



Date:-July 14, 2022

To Whom It May Concern

Subject: Testimony to Dr. Hamzah Hasyim's Voluntary Expertise Service

Dear Sir/Madam,

As the Editor- In-Chief of the Ethiopian Journal of Health Sciences, I certify that **Dr. Hamzah <u>Hasyim</u>** has been serving ETHIOPIAN JOURNAL OF HEALTH SCIENCES as a reviewer. Hence, we are writing him/her this letter of acknowledgement for the service s/he gave to the progress of our Journal. His/her expertise views on manuscripts s/he reviewed were instrumental for the betterment of the journal in particular and the scientific world in general. We really thank him/her for the contribution.

The Editorial Board of the Ethiopian Journal of health sciences looks forward for the continued contribution.

f.Abraham Haileamłak Sincerely Editor-in-Chief Prof. Abraham Haileamlak Editor-in-Chief, Ethiopian Journal of Health Sciences eihs@ju.edu.et



Invitation to Review for the Ethiopian Journal of Health Sciences

2 pesan

Ethiopian Journal of Health Sciences <onbehalfof@manuscriptcentral.com> Balas Ke: kasechab@gmail.com Kepada: hamzah_hasyim@fkm.unsri.ac.id

20 September 2021 20.40

20-Sep-2021

Dear Dr. Hasyim:

Manuscript ID EJHS-2021-0721.R1 entitled "Prevalence and Risk Factors of Isolated Systolic Hypertension among Diabetes Mellitus Subjects; a national cross-sectional study in Indonesia" has been RE-submitted to the Ethiopian Journal of Health Sciences. AUTHORS CLAIMED ACCOMMODATING YOUR PREVIOUS COMMENTS- SHOWN IN TRACK CHANGES.

THANKING YOU FOR THE PREVIOUS REVIEW, I ASK YOU TO CHECK IF YOUR MAJOR CONCERNS ARE ADDRESSED. The abstract appears at the end of this letter. Please let me know as soon as possible if you will be able to accept my invitation to review. If you are unable to review at this time, I would appreciate you recommending another expert reviewer. You may e-mail me with your reply or click the appropriate link at the bottom of the page to automatically register your reply with our online manuscript submission and review system.

Once you accept my invitation to review this manuscript, you will be notified via e-mail about how to access ScholarOne Manuscripts, our online manuscript submission and review system. You will then have access to the manuscript and reviewer instructions in your Reviewer Center.

I realize that our expert reviewers greatly contribute to the high standards of the Journal, and I thank you for your present and/or future participation.

Sincerely, Prof. Abraham Haileamlak Ethiopian Journal of Health Sciences Associate Editor kasechab@gmail.com

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MANUSCRIPT DETAILS

TITLE: Prevalence and Risk Factors of Isolated Systolic Hypertension among Diabetes Mellitus Subjects; a national cross-sectional study in Indonesia

ABSTRACT: BACKGROUND: Isolated systolic hypertension (ISH) is the most frequent hypertension. ISH reflects atherosclerosis. Studies reported hypertension prevalence among diabetes mellitus (DM); however, limited studies provided community prevalence. Present study aimed to explore ISH prevalence and its risk factors among DM in the community setting in Indonesia. METHODS: Cross-sectional study extracted data from basic health survey (Riset Kesehatan Dasar; RISKESDAS) conducted in 2018. DM subjects were defined based on fasting blood glucose level ≥ 126 mg/dL or 2 hours postprandial and random blood glucose level ≥ 200 mg/dL or previously had been diagnosed by a doctor, while ISH was determined based on systolic blood pressure ≥ 140 mmHg and diastolic blood pressure < 90 mmHg. We also observed the subject's characteristics, such as demography, lipid profile, and subject's compliance. Data were then analyzed using Chi-square and Binary logistic regression. RESULTS: Study involved 3,911 subjects, revealed overall ISH prevalence 17.5%. Older subjects (prevalence odds ratio (POR)=4.70; 95% CI: 3.553-6.222), high HDL cholesterol (POR=0.80; 95% CI: 0.653-0.972), and longer duration of DM (POR=1.82; 95% CI: 1.181-2.218), all together were associated with the ISH. Subjects with the older age category tend to get higher POR, i.e., 69.16, 57.19, 38.02, 20.88, and 10.13 for the age category of ≥75, 65-74, 55-64, 45-54, and 35-44 years old, respectively. CONCLUSION: Older DM subjects, low HDL, and longer duration of DM were associated with the ISH, suggesting that modification lipid profile, especially the HDL, is an important measure to delay ISH in the elderly and long-duration DM subjects 20-Sep-2021

Dear Dr. Hasyim:

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Sincerely, Prof. Abraham Haileamlak Ethiopian Journal of Health Sciences Associate Editor kasechab@gmail.com

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Reminder: Ethiopian Journal of Health Sciences

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23 September 2021 18.13

23-Sep-2021

Dear Dr. Hasyim:

Recently, I invited you to review Manuscript ID EJHS-2021-0721.R1, entitled "Prevalence and Risk Factors of Isolated Systolic Hypertension among Diabetes Mellitus Subjects; a national cross-sectional study in Indonesia." I have yet to hear from you about this.

This e-mail is simply a reminder to respond to the invitation to review. I appreciate your help in accomplishing our goal of having an expedited reviewing process.

You may e-mail me with your reply or click the appropriate link at the bottom of the page to automatically register your reply with our online manuscript submission and review system. If you are unable to review at this time, I would appreciate you recommending another expert reviewer.

Please do not hesitate to contact me if I can be of any assistance.

Sincerely, EJHS Admin Ethiopian Journal of Health Sciences Editorial Office yibeltal_siraneh@yahoo.com, tekle.ferede2014@gmail.com, enatfentasewmehone@gmail.com

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16-Oct-2021

Dear Dr. Hasyim:

Recently, you agreed to review Manuscript ID EJHS-2021-0721.R1, entitled "Prevalence and Risk Factors of Isolated Systolic Hypertension among Diabetes Mellitus Subjects; a national cross-sectional study in Indonesia." The manuscript is located in your Reviewer Center at https://mc.manuscriptcentral.com/ju-ejhs.

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Sincerely, Prof. Abraham Haileamlak Editor in Cheif, Ethiopian Journal of Health Sciences kasechab@gmail.com

Overall reflections and a summary of the research - for

Manuscript ID	EJHS-2021-0721
Full Title:	Prevalence of Isolated Systolic Hypertension among People with
	Diabetes in Indonesia
Manuscript Type:	Original Article

Reviewer

Dear authors,

Isolated systolic hypertension (ISH) is the most common form of atherosclerosis. Studies found hypertension in diabetics, but few saw it in the general population. The current study examined ISH prevalence and risk variables among DM in Indonesian communities. Manuscript ID EJHS-2021-0721.R1 attracted a reviewer.

However, there are some recommendations and questions that should be clarifying below.

The introduction contains the research background and research objectives. Its contents include

What is the research question (problem)?

What is a state-of-the-art study to solve the problem?

How to address the problem: Gap analysis (what solutions are offered) is different from previous research? On the other hand, what is the novelty of the article?

What are the advantages of the paper compared to other similar articles? The benefit of the article is following the formulation of the problem, specific research objectives, and research urgency.

Mistakes that often include: The formulation of the problem is weak, lacks direction, the research objectives and contributions are not clear, the researcher's power of expression about the situation is minimal, more "clippings" from readings that are considered relevant. The description is too long, not direct in the description of the problem is formulated not supported by the latest literature/information (state of the art) Unable to determine gap analysis and not associated with novelty.

The study's research must give the impression that there will be changes (implications) of the research results (for example, changes in policy/science and technology, not just new information).

The method section includes a research flow chart outlining what has been accomplished and accomplished during the proposed period. The research chart must be made in its entirety with clear stages, starting from the beginning of the process and outputs and the targeted achievement indicators. Additionally, it would be best to detail each proposer authorships responsibilities according to the stages of the proposed research in this section.

I suggest publishing the manuscript after a significant edit.

Best,

Reviewer

Confidential Comments to the EIC

Dear EIC,

This manuscript describes national secondary data aimed at determining ISH prevalence and its risk variables among people with diabetes in Indonesia. At the same time, the subject area is indeed attractive. I am afraid that this manuscript, at least in its current form, fails to meet publication standards in this journal. If the author decides to submit the manuscript, make necessary changes to this paper by completing the relevant recommendations of items in the article. After completing each offer, the reviewer can determine whether the authors' statement is appropriate. The author should read these recommendations for improving the study's reporting and respond to comments and suggestions on the page/line for each advice below. I recommend that the manuscript be published following a significant revision. Besides, please consider extensive editing of English grammar and usage by a native speaker directly.

Dear Authors,

Prevalence of Isolated Systolic Hypertension in Diabetes in Indonesia attracted a reviewer. The current study determines ISH prevalence and its risk variables among people with diabetes in Indonesia; it uses secondary data from the 2018 Basic Health Survey (RISKESDAS). This study revealed that there was a 17,5% ISH prevalence in 3,911 DM patients. The PORs for DM patients variated among aged groups. Besides, low HDL cholesterol and duration of DM were associated with the ISH. Modifying lipid profiles, particularly HDL cholesterol levels, may help delay ISH in elderly and long-term DM patients.

However, as with the abstract, the background section does not explain why this research was undertaken. The duration of DM should be specified again. In a result section, the reader cannot deduce what the duration of DM signifies, whether it is a long or short period (if there is a criterion, how many years is meant). Because if you look at the conclusion, what is written throughout DM's lengthy duration. It will be more apparent if you can determine the age of DM subjects and the duration of DM, the most influential age criteria, and the number of years of DM duration. As given, the methods lacked sufficient information. If the author decides to submit the manuscript, the authors should revise it to incorporate the pertinent advice made in the article.



Prevalence of Isolated Systolic Hypertension among People with Diabetes in Indonesia

Journal:	Ethiopian Journal of Health Sciences
Manuscript ID	EJHS-2021-0721
Manuscript Type:	Original Article
Keyword:	diabetes, isolated systolic hypertension, prevalence, risk factor, Indonesia



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2 3	1	Duranalance of Icoloted Systelie Hypertension among Deeple with
4	1	Prevalence of Isolated Systolic Hypertension among People with
5 6 7	2	Diabetes in Indonesia
8 9 10	3	ABSTRACT
11	4	BACKGROUND : The present study aimed to explore the prevalence of isolated systolic
12 13	5	hypertension (ISH) and its risk factors among diabetes mellitus (DM) subjects in the
14	6	community setting study in Indonesia.
15	7	METHODS: This cross-sectional study extracted secondary data from basic health survey
16	8	(Riset Kesehatan Dasar; RISKESDAS) conducted in 2018. DM subjects were defined based
17	9	on fasting blood glucose level \geq 126 mg/dL or 2 hours postprandial and random blood
18 19	10	glucose level \geq 200 mg/dL or previously had been diagnosed by a doctor, while ISH was
20	11	determined based on systolic blood pressure \geq 140 mmHg and diastolic blood pressure $<$ 90
21	12	mmHg. We also observed the subject's characteristics, such as demography, lipid profile, and
22	13	subject's compliance. Data were then analyzed using Chi-square and Binary logistic
23	14	regression.
24	15	RESULTS: Study involved 3,911 DM subjects, revealed the overall prevalence of ISH
25	16	17.5%. Age category of 35-44 years old (POR= 10.80; 95%CI: 2.595-44.957), 45-54 years
26 27	17	old (POR=22.81; 95%CI: 5.616-92.677), 55-64 years old (POR=46.12; 95% CI: 11.393-
27	18	186.720); 65-74 years old (POR= 81.82; 95% CI: 20.110-332.868); ≥75 years old (POR=
29	19	109.64; 95% CI: 26.373-455.789), low HDL cholesterol (POR= 0,80; 95% CI: 0.653-0.972);
30	20	duration of DM (POR= 1.73; 95% CI: 1.257-2.389) were associated with the ISH. The
31	21	prevalence of ISH among DM subjects was 17.5%.
32	22	CONCLUSION: Older DM subjects, low HDL cholesterol, and duration of DM were
33	23	associated with the ISH, suggesting that modification lipid profile, especially the HDL
34 25	24	cholesterol level, is an important measure to delay ISH in elderly and long-duration DM
35 36	25	subjects.
37	26	5
38	27	Keywords: diabetes, isolated systolic hypertension, prevalence, risk factor, Indonesia
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40	28	
41	20	
42 43	29	INTRODUCTION
43 44	29	INTRODUCTION
45	20	
46	30	International Diabetes Federation reports 463 million people globally, and 10.7
47	2.1	
48	31	million people in Indonesia living with diabetes placing Indonesia in the 7 th rank among
49 50	22	
50 51	32	countries for the number of adults with diabetes (1). Hypertension is the most frequent
52	22	
53	33	comorbidity for diabetes (2–4). Both hypertension and diabetes are the major risk factors for
54	2.4	
55	34	cardiovascular diseases due to the vascular mechanism (5). Hypertension is associated with
56	25	
57 58	35	30% of death and 25% of cardiovascular events among diabetes mellitus (DM) subjects (6).
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36 DM subjects with hypertension have seven times likely to experience end-stage renal disease
37 and 2-4 times to get myocardial infarction and stroke (6).

