqh, *istitha'ah* (steadfastness), encompasses medical and religious fitness and is mandatory for participating in the pilgrimage. *Istitha'ah* determines the ability of pilgrims to participate in various activities on the pillars of Hajj.¹ The results of health examinations during the *istitha'ah* preparation of pilgrims are used as a basis for health coaching. Forms of guidance include counselling, integrated coaching posts, information dissemination through various media, home visits, and Hajj rituals.³

The indirect impact of *istitha'ah* control is a reduction in morbidity and mortality rates among Hajj pilgrims. A common misconception among pilgrims is that dying while participating in the Hajj in the holy city of Mecca is a blessing from God. Consequently, many pilgrims fail to recognise the importance of pre-Hajj fitness. This problem can be avoided by making *istitha'ah* a ritual requirement of the Hajj rather than using it to reduce mortality.⁴

Physical fitness is crucial for participating in the Hajj pilgrimage, as it requires good physical status to fully participate in all activities. Physical fitness as a daily activity is influenced by muscle strength, flexibility, balance, agility, gait

velocity, and cardiorespiratory fitness.⁵ Cardiorespiratory measurements are components of health-related physical fitness that measure maximum oxygen consumption during activity.^{6,7}

The six-minute walk test (6-MWT) that proceeds during *istitha'ah* is a submaximal effort test that is inexpensive, easy to implement, and reflects activities of daily life. The results can predict mileage capability and maximal oxygen consumption. The 6-MWT has been extensively validated and provides valuable insights into the impact of pathological conditions on function and prognosis. Moreover, it can evaluate the effectiveness of interventions.^{8,9} Age, body mass index (BMI), body composition, and strength affect 6-MWT findings in persons with obesity.¹⁰ The 6-MWT can predict cardiovascular events in patients with stable coronary heart disease.¹¹ The distance walked in the 6-MWT by patients undergoing haemodialysis is influenced by muscle strength, iron deficiency anaemia, and prior coronary artery disease.¹² Patients on haemodialysis often have end-stage renal disease, which is associated with high serum creatinine levels due to free filtration through renal glomeruli.¹³ Serum creatinine values can predict all-cause mortality in persons with hypertension and in those with advanced age.^{14,15}

This cross-sectional study aimed to reduce illness and mortality rates among persons who embark on Hajj pilgrimages by analysing clinical health data obtained from pilgrims. The results of health examinations will serve as primary data to predict the functional capacity of Hajj pilgrims.

METHODS

We obtained secondary health information from the Ministry of Religious Affairs about Indonesian Hajj pilgrims

during the (*istitha'ah*) pre-departure period of May 2022. The health examinations implemented by health professionals at the Indonesian Ministry of Religious Affairs included medical, clinical, and family histories, a physical examination, and laboratory tests. The Health Research Ethics Committee, Faculty of Medicine, Airlangga University, approved the data collection and review procedures (Approval ID: 103/EC/KEPK/FKUA/2023) and waived the need for written consent because we analysed secondary innominate data with minimal risk to participants.

Participants

We selected data from 6,325 consecutive Hajj pilgrims in Indonesia during 2022, out of these 2,933 met the following inclusion criteria: age ≥ 60 and at least one comorbidity. We examined the data to ensure completeness, and records with incomplete data were excluded.

Data collection

We collected secondary data about the clinical characteristics of Indonesian Hajj pilgrims in 2022. The data included demographic information (age and gender), basic anthropometry (weight, height, and BMI), and medical history data, such as cigarette smoking, hypertension, heart disease, diabetes mellitus, stroke, asthma, chronic renal failure, hyperthyroidism, and previous hospitalisation.

Haemoglobin, leukocytes, platelets, uric acid, creatinine, aspartic aminotransferase (AST), *alanine transaminase* (ALT), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), triglycerides, fasting plasma glucose (FPG), and 2-h postprandial plasma glucose (2HPP) were routinely assessed in fresh serum before departure.

