

Ultrasound-based prevalence of polyvascular disease and its association with adverse outcome in patients undergoing coronary artery bypass grafting

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Abstract

Objective: Polyvascular disease (polyVD) often coexists with coronary artery disease (CAD). We aim to investigate the prevalence of polyVD using the method of ultrasound and find its association with adverse outcomes in coronary artery bypass grafting (CABG) patients. **Methods:** This retrospective and cross-sectional study included 1344 patients with a mean age of 61.4 years. Presence of peripheral artery atherosclerotic plaque and stenosis was assessed using the method of ultrasound. Receiver operating characteristic (ROC) analysis and multivariate logistic regression analysis were performed to investigate the association of polyVD with in-hospital all-cause death. **Results:** 52.1% of the patients had polyVD and among which 31.9% had one additional arterial bed involvement and 20.2% had two or three additional arterial beds involvement. Patients with two or three involved arterial beds had worse baseline characteristics. In-hospital all-cause death rate increased with the number of involved arterial beds (1.1% in patients with only CAD vs 3.7% in patients with two or three involved arterial beds), and this trend was more prominent in elderly patients. Multivariate logistic regression analysis confirmed that polyVD patients with two or three involved arterial beds had about three times the risk for all-cause death. **Conclusions:** Prevalence of polyVD assessed by ultrasound was high in CABG patients and it was significantly associated with in-hospital all-cause death. Our study may provide additive information for preoperative risk stratification in CABG patients.

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Keywords

Polyvascular disease (polyVD), carotid artery, vertebrate artery, lower extremity artery, coronary artery bypass grafting

Introduction

Polyvascular disease (polyVD) is defined as atherosclerotic lesions in at least two arterial beds such as coronary artery, carotid artery, and lower extremity artery.¹ Recently, patients with polyVD have been categorized as “very high-risk,” and polyVD is gaining extensive attention.² Studies have been conducted on the prevalence of polyVD in various populations. Most recently, Pan and colleagues³ reported the prevalence and vascular distribution of multiterritorial atherosclerotic plaque and stenosis in an old community-dwelling population.

Cardiovascular disease (CVD) has been correlated with systemic atherosclerotic vascular disease which raised the interest of screening polyVD in this population.⁴ The prognosis of CVD patients with multi arterial beds involvement is significantly worse than those without polyVD.^{2,5,6} Meizels et al.⁷ found that acute myocardial infarction (AMI) patients with PolyVD represented a significantly higher in-hospital mortality. Similarly, Arai and colleagues⁸ reviewed 3411 AMI patients and reported that polyVD was significantly associated with 1-year all-cause death. Recently, Bansal and colleagues⁹ reviewed 443 thousand patients with severe aortic stenosis undergoing transcatheter aortic valve replacement (TAVR) and found that polyVD is associated with worse outcomes, and the risk is highest in patients with three vascular beds involvement.

Carotid and lower extremity arteries are frequently used to implicate systemic vascular atherosclerosis involvement.^{1,10} In previous studies, magnetic resonance imaging (MRI) and ankle-brachial index (ABI) were frequently used to evaluate carotid artery disease and lower extremity artery disease, respectively.^{3,11} However, the application of MRI in carotid artery screening is limited in daily clinical use due to its time-consuming feature and expensiveness.¹² When detecting lower extremity artery disease, ABI could be falsely high in the presence of arterial wall calcification, a condition often observed in patients with severe cardiovascular disease.¹³ As a convenient, cheap, and time-saving method, ultrasound makes it possible to reveal peripheral artery atherosclerotic lesions directly and accurately.^{14,15} Few studies evaluated polyVD using the method of ultrasound in CABG patients. Our previous study¹⁶ is the first known to report the association of lipoprotein(a) with lower extremity artery disease diagnosed by ultrasound in a CABG population.

In this study, our aims include (1) to investigate the prevalence of polyVD, (2) to investigate the prevalence of plaque and arterial stenosis in different vascular territories, and (3) to find the association of polyVD with in-hospital all-cause death in a CABG population.

Methods

Patients

In this retrospective cross-sectional study, we reviewed 1500 consecutive patients undergoing CABG in the Department of Cardiology at Beijing Anzhen Hospital between 2018.1 and 2020.1. After excluding patients with incomplete or missing data, 1344

patients were finally included. All patients had established severe coronary artery disease (CAD). The patients were divided into groups G1, G2, and G3 according to the number of arterial beds involvement: G1 included patients with only CAD; G2 included patients with CAD and one peripheral arterial bed (either carotid, vertebrate, or lower extremity artery) involvement; G3 included patients with CAD and two or three peripheral arterial beds involvement. Patients ≥ 65 years were defined as the elderly group, and patients < 65 years were defined as the young group. The flow chart of the study is shown in Figure 1.

Baseline characteristics including age, sex, family history of CAD, smoking history, hypertension (HTN) history, and diabetes mellitus (DM) history were collected from hospital records. Venous blood samples were obtained from fasting patients early in the morning. Beckman AU5400 (US) and Cobas8000 c701 (GER) automatic biochemical analyzers were used to measure novel and traditional lipid parameters and biochemical indicators, including small dense low-density lipoprotein (sdLDL-C), Lp(a), total cholesterol (TCHO), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG). The Sysmex XE-2100 was used to determine complete blood counts. The measurements were all accomplished following the manufacturer's instructions.