Hypertension occurred due to the vascular resistance and increase of fluid volume (7). Vascular resistance in DM subjects is related to vascular remodeling that caused arterial stiffness, while the increase of body fluid volume is associated with resistance-induced hyperinsulinemia and hyperglycemia (7). Isolated systolic hypertension (ISH) is the most frequent form of hypertension among the elderly (8) and the most frequent subtype of uncontrolled hypertension (9). People with diabetes have twice higher risk to get ISH than of those without diabetes (10). ISH reflects widespread atherosclerosis and increases stroke risk of 11% as well as an increase in all-cause mortality risk of 16% (10). Alongside the ISH, the pulse pressure (PP) and mean arterial pressure (MAP) is the independent predictors of cardiovascular events and all-cause mortality (10–13).

A previous study(14) based on the hospital-based data reported that the prevalence of ISH among DM subjects was 37.4%, and age was the most related factor. Another study reported that the prevalence of ISH among DM subjects was 27.6%(15); male, older age, obesity, and smoking were its risk factors (15,16). A study in Indonesia reported risk factors of hypertension among DM subjects such as age, mental health disorders, obesity, physical activities, duration of diabetes, dyslipidemia, and patient compliance (17). However, limited information regarding prevalence and risk factors of ISH among DM subjects based on population-based data. The present study aimed to explore the prevalence of ISH and its risk factors among DM subjects based on community setting study in Indonesia.

METHODS

Design and study population

59 This cross-sectional study extracted secondary data from the basic health survey
60 (Riset Kesehatan Dasar; RISKESDAS) 2018, the latest five-annual national scope cross-

sectional study, conducted by the National Institute of Research and Development, Ministry of Health, the Republic of Indonesia. The survey was conducted and delivered for households systematic-randomly selected from 514 districts/cities in 34 provinces. For each province and district/city, the number of proportional census blocks was determined systematically. Three hundred households or 30.000 census blocks were then determined to be involved in the survey. Of them, 94.2 % or 282,654 households completed the questionnaire consist of 1,017,290 individual subjects(18). The study population involved subjects with DM in the RISKESDAS 2018 data. Subjects with DM were determined by fasting blood glucose level \geq 126 mg/dL or 2 hours postprandial and random blood glucose level \geq 200 mg/dL or previously had been diagnosed by a doctor.

72 Data collection

Ethical clearance for the RISKESDAS 2018 study was obtained from the Ethics Committee, the National Institute of Health Research and Development (NIHRD), the Ministry of Health, Republic of Indonesia. Subject with ISH was defined as those with systolic blood pressure \geq 140 mmHg and diastolic blood pressure < 90 mmHg (19). We categorized the subject as non-hypertensive when meet the criteria of optimal (<120 mmHg and <80 mmHg), or normal (120 mmHg-129 mmHg and/or 80-84 mmHg), or high normal (130-139 mmHg and/or 85-89 mmHg). While non ISH hypertension were categorized for grade 1-3 hypertension; grade 1 hypertension: 140-159 mmHg and/or 90-99 mmHg; grade 2 hypertension: 160-179 mmHg and/or 100-109 mmHg; grade 3 hypertension: ≥ 180 mmHg and or ≥ 110 mmHg (19). Based on the measurement of blood pressure, we also calculated pulse pressure (PP) and mean arterial pressure (MAP). PP was calculated as a result of the formula (PP = systolic blood pressure (SBP) – diastolic blood pressure (DBP)), while the MAP was calculated as the formula of $(MAP = \frac{(SBP + 2 * DBP)}{3})$.

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2 3 4	86	Secondary data acquired from RISKESDAS 2018 were age, sex, urban-rural
5 6	87	residence status, marital status, educational level, employment status, total cholesterol level,
7 8 9 10 11	88	HDL-cholesterol level, triglycerides level, history of hypertension, smoking, physical activity
	89	status, alcohol consumption, body mass index (BMI), duration of DM, type of medication,
12 13	90	and medication compliance.
14 15	91	
16 17 18	92	Statistical analysis
19 20	93	Characteristics of the subjects were presented as proportions since they are categorical
21 22	94	type of data. The association between ISH status were analyzed using the Chi-square test.
23 24 25	95	The p-values <0.05 were considered statistically significant. Parameters that had p-value
26 27	96	< 0.25 were then involved in the multivariate analysis using binary logistic regression. All
28 29 30 31 32	97	statistical analyses were performed using the Statistical Package for the Social Sciences
	98	(SPSS) software (version 23.0 for Windows, IBM SPSS Inc., Chicago, IL).
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100	RESULTS
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5 5 7	101	Data extracted from the RISKESDAS 2018 consisted of 3,911 DM subjects that were
3 9	102	included in the final analysis. Study population consisted of 1,289 (33%) male and 2,622
10 11	103	(67%) female. The most frequent age category was 45-54 years old (29.3 %). More than half
12 13 14	104	of the study population was live in the urban area with a low level of education and were
14 15 16	105	employed in various sectors. Most of the study population had lower total cholesterol levels,
17 18	106	lower high-density lipoprotein (HDL) cholesterol level, higher low-density lipoprotein (LDL)
19 20	107	cholesterol level, and lower triglyceride levels. Most of them had a history of hypertension,
21 22 23	108	non-smoking, active physical activity, and fair medication compliance. The detailed subjects'
24 25	109	characteristics are presented in Table 1.
26 27	110	Based on the result of blood pressure measurement, a total of 1,903 (48.7%) subjects
28 29 30	111	were categorized as normal, while the rest of 2,008 (51.3%) were categorized as
30 31 32	112	hypertension, whether grade 1,2,3 or ISH. ISH was the most frequent form of hypertension in
33 34	113	the study population (Fig. 1). The highest mean MAP was in non-ISH hypertension group,
35 36	114	while the highest mean PP was in the ISH group (Fig. 2)
37 38 39	115	Of the total 3,911 study population of DM subjects, 685 subjects were identified as
40 41	116	ISH, indicated that the prevalence of ISH was 17.5%. Table 2 identified variables associated
42 43	117	with the ISH. Older subjects, low educational level, high total cholesterol level, low HDL
44 45 46	118	level, active physical activity, obese, duration of DM, and type of medication were associated
47 48	119	with the ISH status among DM subjects. These variables, combined with other variables that
49 50	120	$p \le 0.25$, i.e., employment status, LDL level, triglyceride, history of hypertension, alcohol
51 52 53	121	consumption, and medication compliance, continued to be involved in the Binary logistic
54 55	122	regression, and the final model of regression showed in Table 3.
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We found that older subjects, low HDL cholesterol (prevalence odds ratio; POR=0.80; 95% CI: 0.653-0.972), and duration of DM (POR=1.73; 95% CI: 1.257-2.389), all together were associated with the ISH. Subjects with the older age category tend to get higher POR, i.e., 10.80, 22.81, 46.81, 81.82, and 109.64 for the age category of 35-44, 45-54, 55-64, 65-74, and \geq 75 years old, respectively (Table 3). DISCUSSION The present study reported a national scope, population-based cross-sectional study that involved 3,911 DM subjects in Indonesia. Of them, 685 experienced ISH, indicated that the prevalence of ISH among DM subjects in this population study was 17.5%. The prevalence of ISH among DM subjects in Indonesia based on this study population was lower than the prevalence of ISH in Ghana, i.e., 37.4% based on the out-patient diabetes clinic in the teaching hospital of Tamale (14). Similarly, as a hospital-based study, a study in Jimma, Ethiopia, found that the prevalence of ISH among DM patients was 27.6% (15). A

population-based study in district Chiem Hoa, Vietnam, observed the general elderly

population aged >60 years old found a prevalence of 22.9 % (20). Another national

population-based study in the USA revealed that the prevalence of ISH in the general

population was 9.4% (21). A similar result as the current study reported by a hospital-based

cohort study in Italy that observed ISH among type 2 DM and found a prevalence of 20.3 %

7 143 (22).

The present study also added evidence that DM subjects with older age, i.e., ≥ 75 years old, was the most influential risk factor of ISH. This finding is in accordance with the previous cohort study in Italy which concluded that the mean age of type 2 DM subjects experienced ISH was 74.3 years old (22). On the other hand, a study in Ethiopia reported that DM subjects aged ≥ 60 years old were the protective factor for ISH, while the age category of Page 7 of 21

47-55 years old was the risk factor with the highest OR, i.e., 2.63 (15). Similarly, the study in Ghana showed the most frequent ISH in the DM subjects aged 50-69 years old (14). Regarding the study population, a study in Italy and Ethiopia comparing ISH to non-ISH, including other forms of hypertension, while a study in Ghana comparing ISH to normal subjects (14,15,22). The previous review concluded that ISH affects 10-20% of the elderly, systolic blood pressure increase with age, while diastolic blood pressure rises until the age of 50 years and then decreases after that (23). Increase in blood pressure with age is mostly associated with arterial stiffness. Degenerative processes such as calcification and alteration of arteriosclerotic structure play a pivotal role in the formation of large artery stiffness as well as in the small vessels. Small vessel stiffness leads to the condition of peripheral vascular resistance that influences the increase of both systolic and diastolic blood pressure. The existence of large artery stiffness increases systolic blood pressure and, conversely, decreases diastolic blood pressure. The acceleration of large artery stiffness after 50 years old lead to the steeper increase of systolic blood pressure that caused the ISH condition (24). Lipid profile leads to the process of endothelial dysfunction that affects blood pressure. HDL cholesterol tends to have inversely associated with hypertension, while non-HDL cholesterol has a positive association (25). The present study found that HDL was inversely associated with the ISH, while in the bivariate analysis, total cholesterol showed a positive association with ISH. High HDL level, i.e., \geq 40 mg/dL, was concluded as the protective factor for ISH in this study. This finding was in accordance with the Physician Health Study that reported the highest quartile of HDL level, i.e., >53 mg/dL had the lowest adjusted-RR (0.68) compared to the other quartile (26). A study in China also reported that HDL level was inversely related to the blood pressure as well as brachial-ankle pulse-wave velocity, a marker of arterial stiffness development (25). The atherosclerotic formation structure of the vessels also influenced by the oxidative activity of LDL cholesterol that is

Page 8 of 21

1 2		
3 4	174	also inhibited by HDL (27,28). However, a previous study in Japan reported a positive
5 6	175	correlation between HDL and hypertension in apparently healthy people (29). Another study
7 8 9	176	revealed that a positive association between HDL and hypertension occurred in the subjects
9 10 11	177	with high-level circulation CD34-positive cells, a bone marrow-derived endothelial
12 13	178	progenitor. The level of circulating CD-34 increases as a response of the endothelial damage,
14 15	179	therefore masking the role of HDL as endothelial protective in healthy subjects (30).
16 17	180	The current study also found that duration of DM, i.e., more than five years, was
18 19 20	181	significantly associated with ISH, PR=1.73 (95% CI: 1.257-2.389). This finding adds the
21 22	182	evidence that previously reported elsewhere that revealed diabetes duration and insulin
23 24	183	treatment status were the independent predictor of ISH (31). The progression and duration of
25 26 27	184	diabetes increase complications. Duration of diabetes is associated with arterial stiffness,
28 29	185	while arterial stiffness plays a pivotal role in ISH (31). The gradation of DM duration as a
30 31	186	dose-response relationship with hypertension was also described in the previous study (32).
32 33	187	These findings strengthen the hypothesis that diabetes precedes arterial stiffness that caused
34 35 36	188	ISH; however, another study found that onset on diabetes and brachial-ankle pulse wave
37 38	189	velocity occurred simultaneously after a longitudinal observation indicates conversely
39 40	190	condition (33). Indeed, there are roles of multifactor that contributed to the arterial stiffness
41 42 43	191	as a major cause of ISH. Arterial stiffness is a result of degenerative processes in the
43 44 45	192	extracellular matrix of elastic arteries caused by aging and many other risk factors (34).
46 47	193	The final model of Binary logistic regression in this study involved a history of
48 49	194	hypertension; however, the p-value did not meet to be considered significant. The previous
50 51 52	195	history of hypertension describes the condition of individuals who tend to have a genetic
53 54	196	predisposition (35). Hypertension is the form of the complex trait that involved multiple
55 56	197	organs and pathways (35,36). Comprehensive understanding of genomics, epigenomics,
57 58	198	metabolomics, proteomics, and transcriptomics of blood pressure plays a pivotal role in the
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99 context of the previous history of hypertension (35). Further study that observed the detailed 00 genetic role should be conducted to elucidate the novel hypertension pathophysiology and 01 dissect and characterize the disorder's mechanism.