The World Health Organisation classifies BMI (kg/m^2) of <18.5 , $18.5\text{--}22.9$, $23.0\text{--}24.9$, $25.0\text{--}29.9$, and ≥ 30 kg/m^2 in Asian populations as underweight, normal weight, overweight, and obesity classes I and II, respectively.¹⁶

Hypertension is defined as systolic blood pressure (SBP) >140 mmHg and/or diastolic blood pressure (DBP) >90 mmHg, according to the American College of Cardiology (ACC), the American Heart Association (AHA), and the European Society of Cardiology 2018 (ESC 2018). Hypertension is graded as 1–3 based on respective SBP or DBP values of 140–159 and/or 90–99, 160–179 and/or 100–109, and >110 mmHg.¹⁷ According to the American Diabetes Association, a diagnosis of diabetes can be reported by a healthcare professional or determined by an oral glucose tolerance test with a 2-h plasma glucose level of 200 mg/dL (11.1 mmol/L) for persons without self-reported diabetes.¹⁸

The functional capacity of Hajj pilgrims was assessed using the standardised 6-MWT developed by the American Thoracic Society (ATS). This test requires a simple walk of 100 m on a flat, hard surface without the use of exercise equipment or trained technicians. The distance walked in 6 min can be used to evaluate the integrated responses of various physiological systems, including the pulmonary, cardiovascular, systemic, and peripheral circulation, neuromuscular unit, blood, and muscle metabolism.¹⁹

Participants walked at their own pace along a 30-m flat, straight track for 6 min with options to stop and rest as necessary. The total distance walked was then measured, and participants were categorised into age groups based on the results (Tables 1 and 2).⁹

Table 1. Cardiorespiratory fitness of males measured using 6-MWT⁹

Category	Distance (m) walked according to age (y)						
	60–64	65–69	70–74	75–79	80–84	85–89	90–94
Excellent	700	650	600	550	500	450	400
Good	650	600	550	500	450	400	350
Fair	600	550	500	450	400	350	300
Poor	550	500	450	400	350	300	250
Very poor	500	450	400	350	300	250	200

Table 2. Cardiorespiratory fitness of females measured using 6-MWT for participants⁹

Category	Distance (m) walked according to age (y)						
	60–64	65–69	70–74	75–79	80–84	85–89	90–94
Excellent	650	600	550	500	450	400	350
Good	600	550	500	450	400	350	300
Fair	550	500	450	400	350	300	250
Poor	500	450	400	350	300	250	200
Very poor	450	400	350	300	250	200	150

Statistical analysis

All data were statistically analysed using IBM SPSS Statistics for Windows version 20.0 (IBM Corp., Armonk, NY, USA). Normally distributed data were evaluated using the Kolmogorov–Smirnov test. Continuous and categorical variables are presented as medians with 25th–75th percentiles, and as absolute frequencies and ratios (%). Univariate continuous and numeric categorical variables were compared using Pearson correlations (*r*) and independent *t*-tests, respectively. Values with *p* < 0.05 were considered statistically significant.

RESULTS

Baseline characteristics

We included data from 2,933 pilgrims (female, 57.9%; males, 42.1%) in

Indonesia who participated in the Hajj in 2021 who were either aged ≤60 or had comorbidities. All met the inclusion criteria and provided complete demographic data, physical examinations, laboratory results, and clinical manifestations. Table 3 shows their clinical characteristics. The average BMI was approximately 26.08, 10.8% were smokers, and many had the following comorbidities: hypertension (30.8%), heart disease (43%), diabetes mellitus (11.6%), stroke (1.9%), asthma (3.1%), chronic renal failure (0.1%), and hyperthyroidism (0.9%). Furthermore, 1.4% of pilgrims had a history of hospitalization. The 6-MWT results were low (16.4%), sufficient (18.3%), good (39.7%), and excellent (22.5%) (Table 3). Table 4 shows laboratory findings of mildly elevated serum creatinine as well as elevated mean FPG and triglyceride values (Table 4).

Table 3. Clinical characteristics of Hajj pilgrims

Clinical characteristics	(n = 2,933)
Age (y)	54.90 ± 8.35
Sex n (%)	
Male	1,235 (42.1)
Female	1,698 (57.9)
BMI (kg/m ²)	26.08 ± 4.57
Smoker n (%)	317 (10.8)
Comorbidity n (%)	
Hypertension	903 (30.8)
Heart Disease	126 (4.3)
Diabetes Mellitus	340 (11.6)
Stroke	56 (1.9)
Asthma	91 (3.1)
Chronic Kidney Disease	3 (0.1)
Hyperthyroidism	27 (0.9)
Previous hospitalisation	41 (1.4)
6-MWT n (%)	
Low	481 (16.4)
Sufficient	537 (18.3)
Good	1,164 (39.7)
Excellent	660 (22.5)

