Prevalence and Risk Factors of Peripheral Arterial Disease in type 2 Diabetes Mellitus in Yogyakarta, Indonesia

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ABSTRACT

Aim: Diabetes mellitus increases the risk of peripheral artery disease (PAD) 2 times. PAD is diagnosed by ABI (Ankle Brachial Index). PAD increases mortality and morbidity of patient with Diabetes Mellitus (DM) Type 2. This study aims to determine the prevalence and risk factors of PAD in the population of type 2 diabetes mellitus (DM) in Yogyakarta, Indonesia.

Methods: This study was a community-based descriptive and analytic observational study that examines the prevalence and risk factors of PAD in type 2 diabetes mellitus. Diagnosis of PAD was detected by ABI examination using VaSera VS-1500N. All patients with type 2 diabetes mellitus in Yogyakarta who meet the inclusion criteria will be enrolled in this study. The research subjects were taken in multi-stage, cluster-random sampling in Yogyakarta. The patient will undergo an interview of demographic data which were assessed by one assessor. Data from interviews and ABI examinations were analysed statistically.

Results: Two hundred and fifty-six (256) patients with type 2 DM consisted of 188 patients (73.4%) women and 68 patients (26.6%) men. Prevalence of PAD diagnosed by abnormal ABI was found in 41 (16%) of 256 patients. Subjects with age more than 67 years old was significantly associated with PAD occurrence (P=0,001) in type 2 DM population.

Conclusion: The prevalence of PAD was 16% of 256 type 2 DM patients. Age more than 67 years old was the strong risk factor of PAD in type 2 DM.

INTISARI

Tujuan: Diabetes melitus meningkatkan risiko penyakit arteri perifer (PAD) 2 kali lipat. PAD didiagnosis dengan ABI (Ankle Brachial Index). PAD meningkatkan mortalitas dan morbiditas penderita Diabetes Mellitus (DM) Tipe 2. Penelitian ini bertujuan untuk mengetahui prevalensi PAD pada populasi penderita Diabetes Mellitus (DM) tipe 2 di Yogyakarta.

Metode: Penelitian ini merupakan penelitian deskriptif observasional dan analitik berbasis komunitas untuk mengetahui prevalensi dan faktor risiko PAD pada diabetes mellitus tipe 2. Diagnosis PAD berdasarkan pemeriksaan ABI dan dinilai menggunakan VaSera VS-1500N. Seluruh pasien diabetes melitus tipe 2 di Yogyakarta yang memenuhi kriteria inklusi akan menjadi subyek dalam penelitian ini. Subyek penelitian diambil secara multi stage, cluster-random sampling di Yogyakarta. Pasien akan menjalani wawancara, serta pemeriksaan ABI yang dinilai oleh satu asesor. Dengan demikian, data hasil wawancara, pemeriksaan ABI dianalisis secara statistik.

Hasil: Dua ratus lima puluh enam (256) pasien DM tipe 2 terdiri dari 188 pasien (73,4%) perempuan dan 68 pasien (26,6%) laki-laki. ABI abnormal ditemukan pada 41 (16%) dari 256 pasien. Subjek dengan usia lebih dari 67 tahun berhubungan bermakna dengan kejadian PAD (P=0,001) sedangkan faktor risiko lain seperti usia kurang dari 67 tahun, jenis kelamin, hipertensi, merokok, dan dislipidemia tidak berhubungan dengan kejadian PAD.

Kesimpulan: Prevalensi PAD adalah 16% dari 256 pasien DM tipe 2. Usia lebih dari 67 tahun merupakan faktor risiko yang kuat pada pasien PAD dengan DM tipe 2.*Latar Belakang*: Gagal jantung masih menjadi salah satu problematika di Indonesia saat ini terkait masih tingginya angka morbiditas, mortalitas serta rehospitalisasinya. Gagal jantung juga menjadi salah satu penyakit yang menggunakan dana kesehatan paling banyak. Penyakit jantung coroner merupakan penyebab gagal jantung yang paling banyak ditemukan. Data mengenai epidemiologi gagal jantung masih terbatas di Indonesia. Memahami epidemiologi gagal jantung dari praklinis hingga klinis dapat meningkatkan upaya strategi pencegahan terhadap kejadian gagal jantung. Studi ini bertujuan untuk mengetahui data epidemiologi pasien gagal jantung di Yogyakarta, dimulai dari populasi di rumah sakit, khususnya di RSUP Dr.Sardjito.

