Original Article

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Survival Rates in Peripheral Artery Disease

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Objective: The aim of this study was to analyze the long-term survival of subjects with peripheral artery disease (PAD).
Methods: The data included 415 Korean PAD patients aged ≥20 years hospitalized from 1994 through 2004 at a single tertiary center in Korea. Death data were obtained from all participants between 1994 and 2009.
Results: The mean of age was 64.4±9.3 years in PAD. The proportion of peripheral vascular bypass operation (re-vascularized) was about 50%. The proportion of males was 90.6% in PAD. Five- and 10- year survival rates were 79.2% and 60.5% in PAD, respectively. The 5- and 10- year survival rates were 83.0% and 64.1% in re-vascularized group, and 75.5% and 56.3% in non-revascularized group ($p<0.05$). For PAD, the adjusted hazard ratios (HRs) were 1.75 (95% confidence interval (CI) 1.17-2.68) in over 65 years, 1.53 (95% CI 1.05-2.27) in diabetes, and 2.21 (95% CI 1.51-3.23) in chronic kidney disease (CKD). Interestingly, HRs in PAD were 0.55 (95% CI 0.34-0.84) in overweight and 0.45 (95% CI 0.25-0.76) in obesity.
Conclusions: The 5- and 10- year survival rates were 79.2% and 60.5% in PAD. The survival rate in re-vascularized group was higher than that in non-revascularized group. Independent predictors of mortality were age, diabetes, and CKD in PAD. Obesity showed improved survival rates. **(J Lipid Atheroscler 2017 June;6(1):39-45)**

Key Words: Peripheral artery disease, Survival rates

INTRODUCTION

Atherosclerosis is one of the main causes of death with peripheral artery disease (PAD). Notably, atherosclerotic disease mortality has increased due to the aging population and the increasingly westernized life-style in Korea.[1] PAD patients with more than 50% of peripheral artery stenosis showed ankle brachial index (ABI) <0.9. They showed the intermittent claudication, gangrene of extremities, and pain caused by arterial atherosclerosis progression. The pain for a long time was caused insomnia at day and night that was put them to mental instability and uncomfortable daily life. If PAD has progressed a lot, they also were struggle muscle atrophy and depression because of limitation of activity and impossible exercises. However, few studies have analyzed long-term survival of the status of PAD progress much. Therefore, our objectives in the present study were to analyze long-term survival in subjects with progressed PAD.

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METHODS

This study is the extension study of 'Comparison of cardiovascular risk factors for peripheral artery disease and coronary artery disease in the Korean population'.[2] Study population, cardiovascular risk factors, and study design have been previously described in detail.

1. Study Population and Design

Briefly, we reviewed the records of patients diagnosed with PAD at the Cardiac and Vascular Center, Samsung Medical Center, Seoul, Korea, from November 1994 to November 2004. The subjects were patients with PAD (n=415) with over 50% peripheral artery stenosis confirmed by lower extremities computed tomography. We categorized the patients into two groups; one is peripheral vascular bypass operation (revascularized, n=218) group, and the other is non-revascularization group. Clinical information was obtained retrospectively by reviewing electronic medical charts and death data were offered by the Korea Statistics Promotion Institute. The all-cause cumulative fatality rate and survival duration were assessed in this study. We analyzed death data from Dec. 1994 until Dec. 2009. All-cause mortality was measured over 5 to 15 years. The Samsung Medical Center institutional review board approved this study. Informed consent was waived for this retrospective study.