6-MWT, six-minute walk test; BMI, body mass index

Table 4. Mean laboratory findings of Hajj pilgrims

Parameters	Mean	Normal range
Heamoglobin (g/dL)	14.36 ± 28	M: 13.5–17.5 F: 11.5–15.5
Leukocyte (/mm ³)	8.03 ± 5	3.37–10.0
Platelets (10 ³ /μL)	281 ± 74	150–450
Uric Acid (mg/dL)	5.64 ± 11	M: 3.4–7.0 F: 2.4–5.7
Creatinine (mg/dL)	1.40 ± 5	0.5–1.2
AST (U/L)	24.02 ± 10	0–37
ALT (U/L)	34.35 ± 5	0–55
FPG (mg/dL)	112.35 ± 52	<100
2HPP (mg/dL)	148.97 ± 21	<200
HDL (mg/dL)	71.75 ± 59	>60
LDL (mg/dL)	127.90 ± 45	<100
Triglycerides (mg/dL)	241.12 ± 39	<150

2HPP, 2-h postprandial plasma glucose; ALT, alanine aminotransferase; AST, aspartate aminotransferase; F, female; FGP, fasting glucose plasma; HDL, high-density lipoprotein; LDL, low-density lipoprotein; M, male

Correlations between laboratory findings and 6-MWT

We investigated relationships between the 6-MWT and laboratory findings of haemoglobin, leukocytes, uric acid, AST, ALT, FPG, HDL, 2-HPP, and triglycerides and observed no significant

correlations ($p > 0.05$). However, 6-MWT and platelets, LDL, and creatinine significantly correlated (two-tailed $P < 0.05$). Platelets and creatinine were weakly correlated ($r = 0.038$ and 0.054 , respectively, $p < 0.05$; Table 5).

Table 5. Correlation coefficients between 6-MWT and laboratory findings

Parameters	r	p
Haemoglobin	0.013	0.476
Leukocyte	0.027	0.143
Platelets	0.038	0.038*
Uric Acid	-0.007	0.718
Creatinine	-0.054	0.003*
AST	0.021	0.258
ALT	0.031	0.096
FPG	0.017	0.360
2HPP	-0.014	0.442
HDL	-0.007	0.690
LDL	0.101	<.001*
Triglycerides	-0.020	0.287

2HPP, 2-h postprandial plasma glucose; r, coefficient correlation; p, probability. ALT, alanine aminotransferase; AST, aspartate aminotransferase; FPG, fasting glucose plasma; HDL, high-density lipoprotein; LDL, low-density lipoprotein; * $p < 0.05$

DISCUSSION

The 6-MWT is a submaximal effort test of functional capacity that can reflect daily life activities inexpensively and easily. Moreover, it can predict prognosis, mortality, and morbidity in patients with lung and/or heart disease, applicable to both adults and children.²⁰ Thus, this test is applied to assess the physical fitness of Hajj pilgrims during *istitha'ah*. Factors that influence the distance walked in the 6-MWT have been investigated in various populations.

Age correlates with the distance walked. This indicates that decreased functional capacity due to ageing leads to reduced muscle strength. The normal ageing process affects changes in type 2 muscle fibres, and reduced capillarity of the

vascular bed and blood flow can cause muscle abnormalities.²¹

One of the factors that influences 6-MWT outcomes is BMI. Body fat mass is a predictor associated with distance walked during the 6-MWT in patients with end-stage renal disease.²² A correlation has been identified between 6-MWT outcomes and each of the mid-thigh area and intraabdominal fat.²³ Weight reduction programmes can significantly increase 6-MWT outcomes among patients with obesity.²⁴

The 6-MWT correlates with various comorbidities and is a predictor of mortality among adult patients undergoing haemodialysis²⁵. Every 100-m increase in the distance indicates a 5.3% increase in life expectancy.²⁵ A study examining psychological factors that can affect the results of the 6-MWT reported that

depressed patients with chronic obstructive pulmonary disease (COPD) might not walk very far due to a lack of encouragement to engage in physical activity in daily life.²⁶ Patients with advanced heart failure have a higher risk of mortality if they are unable to walk more than 200–220 m. These distances have been notably identified as cut-off values for mortality risk.^{27,28}