Triglycerides and glucose (TyG) index was calculated as $\ln [\text{TG (mg/dl)} \times \text{fasting plasma glucose (mg/dL)} / 2]$,¹⁷ and TyG-BMI was calculated as $\text{TyG} \times \text{BMI (kg/m}^2\text{)}$.¹⁸ CKD was defined as having a history of renal failure or an admission estimated glomerular filtration rate (eGFR) $< 60 \text{ mL/min/1.73 m}^2$ according to modification of diet in renal disease (MDRD) formula.¹⁹ In-hospital all-cause death was chosen as the main adverse outcome and was defined as death from any cause during the period of hospitalization.

Each patient received preoperative peripheral vascular ultrasound examination (carotid, vertebrate and lower extremity peripheral arteries). Carotid and vertebral artery examination

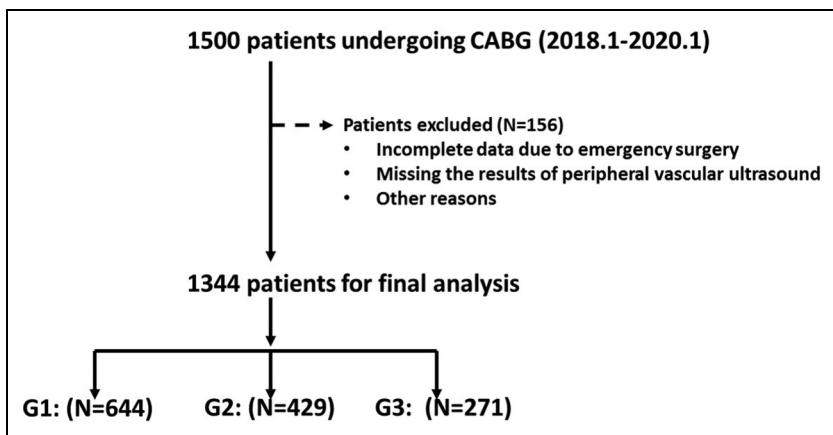


Figure 1. Flow chart of the study.

Abbreviations: CAD: coronary artery disease; polyVD: polyvascular disease; CABG: coronary artery bypass grafting. G1 included patients with only CAD; G2 included patients with CAD and 1 peripheral arterial territory (either carotid, vertebrate or lower extremity artery) involvement; G3 included patients with CAD and 2 or 3 peripheral arterial territories involvement.

included extracranial segments of carotid artery (common carotid artery and internal carotid artery) and extracranial segments of vertebral artery. Lower extremity artery examination included femoral (common femoral artery and superficial femoral artery), popliteal, posterior tibia, and anterior tibia arteries. All images were acquired with Philips (Bothell, WA, USA), GE (Waukesha, Wisconsin, USA) or Hitachi (Tokyo, Japan) ultrasound imaging system by certified experienced ultrasound clinicians. Atherosclerotic plaque is defined as the presence of focal wall thickening that is at least 50% greater than that of the surrounding artery wall.¹⁴ Carotid artery stenosis (CAS) was defined as $\geq 50\%$ diameter stenosis of internal or common carotid artery.²⁰ Vertebrate artery stenosis (VAS) was defined as $\geq 50\%$ diameter stenosis according to local guideline. Lower extremity artery disease (LEAD) is defined as $\geq 50\%$ diameter stenosis of artery segments from femoral artery to tibial artery.^{15,21} For each artery bed $\geq 50\text{--}69\%$ diameter stenosis was defined as moderate stenosis, and $\geq 70\%$ diameter stenosis (includes occlusion) was defined as severe stenosis.⁹

The reporting of this study conforms to STROBE guidelines.²²

Statistical analysis

Continuous variables were assessed for normality using Shapiro-Wilk test and were described as mean \pm standard deviation if normally distributed. For continuous variables not normally distributed, results were expressed as median with interquartile range. Categorical variables were described as numbers and percentages. For continuous variables, results were compared among the groups using one-way ANOVA followed by LSD post-hoc comparison. For categorical variables, comparisons among the groups were performed using the chi-square test. Receiver operating characteristic (ROC) analysis was performed to analyze the association of polyVD with in-hospital all-cause death in the overall patients and subgroups. Multivariate logistic regression analysis was used to investigate potential risk factors for in-hospital all-cause death in the overall patients and subgroups. Analyses were performed using SPSS 26.0 (SPSS, Chicago, IL, USA); $p < .05$ was considered statistically significant.

Ethics approval statement

The protocol of this study was performed in accordance with the ethical standards of the 1975 Declaration of Helsinki and its later amendments in 2013. The study was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University as an observational and retrospective study (Date: 1/15/2024; Number: 2024148X). The committee waived the need for informed consent from the patients for the retrospective nature of this study. All patient details have been de-identified.

Results

Baseline characteristics

The overall patients ($N = 1344$) had a mean age of 61.4 ± 8.5 years and male patients accounted for 76.1%. 700 patients (52.1%) had polyVD: 429 patients (31.9%) had one additional arterial bed involvement and 271 patients (20.2%) had two or three additional

arterial beds involvement. Prevalence of polyVD was 53.4% in men and 48.0% in women (Shown in Table 1). Prevalence of polyVD in the elderly patients was higher (65.2%) than that in the young patients (43.0%)(Shown in Table 2).