02 It is well established that obesity is associated with ISH (37–39). Obesity affects the 03 process of inflammation, cell adhesion, and coagulation that impact in the arterial stiffness 04 (38,40). Obesity is also related to the insulin and leptin resistance that contributes to sodium 205 retention with concomitant cardiac output (39). However, in this study, BMI did not 06 significantly associate with ISH, although involved in the final model. It must be considered 207 that the role of BMI measurement alone is inadequate for accurately predict the disease 08 progression in DM subjects (41). Other parameters such as body composition, total adipose .09 mass, visceral adiposity-accumulation of intra-abdominal fat, and muscle mass should be 210 analyzed to describe the current condition of DM subjects (41–43).

211 The prevalence of ISH among Indonesian DM subjects in the present study was 212 17.5%. Older DM subjects, low HDL cholesterol, and duration of DM were associated with 213 the ISH, suggesting that modify lipid profile, especially HDL cholesterol level, is a needful 214 measure to delay ISH in older and duration DM subjects.

217

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225	curre	nt study. The protocol and reports of the RISKESDAS is published on	
226	<u>https</u>	://www.litbang.kemkes.go.id/laporan-riset-kesehatan-dasar-riskesdas//	
227			
228			
229	References		
230	[1]	International Diabetes Federation, IDF Diabetes atlas 9th edition, Brussel, Belgium,	
231		2019. https://www.diabetesatlas.org.	
232	[2]	B. Tesfaye, A. Alebel, A. Gebrie, A. Zegeye, C. Tesema Leshargie, A. Ferede, H.	
233		Abera, K. Alam, Diabetes Mellitus and Its Association with Hypertension in Ethiopia:	
234		A Systematic Review and Meta-Analysis., Diabetes Res. Clin. Pract. 156 (2019)	
235		107838. https://doi.org/10.1016/j.diabres.2019.107838.	
236	[3]	A.D. Colosia, R. Palencia, S. Khan, Prevalence of hypertension and obesity in patients	
237		with type 2 diabetes mellitus in observational studies: a systematic literature review.,	
238		diabetes. Metab. Syndr. Obes. 6 (2013) 327–338.	
239		https://doi.org/10.2147/DMSO.S51325.	
240	[4]	C.T. Nguyen, N.M. Pham, A.H. Lee, C.W. Binns, Prevalence of and Risk Factors for	
241		Type 2 Diabetes Mellitus in Vietnam: A Systematic Review., Asia-Pacific J. Public	
242		Heal. 27 (2015) 588–600. https://doi.org/10.1177/1010539515595860.	
243	[5]	J.R. Petrie, T.J. Guzik, R.M. Touyz, Diabetes, Hypertension, and Cardiovascular	
244		Disease: Clinical Insights and Vascular Mechanisms., Can. J. Cardiol. 34 (2018) 575-	
245		584. https://doi.org/10.1016/j.cjca.2017.12.005.	
246	[6]	G. Chen, F.A. McAlister, R.L. Walker, B.R. Hemmelgarn, N.R.C. Campbell,	
247		Cardiovascular outcomes in framingham participants with diabetes: The importance of	
248		blood pressure, hypertension. 57 (2011) 891–897.	
249		https://doi.org/10.1161/HYPERTENSIONAHA.110.162446.	
250	[7]	M. Ohishi, Hypertension with diabetes mellitus: physiology and pathology.,	
251		Hypertens. Res. 41 (2018) 389–393. https://doi.org/10.1038/s41440-018-0034-4.	
252	[8]	C. Bavishi, S. Goel, F.H. Messerli, Isolated Systolic Hypertension: An Update After	
253		SPRINT., Am. J. Med. 129 (2016) 1251–1258.	
254		https://doi.org/10.1016/j.amjmed.2016.08.032.	
255	[9]	S.S. Franklin, P. Lapuerta, G.J. L'Italien, N.D. Wong, M.J. Jacobs, Predominance of	
256		Isolated Systolic Hypertension Among Middle-Aged and Elderly US Hypertensives,	
	226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255	2226https22272282228 Refa 229 Refa 230[1]231[2]233[2]233[2]234[3]235[3]236[3]237[3]238[4]240[4]241[5]240[6]241[5]243[5]244[6]245[6]247[4]245[6]247[4]250[7]251[8]253[9]	

2			
3 4	257		Hypertension. 37 (2012) 869-874. https://doi.org/10.1161/01.hyp.37.3.869.
5	258	[10]	I. Os, H. Gudmundsdottir, S.E. Kjeldsen, S. Oparil, Treatment of isolated systolic
6 7	259		hypertension in diabetes mellitus type 2., diabetes. Obes. Metab. 8 (2006) 381-387.
8 9	260		https://doi.org/10.1111/j.1463-1326.2005.00523.x.
10 11	261	[11]	N. Madan, A.K. Lee, K. Matsushita, R.C. Hoogeveen, C.M. Ballantyne, E. Selvin,
12	262		J.W. McEvoy, Relation of Isolated Systolic Hypertension and Pulse Pressure to High-
13 14	263		Sensitivity Cardiac Troponin-T and N-Terminal pro-B-Type Natriuretic Peptide in
15 16	264		Older Adults (from the Atherosclerosis Risk in Communities Study)., Am. J. Cardiol.
17	265		124 (2019) 245-252. https://doi.org/10.1016/j.amjcard.2019.04.030.
18 19	266	[12]	S. Selvaraj, P.G. Steg, Y. Elbez, E. Sorbets, L.J. Feldman, K.A. Eagle, E.M. Ohman, J.
20 21	267		Blacher, D.L. Bhatt, Pulse Pressure and Risk for Cardiovascular Events in Patients
22 23	268		With Atherothrombosis: From the REACH Registry., J. Am. Coll. Cardiol. 67 (2016)
24	269		392-403. https://doi.org/10.1016/j.jacc.2015.10.084.
25 26	270	[13]	G.J. Winston, W. Palmas, J. Lima, J.F. Polak, A.G. Bertoni, G. Burke, J. Eng, R.
27 28	271		Gottesman, S. Shea, Pulse pressure and subclinical cardiovascular disease in the multi-
29	272		ethnic study of atherosclerosis., Am. J. Hypertens. 26 (2013) 636–642.
30 31 32 33	273		https://doi.org/10.1093/ajh/hps092.
	274	[14]	R.K.D. Ephraim, A.R. Saasi, E.O. Anto, P. Adoba, Determinants of isolated systolic
34 35	275		hypertension among diabetic patients visiting the diabetic clinic at the Tamale
36	276		Teaching Hospital, Northern Ghana., Afr. Health Sci. 16 (2016) 1151–1156.
37 38	277		https://doi.org/10.4314/ahs.v16i4.33.
39 40	278	[15]	B. Dagnew, Y. Yeshaw, Predictors of isolated systolic hypertension among type 2
41 42	279		diabetes mellitus patients in Jimma University Specialized Hospital, Southwest
43	280		Ethiopia, BMC Res. Notes. 12 (2019) 1-7. https://doi.org/10.1186/s13104-019-4550-
44 45	281		3.
46 47	282	[16]	R. Grebla, C. Rodriguez, L. Borrell, T. Pickering, Prevalence and determinants of
48	283		isolated systolic hypertension among young adults., J. Am. Soc. Hypertens. 28 (2010)
49 50	284		15-23. https://doi.org/10.1097/HJH.0b013e328331b7ff.Prevalence.
51 52	285	[17]	M. Sihombing, Faktor yang Berhubungan dengan Hipertensi pada Penduduk Indonesia
53 54	286		yang Menderita Diabetes Melitus (Data Riskesdas 2013), Bul. Penelit. Kesehat. 45
55	287		(2017) 53-64. https://doi.org/10.22435/bpk.v45i1.5730.53-64.
56 57	288	[18]	Badan Penelitian dan Pengembangan Kesehatan, Laporan Nasional Riset Kesehatan
58 59	289		Dasar: RISKESDAS (Indonesia Basic Health Survey) tahun 2018, 2018.
60	290		http://labmandat.litbang.kemkes.go.id/images/download/laporan/RKD/2018/Laporan_

3	291		Nasional_RKD2018_FINAL.pdf.
4 5	292	[19]	A.F. Members, G. Mancia, R. Fagard, K. Narkiewicz, J. Redon, A. Zanchetti, M.
6 7	293		Böhm, T. Christiaens, R. Cifkova, G. De Backer, A. Dominiczak, M. Galderisi, D.E.
8 9	294		Grobbee, T. Jaarsma, P. Kirchhof, S.E. Kjeldsen, S. Laurent, A.J. Manolis, P.M.
10	295		Nilsson, L.M. Ruilope, R.E. Schmieder, P.A. Sirnes, P. Sleight, M. Viigimaa, B.
11 12	296		Waeber, F. Zannad, E.S.H.S. Council, J. Redon, A. Dominiczak, K. Narkiewicz, P.M.
13 14	297		Nilsson, M. Burnier, M. Viigimaa, E. Ambrosioni, M. Caufield, A. Coca, M.H. Olsen,
15 16	298		R.E. Schmieder, C. Tsioufis, P. van de Borne, E.S.C.C. for P.G. (CPG), J.L.
17	299		Zamorano, S. Achenbach, H. Baumgartner, J.J. Bax, H. Bueno, V. Dean, C. Deaton, C.
18 19	300		Erol, R. Fagard, R. Ferrari, D. Hasdai, A.W. Hoes, P. Kirchhof, J. Knuuti, P. Kolh, P.
20 21	301		Lancellotti, A. Linhart, P. Nihoyannopoulos, M.F. Piepoli, P. Ponikowski, P.A. Sirnes,
22 23	302		J.L. Tamargo, M. Tendera, A. Torbicki, W. Wijns, S. Windecker, D. Reviewers, D.L.
24	303		Clement, A. Coca, T.C. Gillebert, M. Tendera, E.A. Rosei, E. Ambrosioni, S.D.
25 26	304		Anker, J. Bauersachs, J.B. Hitij, M. Caulfield, M. De Buyzere, S. De Geest, G.A.
27 28	305		Derumeaux, S. Erdine, C. Farsang, C. Funck-Brentano, V. Gerc, G. Germano, S.
29 30	306		Gielen, H. Haller, A.W. Hoes, J. Jordan, T. Kahan, M. Komajda, D. Lovic, H.
31	307		Mahrholdt, M.H. Olsen, J. Ostergren, G. Parati, J. Perk, J. Polonia, B.A. Popescu, Ž.
32 33	308		Reiner, L. Rydén, Y. Sirenko, A. Stanton, H. Struijker-Boudier, C. Tsioufis, P. van de
34 35	309		Borne, C. Vlachopoulos, M. Volpe, D.A. Wood, 2013 ESH/ESC Guidelines for the
36	310		management of arterial hypertension: The Task Force for the management of arterial
37 38	311		hypertension of the European Society of Hypertension (ESH) and of the European
39 40	312		Society of Cardiology (ESC), Eur. Heart J. 34 (2013) 2159–2219.
41 42	313		https://doi.org/10.1093/eurheartj/eht151.
43	314	[20]	N. Bui Van, L. Vo Hoang, T. Bui Van, H.N.S. Anh, H.T. Minh, K. Do Nam, T.N. Tri,
44 45	315		P.L. Show, V.T. Nga, D.B. Thimiri Govinda Raj, DT. Chu, Prevalence and Risk
46 47	316		Factors of Hypertension in the Vietnamese Elderly., High Blood Press. Cardiovasc.
48 49	317		Prev. Off. J. Ital. Soc. Hypertens. 26 (2019) 239-246. https://doi.org/10.1007/s40292-
50	318		019-00314-8.
51 52 53 54 55	319	[21]	X. Liu, C.J. Rodriguez, K. Wang, Prevalence and trends of isolated systolic
	320		hypertension among untreated adults in the United States., J. Am. Soc. Hypertens. 9
	321		(2015) 197-205. https://doi.org/10.1016/j.jash.2015.01.002.
56 57	322	[22]	S. Bo, G. Ciccone, G. Grassi, R. Gancia, R. Rosato, F. Merletti, G. Pagano, Isolated
58 59	323		systolic hypertension in a cohort of type 2 diabetic patients., Nutr. Metab. Cardiovasc.
60	324		Dis. 14 (2004) 157–161. https://doi.org/10.1016/s0939-4753(04)80036-x.