2. DIAGNOSTIC CRITERIA

1) Cardiovascular risk factors

Subjects were defined as having hypertension (HT) if they were taking anti-hypertensive drugs had been clinically diagnosed with HT, had either a systolic blood pressure (SBP) ≥140 mmHg, or a diastolic blood pressure (DBP) ≥90 mmHg. Subjects meeting the following criteria were defined as having diabetes mellitus (DM): taking an oral hyperglycemic agent, using insulin, clinical diagnosis of DM, or a fasting plasma glucose >125 mg/dL. Subjects were defined as having dyslipidemia if they met one of the following requirements: diagnosis of hyperlipidemia, previous treatment of hyperlipidemia, total cholesterol>200 mg/dL or low density lipoprotein cholesterol>130 mg/dL. The following body mass index (BMI = weight (kg)/height (m^2)) categories were recognized: normal (18.5≤BMI<23), overweight (23≤BMI<25), and obese (BMI≥25).[3] Patients who had smoked within one year prior to the study were defined as smokers. The estimated glomerular filtration rate (eGFR), which was used as an indicator of kidney function, was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[4] The CKD-EPI equation, expressed as a single equation, is $GFR = 141 \times \min(\text{serum Cr}/\kappa, 1)^{\alpha} \times \max(\text{serum Cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female], where κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum serum Cr /κ or 1, and max indicates the maximum serum Cr /κ or 1. Chronic kidney disease (CKD) was defined as an eGFR <60 mL/min/1.73m^2. We also showed distribution of anti- platelet, anti-coagulants, prostaglandin 1, angiotensin- converting-enzyme inhibitor and/or angiotensin II receptor blocker, beta-blocker, calcium channel blocker, diuretics and/or spironolactone, lipid lowering agents, and oral hyperglycemia agents or insulin in PAD.

3. Statistical analysis

General and clinical characteristics were shown by mean (± standard deviation; SD) for continuous variables and percentage for categorical variables. The Kaplan-Meier method was used to compare cardiovascular risk factors survival differences for PAD using the log-rank test. Multiple Cox proportional hazard analyses were performed and adjusted variables were age, sex, HT, DM, dyslipidemia, smoking, obesity grade, and CKD.

Table 1. General and clinical characteristics in the peripheral artery disease (PAD) patients groups (n=415)

Variables	PAD n=415
Age (years) mean±SD	64.4±9.3
<65 years	46.5
≥65 years	53.5
Sex (male, %)	90.6
SBP (mmHg)	141.2±22.8
DBP (mmHg)	80.2±12.3
Cholesterol (mg/dL)	
Total cholesterol	176.9±43.4
Triglyceride	163.6±119.4
Low density lipoprotein	112.4±36.6
High density lipoprotein	39.7±10.5
Fasting plasma glucose (mg/dL)	141.5±61.3
Hemoglobin (g/dL)	13.0±1.9
Creatinine (mg/dL)	1.19±0.9
estimated Glomerular Filtration Rate	75.8±1.20
Hypertension (%)	75.2
Diabetes (%)	56.6
Dyslipidemia (%)	44.3
Body mass index (kg) mean±SD	23.0±2.9
Overweight	26.8
Obese	22.1
Smoking (%)	68.1
Chronic kidney disease (%)	24.3
Medication	
Anti-platelet	74.7
Anti-coagulants	30.9
Prostaglandin 1	48.2
Angiotensin-converting-enzyme inhibitor and/or angiotensin II receptor blocker	33.0
Beta-blocker	17.7
Calcium channel blocker	27.6
Diuretics and/or spironolactone	16.6
Lipid lowering agents	47.7
Oral hyperglycemia agents or insulin	16.8
Peripheral revascularization	52.5

Table 2. Associations between clinical variables and overall mortality in patients with peripheral artery disease (PAD)

Variables	PAD* HR and 95% CI	*p* value
Age, 65+ vs. <65 year	1.75 (1.17-2.68)	0.007
Sex, male vs. female	0.88 (0.51-1.63)	0.674
Hypertension	1.46 (0.91-2.46)	0.134
Diabetes	1.53 (1.05-2.27)	0.029
Dyslipidemia	0.70 (0.48-1.01)	0.061
Smoking	1.01 (0.68-1.53)	0.963
Body mass index		
Normal	1.0	
Overweight	0.55 (0.34-0.84)	0.009
Obese	0.45 (0.25-0.76)	0.004
Chronic kidney disease	2.21 (1.51-3.23)	<0.001

*Estimated by Cox proportional hazard model analysis using the variables indicated in the table.