Patients with polyVD had worse baseline characteristics. Age, prevalence of HTN history, DM history, and smoking history increased with the number of involved arterial beds. Left ventricular ejection fraction (LVEF) and eGFR decreased with the number of involved arterial beds. Uric acid (UA), glucose (Glu), TCHO, LDL-C, sd-LDL, and hs-CRP levels increased with the number of involved arterial beds (with or without significance). The proportion of patients with elevated Lp(a) also had similar trend among the three groups. TyG and TyG-BMI were comparable among the groups (shown in Table 1).

In the elderly patients (≥ 65 years), the trends of age, smoking history, and blood lipid levels remained, but prevalence of HTN and DM history and eGFR were comparable among the groups. In the young patients (< 65 years), trends of most of the cardiovascular risk factors remained. Patients with polyVD had higher prevalence of CAD family history although the difference was not significant (shown in Table 2).

Prevalence of plaque and arterial stenosis in different vascular territories

Prevalence of atherosclerotic plaque: Atherosclerotic plaque was frequently observed in carotid artery (96.9%) and lower extremity artery (87.6%). The prevalence of plaque was only 18.7% in extracranial vertebrate artery. Generally, plaque prevalence was higher in men and the elderly patients (shown in Table 3).

Prevalence of CAS and VAS: 24.4% of the patients had $\geq 50\%$ CAS and 6.9% had $\geq 70\%$ CAS. In general, prevalence of CAS of the elderly patients outnumbered that of young patients. However, young women had higher prevalence of CAS compared with young men. Although plaque was not frequently seen in extracranial vertebrate artery, 10.9% of the patients had $\geq 50\%$ stenosis and 4.8% had $\geq 70\%$ stenosis (results are shown in Table 3, Figure 2, and Figure 3).

Prevalence of LEAD: The population had a high prevalence of stenosis in lower extremity artery territory. Approximately half of the patients (40.8%) had $\geq 50\%$ lower extremity artery stenosis and 31.9% had $\geq 70\%$ stenosis. The stenosis was more likely to appear in tibial arteries: prevalence of $\geq 50\%$ tibial artery stenosis outnumbered that of femoral popliteal artery (37.2% vs 23.1%); the prevalence of $\geq 70\%$ tibial artery stenosis was far more higher than that of femoral popliteal artery (30.6% vs 4.8%). For both femoral popliteal and tibial territories, men generally had higher prevalence of stenosis ($\geq 50\%$ and $\geq 70\%$) than women (shown in Table 3 and Figures 2 and 3).

Association of polyVD with in-hospital all-cause death

In the overall patients, in-hospital all-cause death rate was significantly higher in G3 compared with the other groups (3.7% vs 1.1% and 0.7%, $p = .009$) (shown in Table 1). All-cause death rates were comparable between patients with only cerebral vascular stenosis (carotid, vertebrate or both) and patients with only lower extremity artery stenosis (0.7% vs 0.7%) (shown in Table S1). In the elderly patients, G3 had the highest

Table 1. Baseline characteristics of the patients.

