Long-term Clinical Outcomes of Peripheral Arterial Disease Patients Who Underwent Routine Coronary Angiography and Subsequent Percutaneous Coronary Angiography for Severe Coronary Artery Disease

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Disclosure

- Nothing to disclose

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Background

- Peripheral arterial disease (PAD) reduces the quality of life and a coronary artery disease (CAD) is a leading cause of death in many geographies of the world.

Ouriel *et.al*. JAMA 2001;286:1380-1381
Regensteiner *et.al*. Vasc Med 2008;13:15-24.
Roth *et.al*. J Am Coll Cardiol 2017;70:1-25

- Severe CAD has been observed in 54% to 69% of patients with PAD.

Faglia *et.al*. Eur J Vasc Endovasc Surg 2005;29:620-627
Lee *et.al*. J invasive cardiol 2015;27:213-217
Nishijima *et.al*. Plast Reconstr Surg Glob Open 2017;5:e1377

Background

- Patients with PAD particularly have high mortality rates from cardiovascular events. Thus, patients with both PAD and CAD are expected to have a particularly poor long-term prognosis.

Jeremias et.al. Am J Cardiol 2010;105:1268-1271.
Faglia et.al. J Cardiovasc Med (Hagerstown) 2008;9:1030-1036.
Parikh *et.al.* Am J Cardiol 2011;107:959-964.

- Long-term clinical outcomes of symptomatic PAD patients who underwent percutaneous transluminal angioplasty (PTA) who also underwent routine coronary angiography (CAG) and subsequent percutaneous coronary intervention (PCI), if clinically indicated, are not fully elucidated yet.

Lee et.al. J invasive cardiol 2015;27:167-171.

Purpose

- We previously reported the one-year outcomes of the strategy of routine CAG and PCI in patients with PAD who underwent PTA.

Lee et.al. J invasive cardiol 2015;27:167-171.

- In the present study, we evaluated the long-term clinical outcomes of this treatment paradigm.

Methods (1)

- ## Study population
  - ✓ A total of 674 consecutive PAD patients who underwent successful PTA and CAG were enrolled.

- ## Definition of CAD
  - ✓ CAD was defined as angiographic stenosis ≥ 50% and significant CAD as ≥ 70% stenosis.
  - ✓ Total CAD was defined as significant CAD or prior coronary revascularization.

Methods (2)

- Study Definition and Groups
  - ✓ Patients were divided into two groups according to the presence or absence of CAD

> **The CAD group** **(n=413)**
>
> **The non-CAD group** **(n=261)**

Methods (3)

- Study endpoints

  ✓ Primary endpoints were **MACCE** as the composite of total death, MI, stroke, revascularization such as PCI and CABG at 5-year follow-up

  ✓ Secondary endpoints were **Target lesion revascularization (TLR), Target extremity revascularization (TER)**, and **target extremity surgery (TES)** after PTA at 5-year clinical follow-up.

Statistics

1. For continuous variables, differences between the two groups were evaluated using the unpaired t-test or Mann-Whitney rank test. Data were expressed as mean ± standard deviations.

2. For discrete variables, differences were expressed as counts and percentages and analyzed with the χ2 or Fisher's exact test between two groups.

3. To adjust for any potential confounders, propensity score matching (PSM) analysis was performed using the logistic regression model.

4. Matching was performed with a 1:1 matching protocol using the nearest neighbor matching algorithm with a caliper width less than 0.01 the standard deviation of the propensity score, yielding 160 well-matched pairs.

5. Clinical outcomes that occurred over a period of 5 years were analyzed by Kaplan-Meier analysis, and differences between groups were compared with the log-rank test before and after PSM.

6. For all analyses, a two-sided $p < 0.05$ was considered statistically significant. All data were analyzed using SPSS (version 20.0, SPSS-PC, Inc. Chicago, Illinois).

Results (1)

Table. Baseline characteristics of the entire cohort and propensity-matched groups.