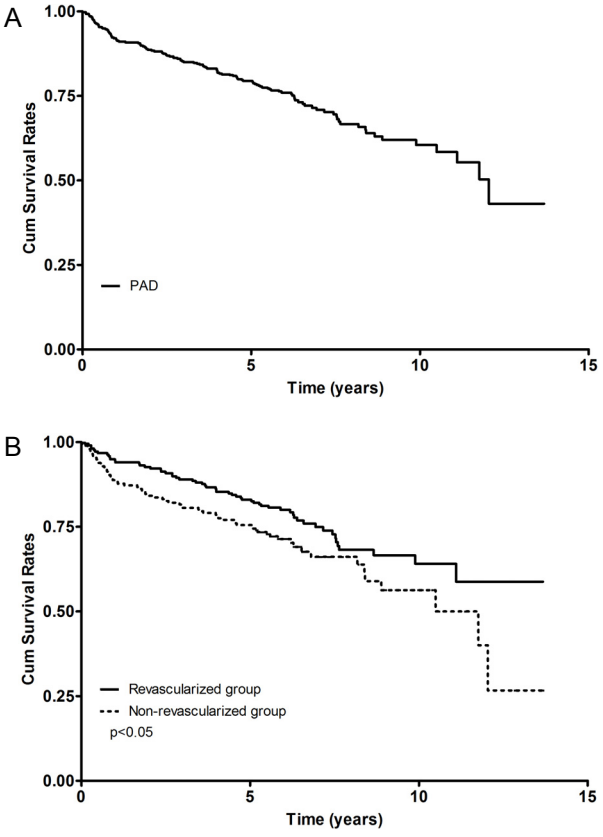

Fig. 1. (A) Cumulative survival rates of the peripheral artery disease (PAD) group and (B) cumulative survival rates with revascularization or not in PAD using Kaplan-Meier curves.

RESULTS

The mean of PAD patients' age was 64.4±9.3 years. The proportion of males was 90.6% for PAD. The proportion of peripheral revascularized group was 52.5% (Table 1).

For the PAD group, the adjusted Hazard ratios (HRs) were 1.75 (95% confidence interval (CI) 1.17-2.68) in patients over 65 years of age, 1.53 (95% CI 1.05-2.27)