1			
2 3	325	[23]	L. Thijs, E. Den Hond, T. Nawrot, J.A. Staessen, Prevalence, pathophysiology and
4 5	326		treatment of isolated systolic hypertension in the elderly, Expert Rev. Cardiovasc.
6 7	327		Ther. 2 (2004) 761–769. https://doi.org/10.1586/14779072.2.5.761.
8 9	328	[24]	E. Pinto, Blood pressure and ageing, Postgrad. Med. J. 83 (2007) 109-114.
10	329		https://doi.org/10.1136/pgmj.2006.048371.
11 12	330	[25]	B. Zhan, X. Huang, J. Wang, X. Qin, J. Zhang, J. Cao, Y. Song, L. Liu, P. Li, R. Yang,
13 14	331		Y. Wu, Q. Wu, Y. Zhang, J. Li, Y. Huo, B. Wang, X. Xu, H. Bao, X. Cheng,
15 16	332		Association Between Lipid Profiles and Arterial Stiffness in Chinese Patients With
17	333		Hypertension: Insights From the CSPPT, Angiology. 70 (2019) 515–522.
18 19	334		https://doi.org/10.1177/0003319718823341.
20 21	335	[26]	HR O., SH D., M. Jing, BJ E., SM J., MG J., Dyslipidemia and the Risk of Incident
22 23	336		Hypertension in Men, Hypertension. 47 (2006) 45–50.
24	337		https://doi.org/10.1161/01.HYP.0000196306.42418.0e.
25 26	338	[27]	F. Brites, M. Martin, I. Guillas, A. Kontush, Antioxidative activity of high-density
27 28	339		lipoprotein (HDL): Mechanistic insights into potential clinical benefit., BBA Clin. 8
29	340		(2017) 66–77. https://doi.org/10.1016/j.bbacli.2017.07.002.
30 31	341	[28]	R. Puri, S.E. Nissen, M. Shao, M.B. Elshazly, Y. Kataoka, S.R. Kapadia, E.M. Tuzcu,
32 33	342		S.J. Nicholls, Non-HDL Cholesterol and Triglycerides: Implications for Coronary
34 35	343		Atheroma Progression and Clinical Events, Arterioscler. Thromb. Vasc. Biol. 36
36	344		(2016) 2220-2228. https://doi.org/10.1161/ATVBAHA.116.307601.
37 38	345	[29]	E. Oda, R. Kawai, High-density lipoprotein cholesterol is positively associated with
39 40	346		hypertension in apparently healthy Japanese men and women, Br. J. Biomed. Sci. 68
41 42	347		(2011) 29-33. https://doi.org/10.1080/09674845.2011.11732838.
43	348	[30]	Y. Shimizu, S. Sato, J. Koyamatsu, H. Yamanashi, M. Nagayoshi, K. Kadota, SY.
44 45	349		Kawashiri, T. Maeda, Association between high-density lipoprotein-cholesterol and
46 47	350		hypertension in relation to circulating CD34-positive cell levels, J. Physiol. Anthropol.
48 49	351		36 (2017) 1-7. https://doi.org/10.1186/s40101-017-0143-9.
50	352	[31]	H. Smulyan, A. Lieber, M.E. Safar, Hypertension, Diabetes Type II, and Their
51 52	353		Association: Role of Arterial Stiffness., Am. J. Hypertens. 29 (2016) 5-13.
53 54	354		https://doi.org/10.1093/ajh/hpv107.
55	355	[32]	M. Berraho, Y. El Achhab, A. Benslimane, K. El Rhazi, M. Chikri, C. Nejjari,
56 57	356		Hypertension and type 2 diabetes: a cross-sectional study in Morocco (EPIDIAM
58 59	357		Study)., Pan Afr. Med. J. 11 (2012) 52.
60	358	[33]	Y. Zhang, P. He, Y. Li, Y. Zhang, J. Li, M. Liang, G. Wang, G. Tang, Y. Song, B.

1			
2 3	359		Wang, C. Liu, L. Liu, Y. Cui, X. Wang, Y. Huo, X. Xu, X. Qin, Positive association
4 5 7 8 9 10 11 12 13 14	360		between baseline brachial-ankle pulse wave velocity and the risk of new-onset
	361		diabetes in hypertensive patients, Cardiovasc. Diabetol. 18 (2019) 111.
	362		https://doi.org/10.1186/s12933-019-0915-0.
	363	[34]	C. Palombo, M. Kozakova, Arterial stiffness, atherosclerosis and cardiovascular risk:
	364		Pathophysiologic mechanisms and emerging clinical indications., Vascul. Pharmacol.
	365		77 (2016) 1-7. https://doi.org/10.1016/j.vph.2015.11.083.
15 16	366	[35]	D.K. Arnett, S.A. Claas, Omics of Blood Pressure and Hypertension., Circ. Res. 122
17	367		(2018) 1409-1419. https://doi.org/10.1161/CIRCRESAHA.118.311342.
18 19	368	[36]	M.L. Lindsey, M. Mayr, A. V Gomes, C. Delles, D.K. Arrell, A.M. Murphy, R.A.
20 21	369		Lange, C.E. Costello, YF. Jin, D.T. Laskowitz, F. Sam, A. Terzic, J. Van Eyk, P.R.
22 23	370		Srinivas, Transformative Impact of Proteomics on Cardiovascular Health and Disease:
24 25	371		A Scientific Statement From the American Heart Association., Circulation. 132
26	372		(2015) 852-872. https://doi.org/10.1161/CIR.000000000000226.
27 28 29 30 31 32 33 34 35	373	[37]	S. Asgari, D. Khalili, Y. Mehrabi, S. Kazempour-Ardebili, F. Azizi, F. Hadaegh,
	374		Incidence and risk factors of isolated systolic and diastolic hypertension: a 10 year
	375		follow-up of the Tehran Lipids and Glucose Study, Blood Press. 25 (2016) 177–183.
	376		https://doi.org/10.3109/08037051.2015.1116221.
	377	[38]	R.P. Wildman, R.H. Mackey, A. Bostom, T. Thompson, K. Sutton-Tyrrell, Measures
36 37	378		of obesity are associated with vascular stiffness in young and older adults,
38	379		hypertension. 42 (2003) 468–473.
39 40	380		https://doi.org/10.1161/01.HYP.0000090360.78539.CD.
41 42	381	[39]	R. and E.R. Zhang, Obesity hypertension: The effects on cardiovascular and renal
43 44	382		systems, Am. J. Hypertens. 13 (2000) 1308–1314.
45	383	[40]	C. Delles, E. Carrick, D. Graham, S.A. Nicklin, Utilizing proteomics to understand and
46 47	384		define hypertension: where are we and where do we go?, Expert Rev. Proteomics. 15
48 49	385		(2018) 581-592. https://doi.org/10.1080/14789450.2018.1493927.
50 51	386	[41]	M. Murea, L. Lenchik, T.C. Register, G.B. Russell, J. Xu, S.C. Smith, D.W. Bowden,
52	387		J. Divers, B.I. Freedman, Psoas and paraspinous muscle index as a predictor of
53 54	388		mortality in African American men with type 2 diabetes mellitus., J. Diabetes
55 56	389		Complications. 32 (2018) 558–564. https://doi.org/10.1016/j.jdiacomp.2018.03.004.
57	390	[42]	E.S.A. Owusu, M. Samanta, J.E. Shaw, A. Majeed, K. Khunti, S.K. Paul, Weight loss
58 59	391		and mortality risk in patients with different adiposity at diagnosis of type 2 diabetes: a
60	392		longitudinal cohort study., Nutr. Diabetes. 8 (2018) 37.

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24	 393 394 395 396 397 398 399 	[43]	https://doi.org/10.1038/s41387-018-0042-0. S. Gullaksen, K.L. Funck, E. Laugesen, T.K. Hansen, D. Dey, P.L. Poulsen, Volumes of coronary plaque disease in relation to body mass index, waist circumference, truncal fat mass and epicardial adipose tissue in patients with type 2 diabetes mellitus and controls., Diabetes Vasc. Dis. Res. 16 (2019) 328–336. https://doi.org/10.1177/1479164119825761.
25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60			

Variable	n	%
Age category (years old)		
≥ 75 × 5 × 5	167	4.3
65-74	502	12.8
55-64	1098	28.1
45-54	1146	29.3
35-44	668	17.1
15-34	330	8.4
Sex	220	0.1
Female	2622	67
Male	1289	33
Residence status	1207	55
Urban	2057	52.6
Rural	1854	47.4
Marital status	10.04	47.4
Un-married	147	3.8
Married	3764	5.8 96.2
Educational level	5/04	90.2
	3006	76.9
Primary high school	3008 905	23.1
Secondary high school or above	903	23.1
Employment status	1(20	41.0
Un-employed	1639	41.9
Employed	2272	58.1
Cotal Cholesterol level	1020	
$\geq 200 \text{ mg/dL}$	1832	46.8
<200 mg/dL	2079	53.2
IDL level	11.40	• • •
$\geq 40 \text{ mg/dL}$	1140	29.1
<40 mg/dL	2771	70.9
DL level		
$\geq 100 \text{ mg/dL}$	3296	84.3
<100 mg/dL	615	15.7
riglyceride		
$\geq 150 \text{ mg/dL}$	1612	41.2
<150 mg/dL	2299	58.8
listory of hypertension		
Yes	1350	34.5
No	2561	65.5
Smoking		
Yes	1002	25.6
No	2909	74.4
hysical activity status		
Sedentary	605	15.5
Active	3306	84.5
Alcohol consumption		
Yes	37	0.9
No	3874	99.1
BMI		· · · · ·
Obese	1262	32.3
	1202	52.5

2			
3	Overweight	603	15.4
4	Normal	1767	45.2
5 6	Underweight	164	4.2
7	Severe Underweight	115	2.9
8	Duration of DM		
9	>5 years	1867	47.7
10	<5 years	2044	52.3
11	Type of DM medication		
12 13	No medication	830	21.2
13 14	OHD+insulin	828	21.2
15	Insulin	770	19.7
16	OHD	1483	37.9
17	Medication compliance		
18	No	1625	41.5
19 20	Yes	2286	58.5
20	401 BMI: body mass index: HDI = high-density line	protein: I DI =low-density linon	rotein

BMI: body mass index; HDL=high-density lipoprotein; LDL=low-density lipoprotein

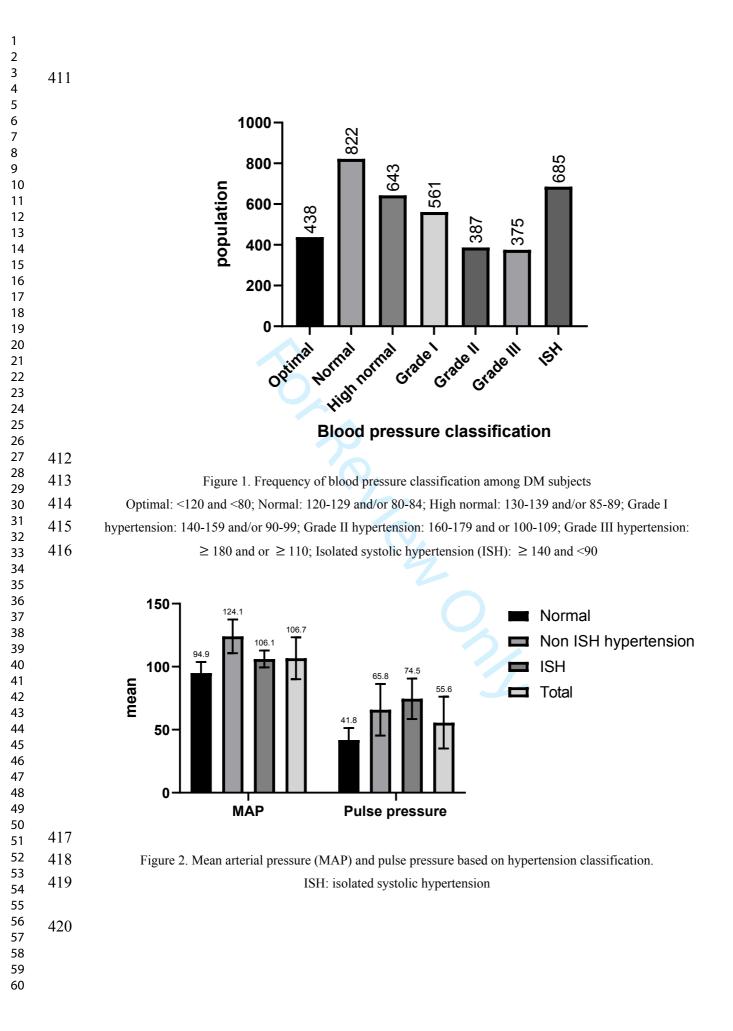
https://mc.manuscriptcentral.com/ju-ejhs