	All (N = 1344)	G1 (N = 644)	G2 (N = 429)	G3 (N = 271)	p Value
Age (year)	61.4 ± 8.5	59.0 ± 8.9	63.4 ± 7.3 ^b	64.2 ± 7.5 ^a	<.001
Male	1023 (76.1%)	477 (74.1%)	321 (74.8%)	225 ^{ac} (83.0%)	.011
BMI (kg/m ²)	25.6 ± 3.1	25.8 ± 3.2	25.5 ± 3.2	25.3 ± 3.0 ^a	.060
Family history of CAD (%)	54 (4.0%)	26 (4.0%)	16 (3.7%)	12 (4.4%)	.900
HTN history (%)	892 (66.4%)	400 (62.1%)	295 (68.8%) ^b	197 (72.7%) ^a	.004
DM history (%)	536 (39.9%)	218 (33.9%)	195 (45.5%) ^b	123 (45.4%) ^a	<.001
Insulin (%)	137 (10.2%)	49 (7.6%)	56 (13.1%) ^b	32 (11.8%) ^a	.010
AF history (%)	34 (2.5%)	13 (2.0%)	11 (2.6%)	10 (3.7%)	.339
MI history (%)	320 (23.8%)	165 (25.6%)	96 (22.4%)	59 (21.8%)	.321
Stroke or TIA history (%)	254 (18.9%)	100 (15.5%)	88 (20.5%) ^b	66 (24.4%) ^a	.005
Previous PCI and stent (%)	204 (15.2%)	108 (16.8%)	60 (14.0%)	36 (13.3%)	.287
CKD history (%)	9 (0.7%)	2 (0.3%)	7 (1.6%) ^b	0 ^c	.009
Smoking history (%)	682 (50.7%)	302 (46.9%)	226 (52.7%)	154 (56.8%) ^a	.014
WBC (G/L)	6.83 ± 1.68	6.79 ± 1.76	6.84 ± 1.63	6.92 ± 1.57	.570
NLR	2.53 ± 1.35	2.52 ± 1.51	2.47 ± 1.11	2.65 ± 1.31	.221
CREA (μmol/L)	71.1 ± 14.8	70.6 ± 14.7	71.3 ± 15.6	72.3 ± 13.5	.296
eGFR (ml/min/1.73m ²)	93.6 ± 12.8	95.4 ± 12.7	92.0 ± 13.2 ^b	91.8 ± 12.0 ^a	<.001
UA (μmol/L)	337.1 ± 85.9	337.2 ± 84.4	334.5 ± 86.6	340.7 ± 88.4	.653
Glu (mmol/L)	5.76 (5.08, 7.34)	5.63 (5.00, 6.94)	5.90 (5.13, 7.75) ^b	5.94 (5.15, 7.51)	.022
TG (mmol/L)	1.35 (1.02, 1.88)	1.38 (1.03, 1.96)	1.35 (1.04, 1.82)	1.30 (0.96, 1.76)	.126
TyG	8.85 ± 0.64	8.85 ± 0.63	8.88 ± 0.65	8.81 ± 0.63	.403
TyG-BMI	666.6 ± 165.3	676.9 ± 169.2	662.0 ± 165.4	649.3 ± 154.4 ^a	.054
TCHO (mmol/L)	4.08 ± 1.09	4.08 ± 1.06	4.04 ± 1.10	4.16 ± 1.13	.397
HDL-C (mmol/L)	1.04 ± 0.26	1.04 ± 0.25	1.04 ± 0.29	1.04 ± 0.23	.996
LDL-C (mmol/L)	2.48 ± 0.93	2.45 ± 0.92	2.44 ± 0.89	2.59 ± 0.99 ^{ac}	.077
Sd-LDL (mmol/L)	0.73 ± 0.34	0.73 ± 0.34	0.73 ± 0.32	0.76 ± 0.37	.500
LP(a) ≥ 30 mg/dL	287 (28.5%)	126 (26.5%)	98 (29.8%)	63 (31.2%)	.378
hs-CRP (mg/L)	1.60 (0.60,4.28)	1.30 (0.52, 4.20)	1.75 (0.67, 4.37)	1.95 (0.71, 4.43)	.061
Preoperative LVEF (%)	59.6 ± 8.8	60.3 ± 8.7	59.1 ± 8.7 ^b	58.9 ± 9.2 ^a	.027

(Continued)

Table 1. (continued)

	All (N = 1344)	G1 (N = 644)	G2 (N = 429)	G3 (N = 271)	p Value
In-hospital all-cause death	20 (1.5%)	7 (1.1%)	3 (0.7%)	10 (3.7%) ^{ac}	.009
In-hospital cardiac death	16 (1.2%)	6 (0.9%)	3 (0.7%)	7 (2.6%)	.092
In-hospital myocardial infarction	1 (0.1%)	0	0	1 (0.4%)	.138
In-hospital stroke	16 (1.2%)	6 (0.9%)	5 (1.2%)	5 (1.8%)	.537

Abbreviations: BMI: body mass index; CAD: coronary artery disease; HTN: hypertension; DM: diabetes mellitus; AF: atrial fibrillation; MI: myocardial infarction; TIA: transient ischemic attack; PCI: percutaneous coronary intervention; CKD: chronic kidney disease; WBC: white blood cell; NLR: neutrophil-to-lymphocyte ratio; CREA: creatinine; eGFR: Estimated glomerular filtration rate; UA: uric acid; Glu: glucose; TG: triglyceride; TyG: triglycerides and glucose index; TyG-BMI: TyG-BMI index; TCHO: total cholesterol; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; Sd-LDL: small dense low density lipoprotein; Lp(a): lipoprotein(a); hs-CRP: high sensitive c-reactive protein; LVEF: left ventricular ejection fraction; CAS: carotid artery stenosis; VAS: vertebrate artery stenosis; LEAD: lower extremity artery disease. G1 included patients with only CAD; G2 included patients with CAD and 1 peripheral arterial beds (either CAS, VAS, or LEAD) involved; G3 included patients with CAD and 2 or 3 peripheral arterial beds involved. Character a: significant post hoc comparison between G3 and G1; Character b: significant post hoc comparison between G2 and G1; Character c: significant post hoc comparison between G2 and G3.

Table 2. Baseline characteristics of the subgroups by age.