Introduction

The global prevalence of diabetes mellitus (DM) is increasing rapidly as a result of increasing age, urbanization, and changes in lifestyle (Zimmet *et al*., 2001). The number of people with diabetes mellitus in the world has more than doubled over the past 3 decades (Danaei *et al.*, 2011). DM disease has become one of the global public health problems and according to the International Diabetes Federation (IDF) in 2012, the number of sufferers is increasing, where more than 371 million people worldwide experience DM, and 4.8 million of them died. In Indonesia alone in 2014 the prevalence was quite high, namely 5.81% (Purnamasari, 2014). In Yogyakarta the prevalence of DM in 2013 according to RISKESDAS was 2.6% or around 91,000 people.

DM complications are divided into macrovascular (coronary artery disease, peripheral artery disease, and stroke) and microvascular (diabetes nephropathy, neuropathy, and retinopathy) (Fowler, 2008). The main mechanism for macrovascular complications is the formation of atherosclerosis which causes narrowing of the artery lumen in the heart, brain and peripheral blood vessels (Fowler, 2008). One of the macrovascular complications that often arise is peripheral artery disease (PAD) which can progress to the final stage of critical limb threatening ischemia (CLTI) (Varu et al., 2010). The presence of diabetes mellitus greatly increases the risk of PAD, as well as accelerates its course, making these patients more susceptible to ischemic events and impaired functional status compared to patients without diabetes (Thiruvoipati, 2015). Approximately 26.3% of DM patients will experience PAD compared to 15.3% in the non-diabetic population. The risk of amputation in these patients also increases compared to nondiabetics. According to the recent study, the proportion of amputations among type 2 DM patients was significantly increased from 2011 to 2016 in Korea (Kim *et al.*, 2019). The prevalence of macrovascular disease, especially peripheral arteries in DM patients using ABI to identify PAD, is estimated to be 20% at the age of 40 years and increases to 29% in patients with DM over 50 years (Thiruvoipati et al., 2015).

Amputation itself will have a major impact on psychological, social, including economic (work) factors so that people with diabetes mellitus are greatly feared (Burger & Marinček, 2007). Type 2 diabetes mellitus was associated with increased risk of all-cause mortality in peripheral vascular disease (Vrsalovic *et al.*, 2017).

According to AHA Guidelines (2016), ABI is a diagnostic tool for PAD. Patient with ABI measurement below or equal to 0,90 is classified as PAD. Those with ABI 0,90 – 0,99 are possibly PAD and should be examined with exercise ABI, if clinically significant. ABI >1,40 indicates that the artery is incompressible which is common in diabetes mellitus and chronic kidney disease patients. (Gerhard-Herman et al., 2017).

Methods

Materials

All patients with type 2 diabetes mellitus in the Community Health Center in Yogyakarta region who meet the inclusion criteria will be subjects in this study. The research subjects were taken in multi-stage, cluster-random sampling from November 2019 to November 2020 was used in this study.

Methods and data analysis

This study was a community-based descriptive and analytic observational study that examines the use of ABI to determine the prevalence and risk factors of PAD in type 2 diabetes mellitus. The research subjects were taken in multi-stage, cluster-random sampling in Yogyakarta. The patient will undergo an interview, which is assessed by one assessor. Data from interviews and ABI examinations were analysed statistically.

Results

Table 1. Demographic data of diabetes subjects comparing between PAD and non-PAD group

	All patients (n=256)	Pad (n=41 (16%))	Non-pad (n=215 (84%))	P-value
Age (years) (mean ± sd)		64,3 ± 10,4	58,6 ± 9,6	
Q1 (<53) [n(%)]		6 (14,6)	60 (27,9)	0,075
Q2 (53-59) [n(%)]	59,5 ± 9,94	6 (14,6)	57 (26,5)	0,106
Q3 (60-67) [n(%)]		12 (29,3)	60 (27,9)	0,859
Q4 (>67) [n(%)]		17 (41,5)	38 (17,7)	0,001*
Gender				
Female [n(%)]	188 (73)	32 (78)	156 (72,6)	0,466
Male [n(%)]	68 (26,6)	9 (21,9)	59 (27,4)	0,466
Hypertension [n(%)]	117 (45,7)	23 (56,1)	94 (43,7)	0,145
Smoking [n(%)]	31 (12,1)	5 (12,2)	26 (12,1)	0,985
Dyslipidemia [n(%)]	79 (30,8)	12 (29,3)	67 (31,2)	0,810