403 Table 2. Subjects' characteristics based on ISH status

_		ISH	_	a.	_	95	%CI
Parameter	Yes	No	Total	_ p*	POR	Lower	Upe
	n(%)	n(%)	n(%)			201101	0
Age (years old)	70 (41 0)	07 (50 1)	1.67	0.001	(0.1.(17 170	070 5
≥75	70 (41.9)	97 (58.1)	167	0.001	69.16	17.172	278.50
65-74	174 (34.7)	328 (65.3)	502	0.001	57.19	14.289	228.9
55-64	253 (23)	845 (77)	1098	0.001	38.02	9.508	152.02
45-54	145 (12.7)	1001 (87.3)	1146	0.001	20.88	5.200	83.82
35-44	41 (6.1)	627 (93.9)	668	0.001	10.13	2.465	41.61
15-34	2 (0.6)	328 (99.4)	330	Reference	1		
Sex							
Female	451 (17.2)	2171 (82.8)	2622	0.489	0.95	0.821	1.09
Male	234 (18.2)	1055 (81.8)	1289				
Residence status							
Urban	370 (18)	1687 (82)	2057	0.437	1.06	0.924	1.214
Rural	315 (17)	1539 (83)	1854				
Marital status							
Un-married	23 (15.6)	124 (84.4)	147	0.619	0.89	0.607	1.303
Married	662 (17.6)	3102 (82.4)	3764				
Education level							
Low	553 (18.4)	2453 (81.6)	3006	0.009	1.26	1.059	1.502
High	132 (14.6)	773 (85.4)	905				
Employment status		4.0					
Un-employed	308 (18.8)	1331 (81.2)	1639	0.081	1.13	0.988	1.298
Employed	377 (16.6)	1895 (83.4)	2272				
Total Cholesterol level	~ /						
≥200 mg/dL	345 (18.8)	1487 (81.2)	1832	0.046	1.15	1.005	1.319
<200 mg/dL	340 (16.4)	1739 (83.6)	2079				
HDL level	~ /	× ,					
$\geq 40 \text{ mg/dL}$	169 (14.8)	971 (85.2)	1140	0.005	0.80	0.679	0.934
<40 mg/dL	516 (18.6)	2255 (81.4)	2771				
LDL level							
$\geq 100 \text{ mg/dL}$	591 (17.9)	2705 (2.1)	3296	0.127	1.17	0.961	1.433
<100 mg/dL	94 (15.3)	521 (84.7)	615	,			
Triglyceride	- (10.0)						
$\geq 150 \text{ mg/dL}$	261 (16.2)	1351 (83.8)	1612	0.075	0.88	0.763	1.010
<150 mg/dL	424 (18.4)	1875 (81.6)	2299	0.070	0.00	0.,00	1.010
History of hypertension	(10.1)	1070 (01.0)	//				
Yes	250 (18.5)	1100 (81.5)	1350	0.248	1.09	0.947	1.25
No	435 (17)	2126 (83)	2561	0.210	1.07	0.717	1.20
Smoking		_ 1 _ 0 (05)					
Yes	182 (18.2)	820 (81.8)	1002	0.563	1.05	0.901	1.225
No	503 (17.3)	2406 (82.7)	2909	0.000	1.00	0.701	1.22.
Physical activity status	505 (17.5)	2700 (02.7)	2707				
Sedentary	131 (21.7)	474 (78.3)	605	0.004	1.29	1.091	1.53
Active	554 (16.8)	2752 (83.2)	3306	0.004	1.47	1.071	1.55
	557 (10.0)	2152 (05.2)	5500				
Alcohol consumption Yes	2 (5.4)	35 (94.6)	37	0.084	0.31	0.080	1.182

1									
2									
3		BMI							
4 5		Obese	165 (13.1)	1097 (86.9)	1262	0.003	0.557	0.389	0.798
6		Overweight	91 (15.1)	512 (84.9)	603	0.037	0.643	0.439	0.940
7		Normal	368 (20.8)	1399 (79.2)	1767	0.576	0.887	0.630	1.249
8		Underweight	34 (20.7)	130 (79.3)	164	0.690	0.883	0.566	1.379
9		Severe underweigth	27 (23.5)	88 (76.5)	115	Reference			
10 11		Duration of DM							
12		>5 years	469 (25.1)	1398 (74.9)	1867	0.001	2.38	2.049	2.758
13		<5 years	216 (10.6)	1828 (89.4)	2044				
14		Type of DM medication					• • • •		
15		No medication	235 (28.3)	595 (71.7)	830	0.001	2.09	1.766	2.471
16		OHD+insulin	158 (19.1)	670 (80.9)	828	0.001	1.41	1.164	1.703
17 18		Insulin	91 (11.8)	679 (88.2)	770	0.261	0.87	0.692	1.099
19		OHD	201 (13.6)	1282 (86.4)	1483	Reference	1		
20		Medication compliance	207(10.0)	1210 (01 1)	1(25	0.0(2	1 1 4	0.007	1 2 1 0
21		No	307 (18.9)	1318 (81.1)	1625	0.062	1.14	0.997	1.310
22	404	Yes * <i>Chi-square</i> test	378 (16.5)	1908 (83.5)	2286				
23 24	404	HDL: high density lipoprotei	in: LDL: low der	nsity lipoprotein: (OHD: oral	hypoglicaemic	drugs: PO	R: prevalenc	e
24 25	406	odds ratio		• • • •				F	-
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	Variables	р	POR	95	5% CI.
	Age (years old)				
	≥75	0.001	109.64	26.373	455.789
	65-74	0.001	81.82	20.110	332.868
	55-64	0.001	46.12	11.393	186.720
	45-54	0.001	22.81	5.616	92.677
	35-44	0.001	10.80	2.595	44.957
	High HDL cholesterol	0.025	0.80	0.653	0.972
	History of hypertension	0.070	1.183	0.986	1.418
	BMI	0.001	0.7(0)	0.450	1.000
	Obese	0.331	0.769	0.453	1.306
	Overweight	0.493	0.825	0.475	1.431
	Normal	0.369	1.241	0.775	1.987
	Underweight	0.857	0.946	0.520	1.722
409	Duration of DM BMI: body mass index; HDL: high de	0.001	1.73	1.257	2.389





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2 pesan

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17-Oct-2021

Dear Dr. Hasyim:

Thank you for reviewing manuscript # EJHS-2021-0721.R1 entitled "Prevalence and Risk Factors of Isolated Systolic Hypertension among Diabetes Mellitus Subjects; a national cross-sectional study in Indonesia" for the Ethiopian Journal of Health Sciences.

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1 Prevalence of Isolated Systolic Hypertension among People with

2 Diabetes in Indonesia

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12 Abstract

- 13 The present study aimed to explore the prevalence of isolated systolic hypertension (ISH) and
- 14 its risk factors among diabetes mellitus (DM) subjects in the community setting study in
- 15 Indonesia. This cross-sectional study extracted secondary data from basic health survey
- 16 (Riset Kesehatan Dasar; RISKESDAS) conducted in 2018. DM subjects were defined based
- 17 on fasting blood glucose level $\geq 126 \text{ mg/dL}$ or 2 hours postprandial and random blood
- 18 glucose level $\geq 200 \text{ mg/dL}$ or previously had been diagnosed by a doctor; while ISH was
- 19 determined based on systolic blood pressure \geq 140 mmHg and diastolic blood pressure < 90
- 20 mmHg. We also observed the subject's characteristics, such as demography, lipid profile, and
- 21 subject's compliance. Data were then analyzed using Chi-square and Binary logistic
- 22 regression. Study involved 3,911 DM subjects, revealed the overall prevalence of ISH 17.5%.
- 23 Age category of 35-44 years old (POR= 10.80; 95%CI: 2.595-44.957), 45-54 years old
- 24 (POR=22.81; 95%CI: 5.616-92.677), 55-64 years old (POR=46.12; 95% CI: 11.393-
- 25 186.720); 65-74 years old (POR= 81.82; 95% CI: 20.110-332.868); ≥75 years old (POR=
- 26 109.64; 95% CI: 26.373-455.789), low HDL cholesterol (POR= 0,80; 95% CI: 0.653-0.972);
- duration of DM (POR= 1.73; 95% CI: 1.257-2.389) were associated with the ISH. The
- 28 prevalence of ISH among DM subjects was 17.5%. Older DM subjects, low HDL cholesterol,
- and duration of DM were associated with the ISH, suggesting that modification lipid profile,
- 30 especially the HDL cholesterol level, is an important measure to delay ISH in elderly and
- 31 long-duration DM subjects.
- 32

33 Keywords: diabetes, isolated systolic hypertension, prevalence, risk factor, Indonesia

34 Introduction

International Diabetes Federation reports 463 million people globally, and 10.7 million people in Indonesia living with diabetes placing Indonesia in the 7th rank among countries for the number of adults with diabetes [1]. Hypertension is the most frequent comorbidity for diabetes [2–4]. Both hypertension and diabetes are the major risk factors for cardiovascular diseases due to the vascular mechanism [5]. Hypertension is associated with

40 30% of death and 25% of cardiovascular events among diabetes mellitus (DM) subjects [6].

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41 DM subjects with hypertension have seven times likely to experience end-stage renal disease 42 and 2-4 times to get myocardial infarction and stroke [6].

43 Hypertension occurred due to the vascular resistance and increase of fluid volume [7]. 44 Vascular resistance in DM subjects is related to vascular remodeling that caused arterial 45 stiffness, while the increase of body fluid volume is associated with resistance-induced 46 hyperinsulinemia and hyperglycemia [7]. Isolated systolic hypertension (ISH) is the most 47 frequent form of hypertension among the elderly [8] and the most frequent subtype of 48 uncontrolled hypertension [9]. People with diabetes have twice higher risk to get ISH than of 49 those without diabetes [10]. ISH reflects widespread atherosclerosis and increases stroke risk 50 of 11% as well as an increase in all-cause mortality risk of 16% [10]. Alongside the ISH, the 51 pulse pressure (PP) and mean arterial pressure (MAP) is the independent predictors of 52 cardiovascular events and all-cause mortality [10–13].

53 A previous study[14] based on the hospital-based data reported that the prevalence of 54 ISH among DM subjects was 37.4%, and age was the most related factor. Another study 55 reported that the prevalence of ISH among DM subjects was 27.6% [15]; male, older age, 56 obesity, and smoking were its risk factors [15,16]. A study in Indonesia reported risk factors 57 of hypertension among DM subjects such as age, mental health disorders, obesity, physical 58 activities, duration of diabetes, dyslipidemia, and patient compliance [17]. However, limited 59 information regarding prevalence and risk factors of ISH among DM subjects based on 60 population-based data. The present study aimed to explore the prevalence of ISH and its risk 61 factors among DM subjects based on community setting study in Indonesia.

62 Materials and Methods

63 **Design and study population**

64 This cross-sectional study extracted secondary data from the basic health survey 65 (Riset Kesehatan Dasar; RISKESDAS) 2018, the latest five-annual national scope cross-66 sectional study, conducted by the National Institute of Research and Development, Ministry 67 of Health, the Republic of Indonesia. The survey was conducted and delivered for households 68 systematic-randomly selected from 514 districts/cities in 34 provinces. For each province and 69 district/city, the number of proportional census blocks was determined systematically. Three 70 hundred households or 30.000 census blocks were then determined to be involved in the survey. Of them, 94.2 % or 282,654 households completed the questionnaire consist of 71 72 1,017,290 individual subjects [18]. The study population involved subjects with DM in the 73 RISKESDAS 2018 data. Subjects with DM were determined by fasting blood glucose level \geq 74 126 mg/dL or 2 hours postprandial and random blood glucose level \geq 200 mg/dL or 75 previously had been diagnosed by a doctor.