	≥65 years		N = 551		<65 years		N = 793		p Value	p Value
	GI (N = 192)	G2 (N = 222)	G3 (N = 137)	p Value	GI (N = 452)	G2 (N = 207)	G3 (N = 134)			
Age (year)	69.0 ± 3.5	68.9 ± 3.8	69.9 ± 4.3 ^{ac}	0.032	54.8 ± 6.9	57.5 ± 5.4 ^b	58.3 ± 5.2 ^a	<.001		
Male (%)	118(61.5%)	146(65.8%)	113(82.5%) ^{bc}	p < 0.001	359(79.4%)	175(84.5%)	112(83.6%)	.230		
BMI (kg/m ²)	25.5 ± 3.2	25.5 ± 3.3	25.3 ± 3.1	0.762	26.0 ± 3.2	25.6 ± 3.0	25.3 ± 2.9 ^a	.071		
Family history of CAD (%)	9(4.7%)	10(4.5%)	4(2.9%)	0.696	170(37.4%)	6(2.9%)	8(6.0%)	.349		
HTN history (%)	130(67.7%)	156(70.3%)	100(73.0%)	0.585	270(59.7%)	139(67.1%)	97(72.4%) ^a	.014		
DM history (%)	67(34.9%)	98(44.1%)	61(44.5%)	0.102	151(33.4%)	97(46.9%) ^b	62(46.3%) ^a	.001		
Insulin (%)	17(8.9%)	25(11.3%)	18(13.1%)	0.457	32(7.1%)	31(15.0%) ^b	14(10.4%)	.006		
AF history (%)	7(3.6%)	8(3.6%)	7(5.1%)	0.743	6(1.3%)	3(1.4%)	3(2.2%)	.768		
MI history (%)	40(20.8%)	52(23.4%)	27(19.7%)	0.673	125(27.7%)	44(21.3%)	32(23.9%)	.196		
Stroke or TIA history (%)	39(20.3%)	44(19.8%)	36(26.3%)	0.305	61(13.5%)	44(21.3%) ^b	30(22.4%) ^a	.009		
Previous PCI and stent (%)	26(13.5%)	26(11.7%)	16(11.7%)	0.822	82(18.1%)	34(16.4%)	20(14.9%)	.652		
CKD history (%)	1(0.5%)	5(2.3%)	0	0.087	1(0.2%)	2(1.0%)	0	.261		
Smoking history (%)	65(33.9%)	94(42.3%)	65(47.4%) ^a	0.038	237(52.4%)	132(63.8%) ^b	89(66.4%) ^a	.002		
WBC (G/L)	6.62 ± 1.82	6.67 ± 1.61	6.87 ± 1.53	0.380	6.86 ± 1.73	7.01 ± 1.64	6.97 ± 1.61	.523		
NLR	2.64 ± 2.12	2.51 ± 1.16	2.67 ± 1.29	0.591	2.47 ± 1.15	2.43 ± 1.05	2.63 ± 1.34	.257		
CREA (μmol/L)	70.4 ± 15.6	71.0 ± 15.3	73.4 ± 12.9	0.180	70.7 ± 14.3	71.5 ± 16.0	71.1 ± 14.1	.792		
eGFR(ml/min/1.73m ²)	87.2 ± 10.7	87.3 ± 11.8	87.4 ± 10.3	0.993	98.8 ± 11.9	97.1 ± 12.7	96.4 ± 11.9 ^a	.066		
UA (μmol/L)	377.8 ± 81.1	326.8 ± 84.4	337.1 ± 83.9	0.484	341.3 ± 85.5	342.9 ± 88.4	344.4 ± 93.0	.931		
Glu (mmol/L)	5.66 (4.99, 6.69)	5.85 (5.13, 7.56)	5.99 (5.19, 7.24)	0.643	5.62 (5.00, 7.09)	5.92 (5.11, 7.99) ^b	5.92 (5.13, 7.75) ^a	.007		
TG (mmol/L)	1.26 (0.92, 1.65)	1.27 (1.01, 1.81)	1.19 (0.87, 1.59)	0.100	1.49 (1.09, 2.10)	1.43 (1.08, 1.85)	1.47 (1.08, 1.91)	.577		
TyG	8.74 ± 0.62	8.83 ± 0.62	8.71 ± 0.63	0.158	8.90 ± 0.63	8.94 ± 0.69	8.92 ± 0.62	.808		
TyG-BMI	658.1 ± 162.9	661.5 ± 173.0	647.6 ± 159.8	0.736	685.0 ± 171.4	662.5 ± 157.2	651.0 ± 149.3 ^a	.060		
TCHO (mmol/L)	3.87 ± 0.83	4.00 ± 1.06	4.11 ± 1.09 ^a	0.096	4.17 ± 1.14	4.09 ± 1.15	4.21 ± 1.16	.641		
HDL-C (mmol/L)	1.09 ± 0.25	1.04 ± 0.24 ^b	1.07 ± 0.26	0.104	1.02 ± 0.24	1.04 ± 0.33	1.00 ± 0.19	.495		
LDL-C (mmol/L)	2.26 ± 0.69	2.39 ± 0.87	2.54 ± 0.96 ^a	0.009	2.54 ± 0.99	2.50 ± 0.92	2.64 ± 1.03	.419		
Sd-LDL (mmol/L)	0.64 ± 0.25	0.68 ± 0.31	0.71 ± 0.34 ^a	0.103	0.76 ± 0.36	0.77 ± 0.33	0.80 ± 0.40	.580		
LP(a) ≥ 30 mg/dL	38(26.6%)	51(29.7%)	35(32.7%)	0.571	88(26.4%)	47(29.9%)	28(29.5%)	.670		
hs-CRP (mg/L)	1.20 (0.46, 4.25)	1.46 (0.55, 4.32)	1.90 (0.70, 4.45)	0.309	1.35 (0.54, 4.19)	2.16 (0.79, 4.52)	2.10 (0.70, 4.39)	.046		
Preoperative LVEF (%)	61.8 ± 7.2	60.4 ± 7.6	59.7 ± 8.8 ^a	0.038	59.7 ± 9.3	57.6 ± 9.6 ^b	58.2 ± 9.5	.023		

(Continued)

Table 2. (continued)