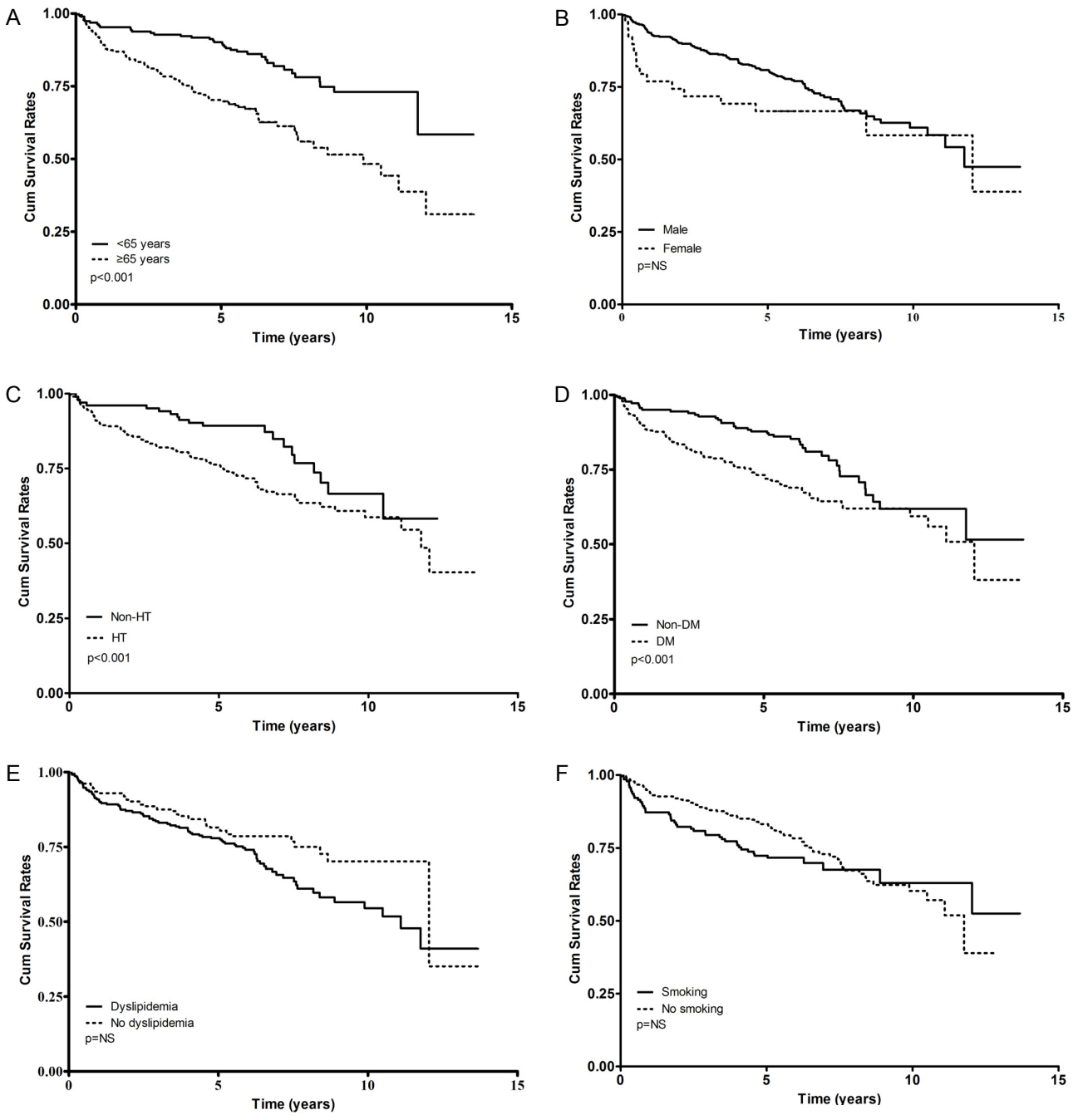

Fig. 2. (A) Cumulative survival rates by over 65 years old and under with peripheral artery disease (PAD) using Kaplan-Meier curves (p<0.001), (B) cumulative survival rates by gender with PAD using Kaplan-Meier curves (p<0.001), (C) cumulative survival rates in hypertension (HT) patients with PAD using Kaplan-Meier curves (p<0.001), (D) cumulative survival rates in diabetes mellitus (DM) patients with PAD using Kaplan-Meier curves (p<0.001), (E) cumulative survival rates in dyslipidemia patients with PAD using Kaplan-Meier curves (p<0.001), (F) cumulative survival rates in smoker with PAD using Kaplan-Meier curves (p<0.001)

in patients with diabetes, and 2.21 (95% CI 1.51-3.23) in patients with CKD. Interestingly, in PAD, HRs were 0.55 (95% CI 0.34-0.84) in overweight patients and 0.45 (95% CI 0.25-0.76) in obese patients (Table 2).

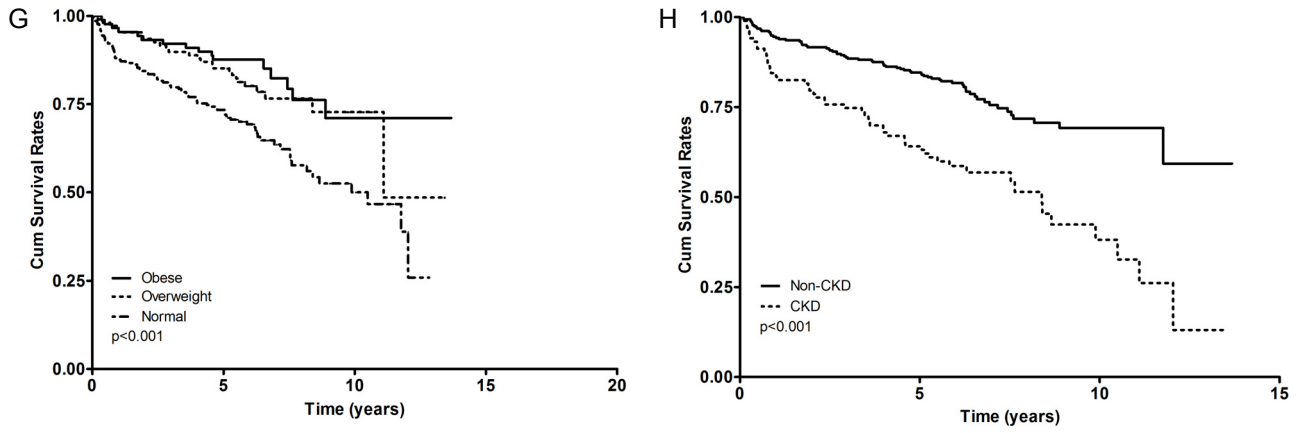

Fig. 2. (G) cumulative survival rates among obese, overweight, and normal weight patients with PAD using Kaplan–Meier curves (p<0.001), and (H) cumulative survival rates in chronic kidney disease (CKD) patients with PAD using Kaplan–Meier curves (p<0.001)