The current study observed that serum creatinine affected the 6-MWT results in Hajj pilgrims. Serum creatinine is routinely measured to assess kidney function²⁹, as it is filtered by glomeruli in the kidneys and can provide estimated glomerular filtration rates.³⁰ Renal function abnormalities increase the risk of poor physical performance and cardiovascular diseases associated with advanced age, such as hypertension, diabetes mellitus, dyslipidaemia, and oxidative stress.³¹⁻³³

Creatinine plays a vital role in energy metabolism in skeletal and heart muscles. As a natural bioenergetic component, it is converted into creatine phosphate, or phosphocreatine, and stored in muscle to produce energy. The phosphorylated isoform of creatinine functions as a temporary buffer to maintain ATP concentrations through ADP re-phosphorylation during intense muscular activity.³⁴ Creatinine is endogenously synthesised in the liver, kidney, and pancreas. Creatine supplementation might increase its availability in muscle, affect ATP regeneration, and potentially improve muscle performance in athletes.^{35, 36} However, creatine does not affect the distance walked during the 6-MWT.³⁶

Physical inactivity is a risk factor for low cardiorespiratory fitness and is indicated by walking short distances during the 6-MWT; this can facilitate the development of atherosclerosis in blood vessels. Atherosclerosis is formed through a complex mechanism involving endothelial dysfunction that leads to vascular inflammation that further damages blood vessels. Such inflammation triggers

the release of pro-inflammatory cytokines, chemokines, and reactive oxygen species, as well as pro-inflammatory leukocyte recruitment, adhesion, and subendothelial transmigration. Platelets play key roles in enhancing the inflammatory process through activation and binding to the endothelium resulting in chemokine release and adhesion molecule expression. The oxidative stress process increases the affinity of LDL for macrophages as a key step in atherosclerotic lesion formation. Plaque rupture or the erosion of lesions can lead to arterial thrombosis.³⁷⁻³⁹ Therefore, LDL and platelet levels reflect atherosclerosis in blood vessels. This is relevant to the current study, which observed a significant correlation between the 6-MWT, LDL, and platelets in Hajj pilgrims.

This study has certain limitations. The sample was considerably smaller than the number of pilgrims that annually depart from Indonesia for the Hajj. We did not accurately represent the age factor that affects functional capacity during the Hajj. The laboratory tests were limited, and we did not measure other parameters of physical fitness, such as strength, flexibility, and balance, among Hajj pilgrims. Therefore, further tests are necessary to identify all factors that affect 6-MWT outcomes.

CONCLUSION AND RECOMMENDATION

Physical fitness is important for pilgrims to participate in and complete all activities associated with the Hajj. The 6-MWT is an economical and simple measurement of physical performance that can be completed during *istitha'ah*. Serum creatinine, LDL-C, and platelet values influenced the 6-MWT, indicating a correlation with functional capacity among pilgrims.

These findings indicate the importance of pre-departure assessments of

physical fitness for Hajj pilgrims. This will help to improve their physical endurance during *istitha'ah* and ensure their full participation in all Hajj activities. Further studies of larger samples are needed to determine additional factors that might influence the functional capacity of Hajj pilgrims.