	≥65 years			<65 years			p Value	p Value
	G1 (N = 192)	G2 (N = 222)	G3 (N = 137)	G1 (N = 452)	G2 (N = 207)	G3 (N = 134)		
In-hospital all-cause death	1(0.5%)	1(0.5%)	7(5.1%) ^{bc}	6(1.3%)	2(1.0%)	3(2.2%)	0.003	.634
In-hospital cardiac death	0	1(0.5%) ^{ac}	5(3.6%) ^{ac}	6(1.3%)	2(1.0%)	2(1.5%)	0.005	.893
In-hospital myocardial infarction	0	0	1(0.7%)	0	0	0	0.248	-
In-hospital stroke	2(1.0%)	2(0.9%)	3(2.2%)	4(0.9%)	3(1.4%)	2(1.5%)	0.573	.749

Abbreviations: BMI: body mass index; CAD: coronary artery disease; HTN: hypertension; DM: diabetes mellitus; AF: atrial fibrillation; MI: myocardial infarction; TIA: transient ischemic attack; PCI: percutaneous coronary intervention; CKD: chronic kidney disease; WBC: white blood cell; NLR: neutrophil-to-lymphocyte ratio; CREA: creatinine; eGFR: estimated glomerular filtration rate; UA: uric acid; Glu: glucose; TyG: triglyceride; TyG: triglycerides and glucose index; TyG-BMI: TyG-BMI index; TCHO: total cholesterol; HDL-C: high density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; Sd-LDL: small dense low-density lipoprotein; Lp(a): lipoprotein(a); hs-CRP: high sensitive c-reactive protein; LVEF: left ventricular ejection fraction; CAS: carotid artery stenosis; VAS: vertebrate artery stenosis; LEAD: lower extremity artery disease. G1 included patients with only CAD; G2 included patients with CAD and 1 peripheral arterial beds (either CAS, VAS, or LEAD) involved; G3 included patients with CAD and 2 or 3 peripheral arterial beds involved. Character a: significant post hoc comparison between G3 and G1; Character b: significant post hoc comparison between G2 and G1; Character c: significant post hoc comparison between G2 and G3.

Table 3. Prevalence of plaque and stenosis of various arterial territories in subgroups by age and sex.

Plaque	≥50% Stenosis				≥70% Stenosis				
	<65 years		≥65 years		<65 years		≥65 years		
	All	All	All	All	All	All	All		
Carotid artery									
All	1303/1344(96.9%)	755/793(95.2%)	548/551(99.5%)	328/1344(24.4%)	173/793(21.8%)	155/551(28.1%)	93/1344(6.9%)	54/793(6.8%)	39/551(7.1%)
Men	993/1023(97.1%)	618/646(95.7%)	375/377(99.5%)	253/1023(24.7%)	139/646(21.5%)	114/377(30.2%)	69/1023(6.7%)	43/646(6.7%)	26/377(6.9%)
Women	310/321(96.6%)	137/147(93.2%)	173/174(99.4%)	75/321(23.4%)	34/147(23.1%)	41/174(23.6%)	24/321(7.5%)	11/147(7.5%)	13/174(7.5%)
Vertebrate artery									
All	251/1344(18.7%)	125/793(15.8%)	126/551(22.9%)	147/1344(10.9%)	69/793(8.7%)	78/551(14.2%)	64/1344(4.8%)	31/793(3.9%)	33/551(6.0%)
Men	211/1023(20.6%)	106/646(16.4%)	105/377(27.9%)	128/1023(12.5%)	59/646(9.1%)	69/377(18.3%)	57/1023(5.6%)	25/646(3.9%)	32/377(8.5%)
Women	40/321(12.5%)	19/147(12.9%)	21/174(12.1%)	19/321(5.9%)	10/147(6.8%)	9/174(5.2%)	7/321(2.2%)	6/147(4.1%)	1/174(0.6%)
Lower extremity artery									
All	1178/1344(87.6%)	678/793(85.5%)	500/551(90.7%)	548/1344(40.8%)	259/793(32.7%)	289/551(52.5%)	429/1344(31.9%)	193/793(24.3%)	236/551(42.8%)
Men	906/1023(88.6%)	561/646(86.8%)	345/377(91.5%)	435/1023(42.5%)	224/646(34.7%)	211/377(56.0%)	338/1023(33.0%)	167/646(25.9%)	171/377(45.4%)
Women	272/321(84.7%)	117/147(79.6%)	155/174(89.1%)	113/321(35.2%)	35/147(23.8%)	78/174(44.8%)	91/321(28.3%)	26/147(17.7%)	65/174(37.4%)
Femoral popliteal artery									
All	311/1344(23.1%)	161/793(20.3%)	150/551(27.2%)	311/1344(23.1%)	161/793(20.3%)	150/551(27.2%)	65/1344(4.8%)	30/793(3.8%)	35/551(6.4%)
Men	245/1023(23.9%)	134/646(20.7%)	111/377(29.4%)	245/1023(23.9%)	134/646(20.7%)	111/377(29.4%)	52/1023(5.1%)	24/646(3.7%)	28/377(7.4%)
Women	66/321(20.6%)	27/147(18.4%)	39/174(22.4%)	66/321(20.6%)	27/147(18.4%)	39/174(22.4%)	13/321(4.0%)	6/147(4.1%)	7/174(4.0%)
Anterior or posterior tibial artery									
All	500/1344(37.2%)	227/793(28.6%)	273/551(49.5%)	500/1344(37.2%)	227/793(28.6%)	273/551(49.5%)	411/1344(30.6%)	182/793(22.9%)	229/551(41.6%)
Men	400/1023(39.1%)	200/646(31.0%)	200/377(53.1%)	400/1023(39.1%)	200/646(31.0%)	200/377(53.1%)	326/1023(31.9%)	159/646(24.7%)	167/377(44.3%)
Women	100/321(31.2%)	27/147(18.4%)	73/174(42.0%)	100/321(31.2%)	27/147(18.4%)	73/174(42.0%)	85/321(26.5%)	23/147(15.6%)	62/174(35.6%)