In patients with PAD, the 5- and 10-year survival rates were 79.2% and 60.5%, respectively. The 5- and 10-year survival rates were 83.0% and 64.1% in revascularized group and in 75.5% and 56.3% in non-revascularized group (p<0.05) (Fig. 1).

The 5- and 10-year survival rates were 90.2% and 73.0% in under 65 year-old group and in 70.3% and 48.3% in greater than 65 year-old group (p<0.001); 89.3% and 66.6% in non-HT group and 76.3% and 58.7% in HT group (p<0.001); 87.8% and 61.9% in non-DM group and 73.2% and 59.4% in DM group (p<0.001); 87.6% and 71.1% in obese, 81.2% and 72.8% in overweight, and 73.4% and 50.0% in normal (p<0.001); 84.6% and 69.2% in non-CKD and 86.4% and 38.1% in CKD (p<0.001) (Fig. 2).

DISCUSSION

Overall, we found that the survival rates were about 80% at the 5- and 60% at 10-years. For PAD, the survival rate in the peripheral revascularized group was higher than that in non-revascularized group. Results of the present study correspond well with those of the earlier studies. The mortality rate for patients with PAD with intermittent claudication is approximately 30% at 5 years, 50% at 10 years, and 70% at 15 years, without any clear decrease in mortality in the time spanning from 1975 to 1998, according to western studies.[5] The follow-up study of 10 years in southern California, United States showed 61.8% of PAD mortality.[6] Bypass versus angioplasty in severe ischemia of the leg (BASIL) clinical trial showed similar overall survival outcomes between a bypass-surgery-first and a balloon-angioplasty-first strategy.[7] In our study, the survival rates in the peripheral revascularized group was higher than non-revascularized group. Although our study does not show any surprising result, it still provides meaningful information about the survival rates based on the peripheral revascularization. There are few studies done on the survival rates based on the peripheral revascularization.

We demonstrated the independent predictors of fatality in PAD. Age,[8] diabetes,[9,10] and CKD[11,12] are risk factors for PAD. Interestingly, being overweight or obese resulted in lower HRs in PAD.

Although obesity is one of the major risk factors for cardiovascular disease (CVD), including PAD[13] and cardiovascular death,[14] a paradoxical decrease in death with increasing BMI has been found. This is partly explained by the obesity paradox.[15,16] Specifically, patients with CAD or PAD show an inversely correlated relationship between

BMI and cardiovascular mortality after adjusting for confounding variables, according to the Fatores Riesgo ENfermedad Arterial (FRENA) registry[17] and the Cooperative Cardiovascular Project.[18] In Japanese patients, lower BMI with PAD resulted in higher all-cause mortality than that of normal, overweight, and obese PAD patients.[10] Their reported J-shaped curve of BMI grade and 5-year mortality was in close agreement with our results (Fig. 2(G)). In this study, the proportion of >65 years with PAD was over 50%. Jee et al.[19] showed that the mortality rate did not increase for elderly Korean individuals with BMI of 25 or higher. And the effect of obesity on mortality in the elderly can be influenced by various parameters such as existing diseases. Accordingly, we could not confirm whether this obesity based on BMI survival difference was real or due to the obesity paradox.[20]

This study showed the survival rates by cardiovascular risk factors for PAD. The group of over 65 years old, HT, DM, normal body weight, and CKD showed significant lower survival rates than that of below 65 years old, non-HT, non-DM, overweight or obese, and non-CKD group, respectively.

This study had several limitations. First, the study was conducted retrospectively at a single center, which may have resulted in selection bias. Also, we were unable to eliminate the possibility of information bias when collecting medical records and laboratory results. Second, we checked the current smoking status, body weight, and clinical data only once, when patients first visited the hospital in this retrospective study. Therefore, there were no available follow-up data. Third, death data in this study were collected from the Korea Statistics Promotion Institute. They did not provide cause of death information, in accordance with their provisions. Thus, we could not specify the number of cardiac events. In the future, a well-designed prospective hospital-based cohort study will be necessary.