76

77 Data collection

78 Ethical clearance for the RISKESDAS 2018 study was obtained from the Ethics 79 Committee, the National Institute of Health Research and Development (NIHRD), the 80 Ministry of Health, Republic of Indonesia. Subject with ISH was defined as those with 81 systolic blood pressure \geq 140 mmHg and diastolic blood pressure < 90 mmHg [19]. We 82 categorized the subject as non-hypertensive when meet the criteria of optimal (<120 mmHg 83 and <80 mmHg), or normal (120 mmHg-129 mmHg and/or 80-84 mmHg), or high normal 84 (130-139 mmHg and/or 85-89 mmHg). While non ISH hypertension were categorized for 85 grade 1-3 hypertension; grade 1 hypertension: 140-159 mmHg and/or 90-99 mmHg; grade 2 86 hypertension: 160-179 mmHg and/or 100-109 mmHg; grade 3 hypertension: ≥180 mmHg 87 and or ≥ 110 mmHg [19]. Based on the measurement of blood pressure, we also calculated 88 pulse pressure (PP) and mean arterial pressure (MAP). PP was calculated as a result of the

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- 89 formula (PP = systolic blood pressure (SBP) diastolic blood pressure (DBP)), while the
- 90 MAP was calculated as the formula of $(MAP = \frac{(SBP+2*DBP)}{3})$.
- Secondary data acquired from RISKESDAS 2018 were age, sex, urban-rural
 residence status, marital status, educational level, employment status, total cholesterol level,
 HDL-cholesterol level, triglycerides level, history of hypertension, smoking, physical activity
 status, alcohol consumption, body mass index (BMI), duration of DM, type of medication,
 and medication compliance.
- 96

97 Statistical analysis

98 Characteristics of the subjects were presented as proportions since they are categorical 99 type of data. The association between ISH status were analyzed using the Chi-square test. 100 The p-values <0.05 were considered statistically significant. Parameters that had p-value 101 <0.25 were then involved in the multivariate analysis using binary logistic regression. All 102 statistical analyses were performed using the Statistical Package for the Social Sciences 103 (SPSS) software (version 23.0 for Windows, IBM SPSS Inc., Chicago, IL).

105 **Results**

106 Data extracted from the RISKESDAS 2018 consisted of 3,911 DM subjects that were 107 included in the final analysis. Study population consisted of 1,289 (33%) male and 2,622 108 (67%) female. The most frequent age category was 45-54 years old (29.3%). More than half 109 of the study population was live in the urban area with a low level of education and were 110 employed in various sectors. Most of the study population had lower total cholesterol levels, 111 lower high-density lipoprotein (HDL) cholesterol level, higher low-density lipoprotein (LDL) 112 cholesterol level, and lower triglyceride levels. Most of them had a history of hypertension, 113 non-smoking, active physical activity, and fair medication compliance. The detailed subjects'

114 characteristics are presented in Table 1.

n	%
167	4.3
502	12.8
1098	28.1
1146	29.3
668	17.1
330	8.4
2622	67
1289	33
2057	52.6
1854	47.4
147	3.8
3764	96.2
3006	76.9
	167 502 1098 1146 668 330 2622 1289 2057 1854 147 3764

115 Table 1. Subjects' characteristics

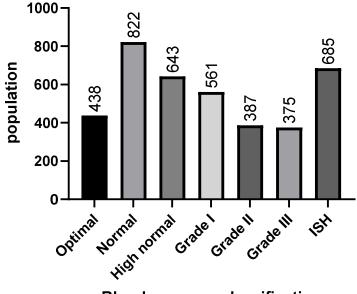
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Casendamy high school on shows	005	02.1
Secondary high school or above	905	23.1
Employment status	1620	41.9
Un-employed Employed	1639 2272	58.1
Total Cholesterol level	2212	38.1
	1022	16.9
$\geq 200 \text{ mg/dL}$	1832	46.8
<200 mg/dL	2079	53.2
HDL level	1140	20.1
$\geq 40 \text{ mg/dL}$	1140	29.1
<40 mg/dL	2771	70.9
LDL level	2204	04.2
$\geq 100 \text{ mg/dL}$	3296	84.3
<100 mg/dL	615	15.7
Triglyceride		
$\geq 150 \text{ mg/dL}$	1612	41.2
<150 mg/dL	2299	58.8
History of hypertension		
Yes	1350	34.5
No	2561	65.5
Smoking		
Yes	1002	25.6
No	2909	74.4
Physical activity status		
Sedentary	605	15.5
Active	3306	84.5
Alcohol consumption		
Yes	37	0.9
No	3874	99.1
BMI	0071	///1
Obese	1262	32.3
Overweight	603	15.4
Normal	1767	45.2
Underweight	164	4.2
Severe Underweight	115	2.9
Duration of DM	115	2.9
>5 years	1867	47.7
<5 years	2044	52.3
•	2044	52.5
Type of DM medication	020	21.2
No medication	830	21.2
OHD+insulin	828	21.2
Insulin	770	19.7
OHD	1483	37.9
Medication compliance		• • •
No	1625	41.5
Yes BMI: body mass index; HDL=high-density lipoprote	2286	58.5

116 BMI: body mass index; HDL=high-density lipoprotein; LDL=low-density lipoprotein

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- Based on the result of blood pressure measurement, a total of 1,903 (48.7%) subjects
- 119 were categorized as normal, while the rest of 2,008 (51.3%) were categorized as
- 120 hypertension, whether grade 1,2,3 or ISH. ISH was the most frequent form of hypertension in
- 121 the study population (Fig. 1). The highest mean MAP was in non-ISH hypertension group,
- 122 while the highest mean PP was in the ISH group (Fig. 2)



Blood pressure classification

124 Figure 1. Frequency of blood pressure	e classification among DM subjects
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- 125 Optimal: <120 and <80; Normal: 120-129 and/or 80-84; High normal: 130-139 and/or 85-89; Grade I
- 126 hypertension: 140-159 and/or 90-99; Grade II hypertension: 160-179 and or 100-109; Grade III hypertension:

127 \geq 180 and or \geq 110; Isolated systolic hypertension (ISH): \geq 140 and <90

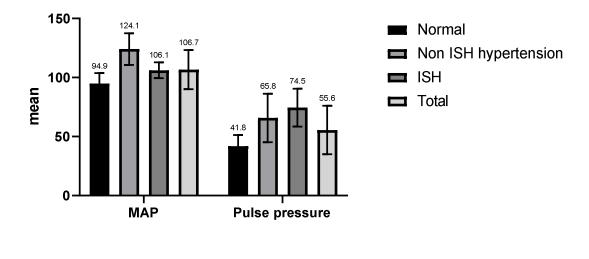






Figure 2. Mean arterial pressure (MAP) and pulse pressure based on hypertension classification.

131	ISH: isolated systolic hypertension
132	Of the total 3,911 study population of DM subjects, 685 subjects were identified as
133	ISH, indicated that the prevalence of ISH was 17.5%. Table 2 identified variables associated
134	with the ISH. Older subjects, low educational level, high total cholesterol level, low HDL
135	level, active physical activity, obese, duration of DM, and type of medication were associated
136	with the ISH status among DM subjects. These variables, combined with other variables that
137	$p \le 0.25$, i.e., employment status, LDL level, triglyceride, history of hypertension, alcohol
138	consumption, and medication compliance, continued to be involved in the Binary logistic
139	regression, and the final model of regression showed in Table 3.
140	
141	Table 2. Subjects' characteristics based on ISH status

5	ISH					95%CI	
Parameter	Yes	No	Total	_ p*	POR	Lower	Uper
Age (years old)	n(%)	n(%)	n(%)				Ĩ
≥ 75	70 (41.9)	97 (58.1)	167	0.001	69.16	17.172	278.560
65-74	174 (34.7)	328 (65.3)	502	0.001	57.19	14.289	228.905
55-64	253 (23)	845 (77)	1098	0.001	38.02	9.508	152.020
45-54	145 (12.7)	1001 (87.3)	1146	0.001	20.88	5.200	83.822
35-44	41 (6.1)	627 (93.9)	668	0.001	10.13	2.465	41.612
15-34	2 (0.6)	328 (99.4)	330	Reference	10.15	2.405	41.012
Sex	2 (0.0)	520 (77.4)	550	Reference	1		
Female	451 (17.2)	2171 (82.8)	2622	0.489	0.95	0.821	1.093
Male	234 (18.2)	1055 (81.8)	1289	0.407	0.75	0.021	1.075
Residence status	234 (10.2)	1055 (01.0)	1207				
Urban	370 (18)	1687 (82)	2057	0.437	1.06	0.924	1.214
Rural	315 (17)	1539 (83)	1854	01127	1.00	0.72	1.211
Marital status	515 (17)	100) (00)	1001				
Un-married	23 (15.6)	124 (84.4)	147	0.619	0.89	0.607	1.303
Married	662 (17.6)	3102 (82.4)	3764	01017	0.07	0.007	1.000
Education level	002 (1110)	0102 (0211)	0701				
Low	553 (18.4)	2453 (81.6)	3006	0.009	1.26	1.059	1.502
High	132 (14.6)	773 (85.4)	905				
Employment status		()					
Un-employed	308 (18.8)	1331 (81.2)	1639	0.081	1.13	0.988	1.298
Employed	377 (16.6)	1895 (83.4)	2272				
Total Cholesterol level		× ,					
≥200 mg/dL	345 (18.8)	1487 (81.2)	1832	0.046	1.15	1.005	1.319
<200 mg/dL	340 (16.4)	1739 (83.6)	2079				
HDL level		× ,					
$\geq 40 \text{ mg/dL}$	169 (14.8)	971 (85.2)	1140	0.005	0.80	0.679	0.934
<40 mg/dL	516 (18.6)	2255 (81.4)	2771				
LDL level	. ,						
≥100 mg/dL	591 (17.9)	2705 (2.1)	3296	0.127	1.17	0.961	1.433
<100 mg/dL	94 (15.3)	521 (84.7)	615				
Triglyceride							
≥150 mg/dL	261 (16.2)	1351 (83.8)	1612	0.075	0.88	0.763	1.010
<150 mg/dL	424 (18.4)	1875 (81.6)	2299				
History of hypertension							
Yes	250 (18.5)	1100 (81.5)	1350	0.248	1.09	0.947	1.255
	. ,	. ,					

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No	435 (17)	2126 (83)	2561				
Smoking							
Yes	182 (18.2)	820 (81.8)	1002	0.563	1.05	0.901	1.225
No	503 (17.3)	2406 (82.7)	2909				
Physical activity status							
Sedentary	131 (21.7)	474 (78.3)	605	0.004	1.29	1.091	1.531
Active	554 (16.8)	2752 (83.2)	3306				
Alcohol consumption							
Yes	2 (5.4)	35 (94.6)	37	0.084	0.31	0.080	1.182
No	683 (17.6)	3191 (82.4)	3874				
BMI							
Obese	165 (13.1)	1097 (86.9)	1262	0.003	0.557	0.389	0.798
Overweight	91 (15.1)	512 (84.9)	603	0.037	0.643	0.439	0.940
Normal	368 (20.8)	1399 (79.2)	1767	0.576	0.887	0.630	1.249
Underweight	34 (20.7)	130 (79.3)	164	0.690	0.883	0.566	1.379
Severe underweigth	27 (23.5)	88 (76.5)	115	Reference			
Duration of DM							
>5 years	469 (25.1)	1398 (74.9)	1867	0.001	2.38	2.049	2.758
<5 years	216 (10.6)	1828 (89.4)	2044				
Type of DM medication							
No medication	235 (28.3)	595 (71.7)	830	0.001	2.09	1.766	2.471
OHD+insulin	158 (19.1)	670 (80.9)	828	0.001	1.41	1.164	1.703
Insulin	91 (11.8)	679 (88.2)	770	0.261	0.87	0.692	1.099
OHD	201 (13.6)	1282 (86.4)	1483	Reference	1		
Medication compliance							
No	307 (18.9)	1318 (81.1)	1625	0.062	1.14	0.997	1.310
Yes	378 (16.5)	1908 (83.5)	2286				
12 * Chi square tost							

142 **Chi-square* test

HDL: high density lipoprotein; LDL: low density lipoprotein; OHD: oral hypoglicaemic drugs; POR:
 prevalence odds ratio

145

146 We found that older subjects, low HDL cholesterol (prevalence odds ratio;

147 POR=0.80; 95% CI: 0.653-0.972), and duration of DM (POR=1.73; 95% CI: 1.257-2.389),

148 all together were associated with the ISH. Subjects with the older age category tend to get

149 higher POR, i.e., 10.80, 22.81, 46.81, 81.82, and 109.64 for the age category of 35-44, 45-54,

150 55-64, 65-74, and \geq 75 years old, respectively (Table 3).