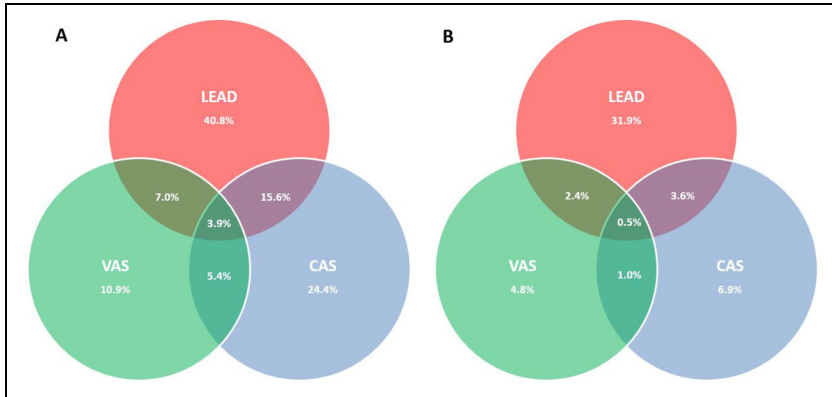


Figure 2. Prevalence of stenosis in various arterial beds: (A) $\geq 50\%$ stenosis; (B) $\geq 70\%$ stenosis. The figure showed the prevalence of $\geq 50\%$ and $\geq 70\%$ stenosis in carotid, vertebrate, and lower extremity arteries. The LEAD prevalence was higher than the other 2 arteries for both $\geq 50\%$ and $\geq 70\%$ stenosis. Abbreviations: CAS: carotid artery stenosis; VAS: vertebrate artery stenosis; LEAD: lower extremity artery disease.

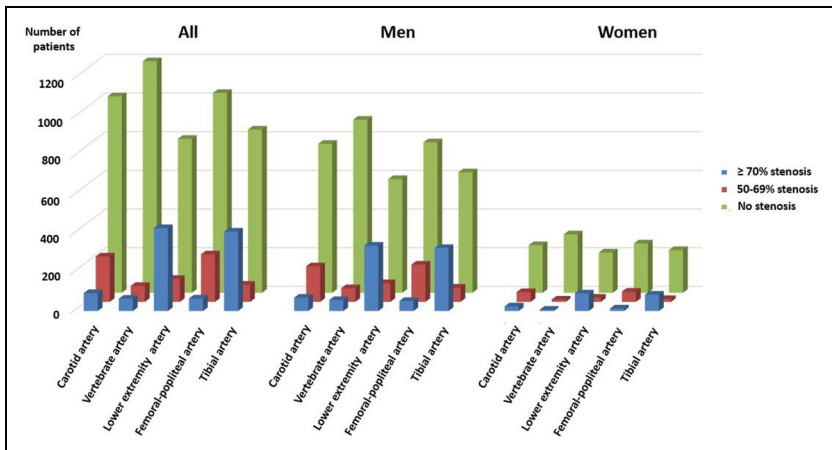


Figure 3. Prevalence of stenosis in various arterial beds in the overall patients, men and women. The figure showed the stenosis was frequently observed in carotid and lower extremity arteries in both sexes. Among patients with lower extremity artery stenosis, most of the stenosis was observed in tibial segments. Tibial segments were also more likely to have severe stenosis than femoral popliteal segments.

in-hospital all-cause death rate (5.1% vs 0.5% and 0.5%, $p = .003$). ROC analysis showed that AUC of affected artery number was 0.761 (95%CI: 0.601, 0.921; $p = .007$). In young patients, all-cause death rate in G3 was still the highest among the three groups but without significance (2.2% vs 1.3% and 1.0%, $p = .609$) (shown in Table 2 and Table S2). Multivariate logistic regression confirmed that polyVD was an independent

risk factor for in-hospital all cause death in the overall patients. Patients in G3 (with two or three peripheral arterial beds involvement) had about three times higher risk of in-hospital death compared with G1 (with only coronary artery involvement) [OR, 3.013, 95%CI (1.075, 8.445), $p = .036$].

Discussion

We are the first known to investigate the prevalence of polyVD using the method of ultrasound in a CABG population. The main findings are as follows: (1) PolyVD is common among CABG patients: 52.1% of the patients had at least one additional arterial bed involvement and 20.2% had two or three additional arterial beds involvement; (2) In-hospital all-cause death rate increased with the number of involved arterial beds, and this trend was more obvious in the elderly (≥ 65 years) group; (3) Atherosclerotic plaque and stenosis were frequently observed in carotid artery and lower extremity artery.