*p<0,05

There were 256 subjected recruited. The prevalence of PAD in our study was 16% (41 of 256 subjects). The mean age of the subjects with PAD were 64,3 years (SD± 10,4) and mean age of the subjects without PAD were 58.64 years (SD:9,6). There were 78% (32/41 subjects) in females and 21,9% (9/41 subjects) in males with PAD. Among 41 subjects with PAD there were 56,1% (23/41 subjects) with hypertension, 12,2% (5/41 subjects) with smoking history, 29,3% (12/41 subjects) with dyslipidemia, otherwise among 215 subjects without PAD there were 43,7% (94/215 subjects) with hypertension, 12,1% (26/215 subjects) with smoking history, 31,2% (67/215 subjects) with dyslipidemia. For bivariate analysis, subjects with age more than 67 years old were significantly associated with PAD occurrence (P=0,001) while other risk factors such as age less than 67 years old, gender, hypertension, smoking, and dyslipidemia were not associated with PAD occurrence. Demographic data of diabetes subjects comparing between PAD and non-PAD group were shown in Table 1.

Multivariable analysis was done to predict which risk factors increase the incidence of PAD. We included age>67 years old as covariable because the comparative analysis revealed that there was a significant difference between PAD and non-PAD groups. As shown in Table 2, our analysis showed that only age>67 years old independently predicts PAD (OR 3.591, 95% CI: 1.694-7.614, p = 0.001). Although covariables hypertension and female gender have odds ratio greater than one, these results are not statistically significant with a p-value of 0.275 and 0.154, respectively.

Table 2. Multivariable analysis to predict PAD

Covariables	OR	95% CI	P-value
Smoking	0.954	0.326-2.791	0.931
Dyslipidemia	0.860	0.401-1.841	0.697
Hypertension	1.481	0.732-2.999	0.275
Female	1.865	0.791-4.394	0.154
Age >67	3.591	1.694-7.614	0.001

Discussion

This study was held in primary care setting. Prevalence of PAD on this study were 41 (16%) subjects. Earlier studies on primary care setting that was held in Thailand (7,2%) and Ecuador (13,9%) showed nearly the same prevalence of PAD with higher population. (Barrera-Guarderas, Carrasco-Tenezaca and De la Torre-Cisneros, 2020; Suwannasrisuk et al., 2020).

The mean age of patients with PAD were 59,5 years (SD: 10,4) years. There was significant relationship between age and PAD in older population. This study in consistency with other study that showed PAD was common in older population (>65 years old) (Li et al., 2012). Wang et al showed that in elderly population with type 2 DM in Wuhan, PAD prevalence was 15,5% among patients aged 60-69 years, 30% among patients aged 70-79 years, and 48,6% among patients older than 80 years. Thus, increasing the age would increase the incidence of PAD (Wang et al., 2011).

In this study, females had a higher frequency of PAD than males (Ali et al., 2012). There were no significant differences among PAD and non-PAD prevalence in female subjects (p = 0,47). This is consistence with other published study that reported no significant differences in the prevalence of PAD between males and females in diabetic subjects (Makdisse et al., 2007). Smoking is one of the important risk factors for PAD in the general population. The low prevalence of smoking (12%) could be associated with the high number of females subjects. We did not find any significant association between current smoking activity and PAD, a similar finding with other studies (Tseng, 2003; Agboghoroma, Akemokwe and Puepet, 2020). This study did not classify the lifetime history of smoking period. Earlier studies showed that type 2 DM participants who suffered from PAD were found to be had a longer duration of smoking than non-PAD subjects (Eason et al., 2005; Rhee et al., 2007).

This study observed that the prevalence of hypertension and dyslipidemia were high in both PAD and non-PAD groups. Hypertension can increase the risk of developing lower extremity PAD in population (Agboghoroma, Akemokwe and Puepet, 2020). Some studies have shown no significant association [Rabia and Khoo, 2007]. Our study did not find any significant

association between hypertension or dyslipidaemia and PAD.

Conclusions

The prevalence of PAD was 16% in type 2 DM among 256 patients. Age more than 67 years old was the strong risk factor while the other risk factors were common for PAD in patients with type 2 DM. With the aging of type 2 diabetes mellitus population, it seems likely that PAD will be increased. Diagnosis of PAD by Toe Brachial Index was not assessed in this study. TBI is reported has better sensitivity than ABI, however in clinical practice, it has several acquirements before tested because its sensitivity of temperature causing high number of false positive result. Further studies are needed to overcome this clinical practice problem.

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Disclosures and Ethics

As a requirement of publication author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations in: authorship, conflicts of interest, privacy and confidentiality and protection of human and animal research subjects.

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