151

152 Table 3. Binary logistic regression of ISH risk factors among DM subjects

• • •		0 0			
Variables	р	POR	95% CI.		
Age (years old)					
≥75	0.001	109.64	26.373	455.789	
65-74	0.001	81.82	20.110	332.868	
55-64	0.001	46.12	11.393	186.720	
45-54	0.001	22.81	5.616	92.677	
35-44	0.001	10.80	2.595	44.957	
High HDL cholesterol	0.025	0.80	0.653	0.972	
History of hypertension	0.070	1.183	0.986	1.418	
BMI					
Obese	0.331	0.769	0.453	1.306	
Overweight	0.493	0.825	0.475	1.431	
-					

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Normal	0.369	1.241	0.775	1.987
Underweight	0.857	0.946	0.520	1.722
Duration of DM	0.001	1.73	1.257	2.389

153 154

BMI: body mass index; HDL: high density lipoprotein; POR: prevalence odds ratio

.54

155 **Discussion**

156 The present study reported a national scope, population-based cross-sectional study 157 that involved 3,911 DM subjects in Indonesia. Of them, 685 experienced ISH, indicated that 158 the prevalence of ISH among DM subjects in this population study was 17.5%. The 159 prevalence of ISH among DM subjects in Indonesia based on this study population was lower 160 than the prevalence of ISH in Ghana, i.e., 37.4% based on the out-patient diabetes clinic in 161 the teaching hospital of Tamale [14]. Similarly, as a hospital-based study, a study in Jimma, 162 Ethiopia, found that the prevalence of ISH among DM patients was 27.6% [15]. A 163 population-based study in district Chiem Hoa, Vietnam, observed the general elderly 164 population aged >60 years old found a prevalence of 22.9 % [20]. Another national 165 population-based study in the USA revealed that the prevalence of ISH in the general 166 population was 9.4% [21]. A similar result as the current study reported by a hospital-based 167 cohort study in Italy that observed ISH among type 2 DM and found a prevalence of 20.3 % 168 [22].

169 The present study also added evidence that DM subjects with older age, i.e., >75170 years old, was the most influential risk factor of ISH. This finding is in accordance with the 171 previous cohort study in Italy which concluded that the mean age of type 2 DM subjects 172 experienced ISH was 74.3 years old [22]. On the other hand, a study in Ethiopia reported that 173 DM subjects aged ≥ 60 years old were the protective factor for ISH, while the age category of 174 47-55 years old was the risk factor with the highest OR, i.e., 2.63 [15]. Similarly, the study in 175 Ghana showed the most frequent ISH in the DM subjects aged 50-69 years old [14]. 176 Regarding the study population, a study in Italy and Ethiopia comparing ISH to non-ISH, 177 including other forms of hypertension, while a study in Ghana comparing ISH to normal 178 subjects [14,15,22]. The previous review concluded that ISH affects 10-20% of the elderly, 179 systolic blood pressure increase with age, while diastolic blood pressure rises until the age of 180 50 years and then decreases after that [23]. Increase in blood pressure with age is mostly 181 associated with arterial stiffness. Degenerative processes such as calcification and alteration 182 of arteriosclerotic structure play a pivotal role in the formation of large artery stiffness as well 183 as in the small vessels. Small vessel stiffness leads to the condition of peripheral vascular 184 resistance that influences the increase of both systolic and diastolic blood pressure. The 185 existence of large artery stiffness increases systolic blood pressure and, conversely, decreases 186 diastolic blood pressure. The acceleration of large artery stiffness after 50 years old lead to 187 the steeper increase of systolic blood pressure that caused the ISH condition [24]. 188 Lipid profile leads to the process of endothelial dysfunction that affects blood 189 pressure. HDL cholesterol tends to have inversely associated with hypertension, while non-190 HDL cholesterol has a positive association [25]. The present study found that HDL was 191 inversely associated with the ISH, while in the bivariate analysis, total cholesterol showed a 192 positive association with ISH. High HDL level, i.e., $\geq 40 \text{ mg/dL}$, was concluded as the 193 protective factor for ISH in this study. This finding was in accordance with the Physician 194 Health Study that reported the highest quartile of HDL level, i.e., >53 mg/dL had the lowest

adjusted-RR (0.68) compared to the other quartile [26]. A study in China also reported that

HDL level was inversely related to the blood pressure as well as brachial-ankle pulse-wave

197 velocity, a marker of arterial stiffness development [25]. The atherosclerotic formation

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198 structure of the vessels also influenced by the oxidative activity of LDL cholesterol that is 199 also inhibited by HDL [27,28]. However, a previous study in Japan reported a positive 200 correlation between HDL and hypertension in apparently healthy people [29]. Another study 201 revealed that a positive association between HDL and hypertension occurred in the subjects 202 with high-level circulation CD34-positive cells, a bone marrow-derived endothelial 203 progenitor. The level of circulating CD-34 increases as a response of the endothelial damage, 204 therefore masking the role of HDL as endothelial protective in healthy subjects [30]. 205 The current study also found that duration of DM, i.e., more than five years, was 206 significantly associated with ISH, PR=1.73 (95% CI: 1.257-2.389). This finding adds the 207 evidence that previously reported elsewhere that revealed diabetes duration and insulin 208 treatment status were the independent predictor of ISH [31]. The progression and duration of 209 diabetes increase complications. Duration of diabetes is associated with arterial stiffness, 210 while arterial stiffness plays a pivotal role in ISH [31]. The gradation of DM duration as a 211 dose-response relationship with hypertension was also described in the previous study [32]. 212 These findings strengthen the hypothesis that diabetes precedes arterial stiffness that caused 213 ISH; however, another study found that onset on diabetes and brachial-ankle pulse wave 214 velocity occurred simultaneously after a longitudinal observation indicates conversely 215 condition [33]. Indeed, there are roles of multifactor that contributed to the arterial stiffness 216 as a major cause of ISH. Arterial stiffness is a result of degenerative processes in the 217 extracellular matrix of elastic arteries caused by aging and many other risk factors [34]. 218 The final model of Binary logistic regression in this study involved a history of 219 hypertension; however, the p-value did not meet to be considered significant. The previous 220 history of hypertension describes the condition of individuals who tend to have a genetic 221 predisposition [35]. Hypertension is the form of the complex trait that involved multiple

organs and pathways [35,36]. Comprehensive understanding of genomics, epigenomics,
 metabolomics, proteomics, and transcriptomics of blood pressure plays a pivotal role in the
 context of the previous history of hypertension [35]. Further study that observed the detailed
 genetic role should be conducted to elucidate the novel hypertension pathophysiology and
 dissect and characterize the disorder's mechanism.

227 It is well established that obesity is associated with ISH [37–39]. Obesity affects the 228 process of inflammation, cell adhesion, and coagulation that impact in the arterial stiffness 229 [38,40]. Obesity is also related to the insulin and leptin resistance that contributes to sodium 230 retention with concomitant cardiac output [39]. However, in this study, BMI did not 231 significantly associate with ISH, although involved in the final model. It must be considered 232 that the role of BMI measurement alone is inadequate for accurately predict the disease 233 progression in DM subjects [41]. Other parameters such as body composition, total adipose mass, visceral adiposity-accumulation of intra-abdominal fat, and muscle mass should be 234 235 analyzed to describe the current condition of DM subjects [41–43].

236

237 Conclusions

The prevalence of ISH among Indonesian DM subjects in the present study was 17.5%. Older DM subjects, low HDL cholesterol, and duration of DM were associated with the ISH, suggesting that modify lipid profile, especially HDL cholesterol level, is a needful measure to delay ISH in older and duration DM subjects.

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242 Data Availability

- 243 The data used in this study are available from the corresponding author Mahalul Azam upon
- request through the email address <u>mahalul.azam@mail.unnes.ac.id</u>. The data set was
- 245 accessed from the RISKESDAS (Riset Kesehatan Dasar); a five-annual national basic health
- survey that conducted and supported by the National Institute of Health Research and
- 247 Development (NIHRD), Ministry of Health, the Republic of Indonesia. The protocol and
- 248 reports of the RISKESDAS is published on https://www.litbang.kemkes.go.id/laporan-riset-
- 249 <u>kesehatan-dasar-riskesdas//</u>

250 Conflicts of Interest

- 251 The authors have declared that there is no conflict of interest exists.
- 252
- 253

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267

268 **References**

- 269 [1] International Diabetes Federation, IDF Diabetes atlas 9th edition, Brussel, Belgium,
- 270 2019. https://www.diabetesatlas.org.
- 271 [2] B. Tesfaye, A. Alebel, A. Gebrie, A. Zegeye, C. Tesema Leshargie, A. Ferede, H.
- 272 Abera, K. Alam, Diabetes Mellitus and Its Association with Hypertension in Ethiopia:
- A Systematic Review and Meta-Analysis., Diabetes Res. Clin. Pract. 156 (2019)
- 274 107838. https://doi.org/10.1016/j.diabres.2019.107838.
- 275 [3] A.D. Colosia, R. Palencia, S. Khan, Prevalence of hypertension and obesity in patients
- with type 2 diabetes mellitus in observational studies: a systematic literature review.,

^{266 &}lt;u>https://www.litbang.kemkes.go.id/laporan-riset-kesehatan-dasar-riskesdas//</u>

277		diabetes. Metab. Syndr. Obes. 6 (2013) 327–338.
278		https://doi.org/10.2147/DMSO.S51325.
279	[4]	C.T. Nguyen, N.M. Pham, A.H. Lee, C.W. Binns, Prevalence of and Risk Factors for
280	[.]	Type 2 Diabetes Mellitus in Vietnam: A Systematic Review., Asia-Pacific J. Public
281		Heal. 27 (2015) 588–600. https://doi.org/10.1177/1010539515595860.
282	[5]	J.R. Petrie, T.J. Guzik, R.M. Touyz, Diabetes, Hypertension, and Cardiovascular
283		Disease: Clinical Insights and Vascular Mechanisms., Can. J. Cardiol. 34 (2018) 575–
284		584. https://doi.org/10.1016/j.cjca.2017.12.005.
285	[6]	G. Chen, F.A. McAlister, R.L. Walker, B.R. Hemmelgarn, N.R.C. Campbell,
286		Cardiovascular outcomes in framingham participants with diabetes: The importance of
287		blood pressure, hypertension. 57 (2011) 891–897.
288		https://doi.org/10.1161/HYPERTENSIONAHA.110.162446.
289	[7]	M. Ohishi, Hypertension with diabetes mellitus: physiology and pathology.,
290		Hypertens. Res. 41 (2018) 389-393. https://doi.org/10.1038/s41440-018-0034-4.
291	[8]	C. Bavishi, S. Goel, F.H. Messerli, Isolated Systolic Hypertension: An Update After
292		SPRINT., Am. J. Med. 129 (2016) 1251–1258.
293		https://doi.org/10.1016/j.amjmed.2016.08.032.
294	[9]	S.S. Franklin, P. Lapuerta, G.J. L'Italien, N.D. Wong, M.J. Jacobs, Predominance of
295		Isolated Systolic Hypertension Among Middle-Aged and Elderly US Hypertensives,
296		Hypertension. 37 (2012) 869-874. https://doi.org/10.1161/01.hyp.37.3.869.
297	[10]	I. Os, H. Gudmundsdottir, S.E. Kjeldsen, S. Oparil, Treatment of isolated systolic
298		hypertension in diabetes mellitus type 2., diabetes. Obes. Metab. 8 (2006) 381-387.
299		https://doi.org/10.1111/j.1463-1326.2005.00523.x.
300	[11]	N. Madan, A.K. Lee, K. Matsushita, R.C. Hoogeveen, C.M. Ballantyne, E. Selvin,
301		J.W. McEvoy, Relation of Isolated Systolic Hypertension and Pulse Pressure to High-
302		Sensitivity Cardiac Troponin-T and N-Terminal pro-B-Type Natriuretic Peptide in
303		Older Adults (from the Atherosclerosis Risk in Communities Study)., Am. J. Cardiol.
304		124 (2019) 245-252. https://doi.org/10.1016/j.amjcard.2019.04.030.
305	[12]	S. Selvaraj, P.G. Steg, Y. Elbez, E. Sorbets, L.J. Feldman, K.A. Eagle, E.M. Ohman, J.
306		Blacher, D.L. Bhatt, Pulse Pressure and Risk for Cardiovascular Events in Patients
307		With Atherothrombosis: From the REACH Registry., J. Am. Coll. Cardiol. 67 (2016)
308		392-403. https://doi.org/10.1016/j.jacc.2015.10.084.
309	[13]	G.J. Winston, W. Palmas, J. Lima, J.F. Polak, A.G. Bertoni, G. Burke, J. Eng, R.
310		Gottesman, S. Shea, Pulse pressure and subclinical cardiovascular disease in the multi-