Numerous studies have reported the high prevalence of polyVD in CAD patients and the results varied due to the heterogeneity of the population and diagnostic method. Syed and colleagues²³ reported that 35% of acute coronary syndrome (ACS) patients had concomitant cerebral vascular disease, LEAD, or both. Song and colleagues²⁴ reported polyVD was present in nearly 30% of CABG patients. Our data showed that the prevalence of polyVD in CABG patients was 52.1% which was higher than previous result. One of the possible reasons might be that we chose a different method. Ultrasonic device makes it possible to reveal the lesion directly and clearly. Thus, asymptomatic stenosis that had invisible impact on ABI (frequently used by most studies) could be detected by ultrasonic device. Additionally, some study reported sex-based disparity of polyVD prevalence.²¹ Our data showed the prevalence of polyVD is similar between men and women in this population. We assume the reason might be that most female patients in our study were in a postmenopausal status.

Atherosclerosis is a systemic disease and involvement of one arterial territory indicates involvement of other arterial territories.²⁵ The presence of CAD often coexists with atherosclerotic lesions in other arterial beds.^{1,26,27} Our result confirmed the high prevalence of plaque and stenosis in different artery territories in CABG patients (with established CAD) and the ultrasound-based result provided supplementary information to this field. Additionally, previous study proposed the distribution disparity of polyVD in various populations.³ Our data showed that LEAD was more frequently observed, and tibial lesions contributed greatly to the prevalence of LEAD. As we mentioned before, the application of ultrasound-based method made it possible to reveal stenosis which maybe neglected by ABI examination. Although the importance of preoperative examination of carotid artery has been proposed,²⁸ lower extremity artery examination is not a routine according to the guidelines of CABG which should not be underestimated according to our result.

Correlation between polyVD and increased risk of adverse outcomes among CAD patients has been well established.^{29,30} In our data, all-cause death rate was 1.1% in patients with only CAD and 3.7% in patients with two or three additional arterial beds involvement. Results from both ROC analysis and multivariate logistic regression analysis confirmed the significant correlation between number of affected vascular beds

and all-cause death and this correlation was more obvious in the elderly patients. Our result was consistent with previous researchers^{8,31,32} who proposed the number of arterial beds affected might be a potential risk factor for adverse outcome. Additionally, Weissler et al.³³ reported the difference of adverse outcomes in different polyVD phenotypes. They found patients with CAD and LEAD had the worst outcome. However, we found all-cause death rates of patients with CAS/VAS and patients with LEAD were of no significant difference.

There are possible explanations for the association of polyVD with adverse outcomes. First, patients with polyVD often have a greater burden of cardiovascular risk factors including smoking, HTN history, DM history and high level of various biomarkers.^{11,34–38} In our study, we also found patients with two or three vascular territories involvement had higher prevalence of HTN and DM history. Song and colleagues²⁴ proposed that high Lp(a) was independently associated with polyvascular disease in CABG patients. Tmoyan and colleagues³⁹ included 1288 healthy subjects and proposed Lp(a), hs-CRP, circulating immune complexes, and neutrophil-to-lymphocyte ratio (NLR) were associated with the stenotic atherosclerosis of different vascular beds. We also found various biomarkers including UA, LDL-C, sd-LDL, hs-CRP levels and proportion of patients with elevated Lp(a) increased with the number of involved arterial beds (with or without significance). Additionally, it has been reported that polyVD patients had prominent microvascular endothelial dysfunction which may be an essential characteristic except the already present systemic atherosclerosis. Thus, the existence of peripheral microvascular endothelial dysfunction might contribute to the poor outcomes of polyVD patients.³⁵

Our study has several limitations. First, this is an observational study and inherent limitations could not be avoided. In addition, we did not evaluate long-term adverse outcome and future study is needed; Secondly, the impact of medication history on the prevalence of polyVD and adverse outcomes was not included, but we assume this would not influence the final result of the study; Third, in-hospital all-cause death was around 1% in our data. Although this is consistent with previous studies, the low incidence of death rate may have influenced the power. However, the focus of our study was to report the prevalence of polyVD in a certain population; The next limitation was that we only included extracranial segments of carotid and vertebrate artery for analysis. Thus, the prevalence of carotid and vertebrate artery atherosclerosis in our data may be underestimated. However, we provided sufficient information and confirmed the association of polyVD and adverse outcome. The fifth limitation was that in our data most patients were male. Although in CABG patients male always outnumbered female, this may have introduced bias.

Conclusion

In conclusion, we reported a high prevalence of polyVD assessed by ultrasound in a CABG population and atherosclerotic plaque and stenosis were frequently observed in carotid artery and lower extremity artery. We found in-hospital all-cause death increased with the number of arterial beds involvement and this trend was more obvious in the elderly patients. For preoperative evaluation of CABG patients, physicians always pay attention to the severity of coronary artery stenosis as well as carotid artery stenosis. Our study may have provided additive information and proposed the necessity of examining various arterial territories preoperatively in this population.

Authors' contributions

Junyi Gao: conceptualization, formal analysis, methodology, writing-original draft. Yi Cheng: data curation, formal analysis, writing-review and editing.

Data availability statement

The data of this study are available from the corresponding author upon reasonable request.

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Supplemental material

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