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REFERENCES

1. Lutfi SH, Rumengan G, Trigono A. Analysis of Istitha'ah Achievement at the Center for Hajj and Umrah Health Integrated Services (P2TKHU) RS Hajj Hospital Jakarta, International Journal of Psychosocial Rehabilitation 2020. Vol. 24, Issue 03.
2. Mas'ud I, Nasir UZ, Pitoyo CW, Rinaldi I. The implementation of health istithaah to the pilgrims with tuberculosis: A cross-sectional study in Jakarta, Indonesia. Medical Journal of Indonesia. 2020;29(2):198-203. doi: 10.13181/mji.oa.203517
3. Aldossari M, Aljoudi A, Celentano D. Health issues in the Hajj pilgrimage: a literature review. East Mediterr Health J. 2019;25(10):744-753. Published 2019 Nov 4. doi:10.26719/2019.25.10.744
4. Mansyur M. Hajj health istithaah amid the COVID-19 pandemic. Med J Indones [Internet]. 2020 Jun 30 [cited 2024 May 27];29(2):115-7.
5. Buchman AS, Boyle PA, Wilson RS, Bienias JL, Bennett DA. Physical activity and motor decline in older persons. *Muscle Nerve*. 2007;35(3): 354-362. doi:10.1002/mus.20702
6. Prasetyo Y, Doewes M, Rahma N, et al. Effects of aerobic exercise and weight training-aerobic towards physical fitness of elderly Hajj candidates. International Journal on Advanced Science, Engineering and Information Technology 2017, 7(1), pp.106-117.
7. Yusri, Y, Zulkarnain M, Sitorus RJ. Faktor yang Mempengaruhi Kebugaran Calon Jemaah Haji Kota Palembang Tahun 2019. Jurnal Epidemiologi Kesehatan Komunitas 2020, 5(1), pp.57-68.
8. Tudor-Locke C, Williams JE, Reis JP, Pluto D. Utility of pedometers for assessing physical activity: convergent validity. *Sports Med*. 2002;32(12): 795-808. doi:10.2165/00007256-200232120-00004
9. Nobel M, Ehrman J, Liguori G, et al. ACSM's Guidelines for Exercise Testing and Prescription. 10th ed. Philadelphia: ACSM; 2018.
10. Donini LM, Poggiogalle E, Mosca V, Pinto A, Brunani A, Capodaglio P. Disability affects the 6-minute walking distance in obese subjects (BMI>40 kg/m²). *PLoS One*. 2013;8(10): e75491. Published 2013 Oct 11. doi:10.1371/journal.pone.0075491
11. Beatty AL, Schiller NB, Whooley MA. Six-minute walk test as a prognostic tool in stable coronary heart disease: data from the heart and soul study. *Arch Intern Med*. 2012;172(14): 1096-1102. doi:10.1001/archinternmed.2012.2198
12. Kono K, Nishida Y, Moriyama Y, Yabe H, Taoka M, Sato T. Investigation of factors affecting the six-minute walk test results in hemodialysis patients. *Ther Apher Dial*. 2014;18(6):623-627. doi:10.1111/1744-9987.12177

13. Bessman SP, Geiger PJ. Transport of energy in muscle: the phosphorylcreatine shuttle. *Science*. 1981;211(4481):448-452. doi:10.1126/science.6450446
14. Shulman NB, Ford CE, Hall WD, et al. Prognostic value of serum creatinine and effect of treatment of hypertension on renal function. Results from the hypertension detection and follow-up program. The Hypertension Detection and Follow-up Program Cooperative Group. *Hypertension*. 1989;13(5 Suppl): I80-I93. doi:10.1161/01.hyp.13.5_suppl.i80
15. Damsgaard EM, Frøland A, Jørgensen OD, Mogensen CE. Microalbuminuria as predictor of increased mortality in elderly people. *BMJ*. 1990;300(6720): 297-300. doi:10.1136/bmj.300.6720.297
16. Choo, V. WHO reassesses appropriate body-mass index for Asian populations. *The Lancet* 2002, 360(9328), p.235.
17. Bakris G, Ali W, Parati G. ACC/AHA versus ESC/ESH on hypertension guidelines: JACC guideline comparison. *Journal of the American College of Cardiology* 2019, 73(23), pp.3018-3026.
18. Gabir MM, Hanson RL, Dabelea D, et al. The 1997 American Diabetes Association and 1999 World Health Organization criteria for hyperglycemia in the diagnosis and prediction of diabetes. *Diabetes Care*. 2000;23(8):1108-1112.
19. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test [published correction appears in *Am J Respir Crit Care Med*. 2016 May 15;193(10):1185]. *Am J Respir Crit Care Med*. 2002;166(1):111-117. doi: 10.1164/ajrccm.166.1.at1102.
20. Solway S, Brooks D, Lacasse Y, Thomas S. A qualitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. *Chest*. 2001;119(1):256-270. doi:10.1378/chest.119.1.256
21. Fernandes AO, Sens YAS, Fonseca Junior PR, Moura RCF, Alves VLS. Impacto do uso do cicloergômetro na função respiratória, cardiovascular, capacidade aeróbica, funcional e qualidade de vida de pacientes com doença renal crônica em hemodiálise. *Fisioter. Bras*. 2019;20(2): 302-309.
22. Bučar Pajek M, Čuk I, Leskošek B, Mlinšek G, Buturović Ponikvar J, Pajek J. Six-Minute Walk Test in Renal Failure Patients: Representative Results, Performance Analysis and Perceived Dyspnea Predictors. *PLoS One*. 2016;11(3):e0150414. Published 2016 Mar 16. doi:10.1371/journal.pone.0150414
23. Martinson M, Ikizler TA, Morrell G, et al. Associations of body size and body composition with functional ability and quality of life in hemodialysis patients. *Clin J Am Soc Nephrol*. 2014; 9(6):1082-1090. doi:10.2215/CJN.09200913
24. Ekman MJ, Klintonberg M, Björck U, Norström F, Ridderstråle M. Six-minute walk test before and after a weight reduction program in obese subjects. *Obesity (Silver Spring)*. 2013;21(3):E236-E243. doi:10.1002/oby.20046
25. Kohl Lde M, Signori LU, Ribeiro RA, et al. Prognostic value of the six-minute walk test in end-stage renal disease life expectancy: a prospective cohort study. *Clinics (Sao Paulo)*. 2012;67(6):581-586. doi:10.6061/clinics/2012(06)06
26. Borgmann M, Ivanda M, Hadizamani Y, et al. Does the 6-minute walk test in hospitalized COPD patients exclusively correlate with lung function parameters or should psychological factors also be taken into account?. *PLoS One*. 2020;15(5):