311		athric study of atherosalerosis Am I Hypertons 26 (2012) 626 642
312		ethnic study of atherosclerosis., Am. J. Hypertens. 26 (2013) 636–642. https://doi.org/10.1093/ajh/hps092.
	F1 41	
313	[14]	R.K.D. Ephraim, A.R. Saasi, E.O. Anto, P. Adoba, Determinants of isolated systolic
314		hypertension among diabetic patients visiting the diabetic clinic at the Tamale
315		Teaching Hospital, Northern Ghana., Afr. Health Sci. 16 (2016) 1151–1156.
316		https://doi.org/10.4314/ahs.v16i4.33.
317	[15]	B. Dagnew, Y. Yeshaw, Predictors of isolated systolic hypertension among type 2
318		diabetes mellitus patients in Jimma University Specialized Hospital, Southwest
319		Ethiopia, BMC Res. Notes. 12 (2019) 1–7. https://doi.org/10.1186/s13104-019-4550-
320		3.
321	[16]	R. Grebla, C. Rodriguez, L. Borrell, T. Pickering, Prevalence and determinants of
322		isolated systolic hypertension among young adults., J. Am. Soc. Hypertens. 28 (2010)
323		15-23. https://doi.org/10.1097/HJH.0b013e328331b7ff.Prevalence.
324	[17]	M. Sihombing, Faktor yang Berhubungan dengan Hipertensi pada Penduduk Indonesia
325		yang Menderita Diabetes Melitus (Data Riskesdas 2013), Bul. Penelit. Kesehat. 45
326		(2017) 53-64. https://doi.org/10.22435/bpk.v45i1.5730.53-64.
327	[18]	Badan Penelitian dan Pengembangan Kesehatan, Laporan Nasional Riset Kesehatan
328		Dasar: RISKESDAS (Indonesia Basic Health Survey) tahun 2018, 2018.
329		http://labmandat.litbang.kemkes.go.id/images/download/laporan/RKD/2018/Laporan_
330		Nasional_RKD2018_FINAL.pdf.
331	[19]	A.F. Members, G. Mancia, R. Fagard, K. Narkiewicz, J. Redon, A. Zanchetti, M.
332		Böhm, T. Christiaens, R. Cifkova, G. De Backer, A. Dominiczak, M. Galderisi, D.E.
333		Grobbee, T. Jaarsma, P. Kirchhof, S.E. Kjeldsen, S. Laurent, A.J. Manolis, P.M.
334		Nilsson, L.M. Ruilope, R.E. Schmieder, P.A. Sirnes, P. Sleight, M. Viigimaa, B.
335		Waeber, F. Zannad, E.S.H.S. Council, J. Redon, A. Dominiczak, K. Narkiewicz, P.M.
336		Nilsson, M. Burnier, M. Viigimaa, E. Ambrosioni, M. Caufield, A. Coca, M.H. Olsen,
337		R.E. Schmieder, C. Tsioufis, P. van de Borne, E.S.C.C. for P.G. (CPG), J.L.
338		Zamorano, S. Achenbach, H. Baumgartner, J.J. Bax, H. Bueno, V. Dean, C. Deaton, C.
339		Erol, R. Fagard, R. Ferrari, D. Hasdai, A.W. Hoes, P. Kirchhof, J. Knuuti, P. Kolh, P.
340		Lancellotti, A. Linhart, P. Nihoyannopoulos, M.F. Piepoli, P. Ponikowski, P.A. Sirnes,
341		J.L. Tamargo, M. Tendera, A. Torbicki, W. Wijns, S. Windecker, D. Reviewers, D.L.
342		Clement, A. Coca, T.C. Gillebert, M. Tendera, E.A. Rosei, E. Ambrosioni, S.D.
343		Anker, J. Bauersachs, J.B. Hitij, M. Caulfield, M. De Buyzere, S. De Geest, G.A.
344		Derumeaux, S. Erdine, C. Farsang, C. Funck-Brentano, V. Gerc, G. Germano, S.
511		2 crantenini, S. Liunio, C. Lubung, C. Lunion Dichano, T. Gere, G. Germano, D.

245		Cisher H Heller AW Here I Lender T Keher M Kennelde D Lende H
345		Gielen, H. Haller, A.W. Hoes, J. Jordan, T. Kahan, M. Komajda, D. Lovic, H.
346		Mahrholdt, M.H. Olsen, J. Ostergren, G. Parati, J. Perk, J. Polonia, B.A. Popescu, Ž.
347		Reiner, L. Rydén, Y. Sirenko, A. Stanton, H. Struijker-Boudier, C. Tsioufis, P. van de
348		Borne, C. Vlachopoulos, M. Volpe, D.A. Wood, 2013 ESH/ESC Guidelines for the
349		management of arterial hypertension: The Task Force for the management of arterial
350		hypertension of the European Society of Hypertension (ESH) and of the European
351		Society of Cardiology (ESC), Eur. Heart J. 34 (2013) 2159–2219.
352		https://doi.org/10.1093/eurheartj/eht151.
353	[20]	N. Bui Van, L. Vo Hoang, T. Bui Van, H.N.S. Anh, H.T. Minh, K. Do Nam, T.N. Tri,
354		P.L. Show, V.T. Nga, D.B. Thimiri Govinda Raj, DT. Chu, Prevalence and Risk
355		Factors of Hypertension in the Vietnamese Elderly., High Blood Press. Cardiovasc.
356		Prev. Off. J. Ital. Soc. Hypertens. 26 (2019) 239-246. https://doi.org/10.1007/s40292-
357		019-00314-8.
358	[21]	X. Liu, C.J. Rodriguez, K. Wang, Prevalence and trends of isolated systolic
359		hypertension among untreated adults in the United States., J. Am. Soc. Hypertens. 9
360		(2015) 197–205. https://doi.org/10.1016/j.jash.2015.01.002.
361	[22]	S. Bo, G. Ciccone, G. Grassi, R. Gancia, R. Rosato, F. Merletti, G. Pagano, Isolated
362		systolic hypertension in a cohort of type 2 diabetic patients., Nutr. Metab. Cardiovasc.
363		Dis. 14 (2004) 157–161. https://doi.org/10.1016/s0939-4753(04)80036-x.
364	[23]	L. Thijs, E. Den Hond, T. Nawrot, J.A. Staessen, Prevalence, pathophysiology and
365		treatment of isolated systolic hypertension in the elderly, Expert Rev. Cardiovasc.
366		Ther. 2 (2004) 761–769. https://doi.org/10.1586/14779072.2.5.761.
367	[24]	E. Pinto, Blood pressure and ageing, Postgrad. Med. J. 83 (2007) 109-114.
368		https://doi.org/10.1136/pgmj.2006.048371.
369	[25]	B. Zhan, X. Huang, J. Wang, X. Qin, J. Zhang, J. Cao, Y. Song, L. Liu, P. Li, R. Yang,
370		Y. Wu, Q. Wu, Y. Zhang, J. Li, Y. Huo, B. Wang, X. Xu, H. Bao, X. Cheng,
371		Association Between Lipid Profiles and Arterial Stiffness in Chinese Patients With
372		Hypertension: Insights From the CSPPT, Angiology. 70 (2019) 515–522.
373		https://doi.org/10.1177/0003319718823341.
374	[26]	HR O., SH D., M. Jing, BJ E., SM J., MG J., Dyslipidemia and the Risk of Incident
375		Hypertension in Men, Hypertension. 47 (2006) 45–50.
376		https://doi.org/10.1161/01.HYP.0000196306.42418.0e.
377	[27]	F. Brites, M. Martin, I. Guillas, A. Kontush, Antioxidative activity of high-density
378		lipoprotein (HDL): Mechanistic insights into potential clinical benefit., BBA Clin. 8

379		(2017) 66-77. https://doi.org/10.1016/j.bbacli.2017.07.002.
380	[28]	R. Puri, S.E. Nissen, M. Shao, M.B. Elshazly, Y. Kataoka, S.R. Kapadia, E.M. Tuzcu,
381		S.J. Nicholls, Non-HDL Cholesterol and Triglycerides: Implications for Coronary
382		Atheroma Progression and Clinical Events, Arterioscler. Thromb. Vasc. Biol. 36
383		(2016) 2220-2228. https://doi.org/10.1161/ATVBAHA.116.307601.
384	[29]	E. Oda, R. Kawai, High-density lipoprotein cholesterol is positively associated with
385		hypertension in apparently healthy Japanese men and women, Br. J. Biomed. Sci. 68
386		(2011) 29-33. https://doi.org/10.1080/09674845.2011.11732838.
387	[30]	Y. Shimizu, S. Sato, J. Koyamatsu, H. Yamanashi, M. Nagayoshi, K. Kadota, SY.
388		Kawashiri, T. Maeda, Association between high-density lipoprotein-cholesterol and
389		hypertension in relation to circulating CD34-positive cell levels, J. Physiol. Anthropol.
390		36 (2017) 1-7. https://doi.org/10.1186/s40101-017-0143-9.
391	[31]	H. Smulyan, A. Lieber, M.E. Safar, Hypertension, Diabetes Type II, and Their
392		Association: Role of Arterial Stiffness., Am. J. Hypertens. 29 (2016) 5-13.
393		https://doi.org/10.1093/ajh/hpv107.
394	[32]	M. Berraho, Y. El Achhab, A. Benslimane, K. El Rhazi, M. Chikri, C. Nejjari,
395		Hypertension and type 2 diabetes: a cross-sectional study in Morocco (EPIDIAM
396		Study)., Pan Afr. Med. J. 11 (2012) 52.
397	[33]	Y. Zhang, P. He, Y. Li, Y. Zhang, J. Li, M. Liang, G. Wang, G. Tang, Y. Song, B.
398		Wang, C. Liu, L. Liu, Y. Cui, X. Wang, Y. Huo, X. Xu, X. Qin, Positive association
399		between baseline brachial-ankle pulse wave velocity and the risk of new-onset
400		diabetes in hypertensive patients, Cardiovasc. Diabetol. 18 (2019) 111.
401		https://doi.org/10.1186/s12933-019-0915-0.
402	[34]	C. Palombo, M. Kozakova, Arterial stiffness, atherosclerosis and cardiovascular risk:
403		Pathophysiologic mechanisms and emerging clinical indications., Vascul. Pharmacol.
404		77 (2016) 1-7. https://doi.org/10.1016/j.vph.2015.11.083.
405	[35]	D.K. Arnett, S.A. Claas, Omics of Blood Pressure and Hypertension., Circ. Res. 122
406		(2018) 1409-1419. https://doi.org/10.1161/CIRCRESAHA.118.311342.
407	[36]	M.L. Lindsey, M. Mayr, A. V Gomes, C. Delles, D.K. Arrell, A.M. Murphy, R.A.
408		Lange, C.E. Costello, YF. Jin, D.T. Laskowitz, F. Sam, A. Terzic, J. Van Eyk, P.R.
409		Srinivas, Transformative Impact of Proteomics on Cardiovascular Health and Disease:
410		A Scientific Statement From the American Heart Association., Circulation. 132
411		(2015) 852-872. https://doi.org/10.1161/CIR.00000000000226.
412	[37]	S. Asgari, D. Khalili, Y. Mehrabi, S. Kazempour-Ardebili, F. Azizi, F. Hadaegh,

It is made available under a CC-BY-NC-ND 4.0 International license .

413		Incidence and risk factors of isolated systolic and diastolic hypertension: a 10 year
414		follow-up of the Tehran Lipids and Glucose Study, Blood Press. 25 (2016) 177–183.
415		https://doi.org/10.3109/08037051.2015.1116221.
416	[38]	R.P. Wildman, R.H. Mackey, A. Bostom, T. Thompson, K. Sutton-Tyrrell, Measures
417		of obesity are associated with vascular stiffness in young and older adults,
418		hypertension. 42 (2003) 468-473.
419		https://doi.org/10.1161/01.HYP.0000090360.78539.CD.
420	[39]	R. and E.R. Zhang, Obesity hypertension: The effects on cardiovascular and renal
421		systems, Am. J. Hypertens. 13 (2000) 1308-1314.
422	[40]	C. Delles, E. Carrick, D. Graham, S.A. Nicklin, Utilizing proteomics to understand and
423		define hypertension: where are we and where do we go?, Expert Rev. Proteomics. 15
424		(2018) 581-592. https://doi.org/10.1080/14789450.2018.1493927.
425	[41]	M. Murea, L. Lenchik, T.C. Register, G.B. Russell, J. Xu, S.C. Smith, D.W. Bowden,
426		J. Divers, B.I. Freedman, Psoas and paraspinous muscle index as a predictor of
427		mortality in African American men with type 2 diabetes mellitus., J. Diabetes
428		Complications. 32 (2018) 558–564. https://doi.org/10.1016/j.jdiacomp.2018.03.004.
429	[42]	E.S.A. Owusu, M. Samanta, J.E. Shaw, A. Majeed, K. Khunti, S.K. Paul, Weight loss
430		and mortality risk in patients with different adiposity at diagnosis of type 2 diabetes: a
431		longitudinal cohort study., Nutr. Diabetes. 8 (2018) 37.
432		https://doi.org/10.1038/s41387-018-0042-0.
433	[43]	S. Gullaksen, K.L. Funck, E. Laugesen, T.K. Hansen, D. Dey, P.L. Poulsen, Volumes
434		of coronary plaque disease in relation to body mass index, waist circumference,
435		truncal fat mass and epicardial adipose tissue in patients with type 2 diabetes mellitus
436		and controls., Diabetes Vasc. Dis. Res. 16 (2019) 328-336.
437		https://doi.org/10.1177/1479164119825761.