CONCLUSIONS

We found that the 5- and 10- year survival rates were 79.2% and 60.5% in PAD. The survival rates in peripheral revascularized group were higher than that in non-revascularized group. For PAD, the independent predictors of fatality were age, diabetes, and CKD. Obesity showed improved survival rates.

REFERENCES

1. Statistics Korea. The statistics of death cause in 2013 [Internet]. Daejeon: Statistics Korea; 2014 [accessed on 1 March 2017]. Available from: http://kostat.go.kr/.
2. Jang SY, Ju EY, Cho SI, Lee SW, Kim DK. Comparison of cardiovascular risk factors for peripheral artery disease and coronary artery disease in the Korean population. Korean Circ J 2013;43:316-328.
3. Weisell RC. Body mass index as an indicator of obesity. Asia Pac J Clin Nutr 2002;11:S681-S684.
4. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139:137-147.
5. Dormandy J, Heeck L, Vig S. The natural history of claudication: risk to life and limb. Semin Vasc Surg 1999;12:123-137.
6. Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. N Engl J Med 1992;326:381-386.
7. Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet 2005;366:1925-1934.
8. Cang Y, Li J, Li YM, Zhou Y, Wu YZ, Li XK, et al. Relationship of a low ankle-brachial index with all-cause mortality and cardiovascular mortality in Chinese patients with metabolic syndrome after a 6-year follow-up: a Chinese prospective cohort study. Intern Med 2012; 51:2847-2856.

9. Ademi Z, Liew D, Gorelik A, Bohensky M, Zomer E, Hollingsworth B, et al. Predictors of health care use among patients with or at high risk of atherothrombotic disease: two-year follow-up data. Int J Cardiol 2014;175:72-77.
10. Kumakura H, Kanai H, Aizaki M, Mitsui K, Araki Y, Kasama S, et al. The influence of the obesity paradox and chronic kidney disease on long-term survival in a Japanese cohort with peripheral arterial disease. J Vasc Surg 2010;52:110-117.
11. Wang Y, Guo X, Li J, Hu D, Zhao D, Ma H, et al. Predictive value of ankle-brachial index to all-cause mortality and cardiovascular mortality in Chinese patients with chronic kidney disease. Vasa 2012;41:205-213.
12. Luo Y, Li X, Li J, Wang X, Xu Y, Qiao Y, et al. Peripheral arterial disease, chronic kidney disease, and mortality: the Chinese Ankle Brachial Index Cohort Study. Vasc Med 2010;15:107-112.
13. Kim S, Popkin BM. Commentary: understanding the epidemiology of overweight and obesity--a real global public health concern. Int J Epidemiol 2006;35:60-67.
14. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. JAMA 2005;293:1861-1867.
15. Galal W, van Gestel YR, Hoeks SE, Sin DD, Winkel TA, Bax JJ, et al. The obesity paradox in patients with peripheral arterial disease. Chest 2008;134:925-930.
16. Romero-Corral A, Montori VM, Somers VK, Korinek J, Thomas RJ, Allison TG, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. Lancet 2006;368:666-678.
17. Barba R, Bisbe J, Pedrajas JN, Toril J, Monte R, Muñoz-Torrero JF, et al. Body mass index and outcome in patients with coronary, cerebrovascular, or peripheral artery disease: findings from the FRENA registry. Eur J Cardiovasc Prev Rehabil 2009;16:457-63.
18. Lea JP, Crenshaw DO, Onufrak SJ, Newsome BB, McClellan WM. Obesity, end-stage renal disease, and survival in an elderly cohort with cardiovascular disease. Obesity (Silver Spring) 2009;17:2216-2222.
19. Jee SH, Sull JW, Park J, Lee SY, Ohrr H, Guallar E, et al. Body-mass index and mortality in Korean men and women. N Engl J Med 2006;355:779-787.
20. Jang SY, Shin YI, Kim DY, Sohn MK, Lee J, Lee SG, et al. Effect of obesity on functional outcomes at 6 months post-stroke among elderly Koreans: a prospective multicentre study. BMJ Open 2015;5:e008712.