- e0232587. Published 2020 May 4. doi:10.1371/journal.pone.0232587
27. Shah MR, Hasselblad V, Gheorghiade M, et al. Prognostic usefulness of the six-minute walk in patients with advanced congestive heart failure secondary to ischemic or nonischemic cardiomyopathy. *Am J Cardiol.* 2001; 88(9):987-993. doi:10.1016/s0002-9149(01)01975-0
 28. Alahdab MT, Mansour IN, Napan S, Stamos TD. Six minute walk test predicts long-term all-cause mortality and heart failure rehospitalization in African-American patients hospitalized with acute decompensated heart failure. *J Card Fail.* 2009;15(2):130-135. doi:10.1016/j.cardfail.2008.10.006
 29. Odden MC, Shlipak MG, Tager IB. Serum creatinine and functional limitation in elderly persons. *J Gerontol A Biol Sci Med Sci.* 2009; 64(3):370-376. doi:10.1093/gerona/gln037
 30. Lamb EJ, O'Riordan SE, Delaney MP. Kidney function in older people: pathology, assessment and management. *Clin Chim Acta.* 2003; 334(1-2):25-40. doi:10.1016/s0009-8981(03)00246-8
 31. Hall WD. Abnormalities of kidney function as a cause and a consequence of cardiovascular disease. *Am J Med Sci.* 1999;317(3):176-182. doi:10.1097/00000441-199903000-00007
 32. Culeton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy D. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. *Kidney Int.* 1999; 56(6):2214-2219. doi:10.1046/j.1523-1755.1999.00773.x
 33. Torino C, Manfredini F, Bolignano D, et al. Physical performance and clinical outcomes in dialysis patients: a secondary analysis of the EXCITE trial. *Kidney Blood Press Res.* 2014; 39(2-3):205-211. doi:10.1159/000355798
 34. de Poli RAB, Roncada LH, Malta ES, Artioli GG, Bertuzzi R, Zagatto AM. Creatine Supplementation Improves Phosphagen Energy Pathway During Supramaximal Effort, but Does Not Improve Anaerobic Capacity or Performance. *Front Physiol.* 2019;10: 352. Published 2019 Apr 10. doi:10.3389/fphys.2019.00352
 35. Mielgo-Ayuso J, Calleja-Gonzalez J, Marqués-Jiménez D, Caballero-García A, Córdova A, Fernández-Lázaro D. Effects of Creatine Supplementation on Athletic Performance in Soccer Players: A Systematic Review and Meta-Analysis. *Nutrients.* 2019;11(4):757. Published 2019 Mar 31. doi:10.3390/nu11040757
 36. Kuethe F, Krack A, Richartz BM, Figulla HR. Creatine supplementation improves muscle strength in patients with congestive heart failure. *Pharmazie.* 2006;61(3):218-222.
 37. Weber C, Noels H. Atherosclerosis: current pathogenesis and therapeutic options. *Nat Med.* 2011;17(11):1410-1422. Published 2011 Nov 7. doi:10.1038/nm.2538
 38. Obermayer G, Afonyushkin T, Binder CJ. Oxidized low-density lipoprotein in inflammation-driven thrombosis. *J Thromb Haemost.* 2018;16(3):418-428. doi:10.1111/jth.13925
 39. Badrnya S, Butler LM, Söderberg-Naucler C, Volf I, Assinger A. Platelets directly enhance neutrophil transmigration in response to oxidised low-density lipoprotein. *Thromb Haemost.* 2012;108(4):719-729. doi:10.1160/TH12-03-0206