Variable, N (%)	All patients				Matched patients			
	CAD (n=413 Pts)	Non-CAD (n=261 Pts)	P value	S.diff	CAD (n=160 Pts)	Non-CAD (n=160 Pts)	P value	S.diff
Sex, male	314 (76.0)	204 (78.1)	0.523	0.24	125 (78.1)	123 (76.8)	0.789	-0.14
Age, years	69.1 ± 9.1	66.3 ± 12.5	0.012	0.26	67.9 ± 9.6	68.8 ± 11.1	0.210	-0.08
Body mass index, kg/m^2	23.1 ± 3.3	23.3 ± 3.2	0.350	-0.08	23.4 ± 3.2	23.4 ± 3.1	0.483	0.02
Final diagnosis								
Diabetic foot ulcer	239 (57.8)	139 (53.2)	0.240	-0.62	96 (60.0)	94 (58.7)	0.820	-0.16
Wound	258 (62.4)	166 (63.6)	0.767	0.14	105 (65.6)	103 (64.3)	0.815	-0.16
Gangrene	138 (33.4)	88 (33.7)	0.935	0.05	57 (35.6)	47 (29.3)	0.233	-1.10
Claudication	73 (17.6)	56 (21.4)	0.224	0.86	31 (19.3)	32 (20.0)	0.888	0.14
Resting pain	44 (10.6)	34 (13.0)	0.348	0.69	21 (13.1)	19 (11.8)	0.735	-0.35
Risk Factors								
Hypertension	302 (73.1)	178 (68.1)	0.169	-0.59	113 (70.6)	117 (73.1)	0.619	0.30
Diabetes mellitus	317 (76.7)	169 (64.7)	0.001	-1.43	122 (76.2)	115 (71.8)	0.372	-0.51
Strokes	90 (21.7)	44 (16.8)	0.118	-1.12	31 (19.3)	33 (20.6)	0.780	0.28
Chronic renal insufficiency	132 (31.9)	67 (25.6)	0.081	-1.17	56 (35.0)	52 (32.5)	0.636	-0.43
Congestive heart failure	29 (7.0)	14 (5.3)	0.391	-0.67	11 (6.8)	12 (7.5)	0.829	0.23
History of smoking	213 (51.5)	148 (56.7)	0.193	0.70	81 (50.6)	83 (51.8)	0.823	0.18
Current of smoking	118 (28.5)	108 (41.3)	0.001	2.17	46 (28.7)	48 (30.0)	0.806	0.23
History of alcohol drinking	131 (31.7)	107 (40.9)	0.014	1.54	52 (32.5)	55 (34.3)	0.722	0.32
Currently alcohol drinking	80 (19.3)	76 (29.1)	0.003	1.98	29 (18.1)	32 (20.0)	0.669	0.43

Data are presented as N (%) or mean ± standard deviation. CAD, coronary artery disease; S.diff, standardized difference

Results (2)

Table. Coronary angiographic and clinical limb characteristics.

Variable, N (%)	All patients				Matched patients			
	CAD (n=413 Pts) (n=545 Limb)	Non-CAD (n=261 Pts) (n=313 Limb)	P value	S.diff	CAD (n=160 Pts) (n=197 Limb)	Non-CAD (n=160 Pts) (n=201 Limb)	P value	S.diff
Coronary artery information (No. patients)								
Treated CAD	296 (71.6)	0 (0.0)	< 0.001	-12.02	113 (70.6)	0 (0.0)	< 0.001	-11.93
PCI	283 (68.5)	0 (0.0)	< 0.001	-11.75	107 (66.8)	0 (0.0)	< 0.001	-11.60
PCI in PTA	214 (51.8)	0 (0.0)	< 0.001	-10.21	84 (52.5)	0 (0.0)	< 0.001	-10.27
Peripheral artery information, limbs								
Ankle brachial index	0.67 ± 0.37	0.72 ± 0.38	0.223	-0.12	0.67 ± 0.40	0.66 ± 0.42	0.863	0.03
Limb site (Right)	289 (53.0)	149 (47.6)	0.126	-0.77	99 (50.2)	96 (47.7)	0.619	-0.36
Rutherford grade, limbs			0.060	-1.58			0.740	1.00
Grade 2	180 (33.0)	114 (36.4)			77 (39.0)	80 (39.8)		
Grade 3	167 (30.6)	85 (27.1)			55 (27.9)	51 (25.3)		
Location, limbs								
Iliac artery	164 (30.0)	81 (25.8)	0.188	-0.80	59 (29.9)	52 (25.8)	0.364	-0.77
Femoral artery	272 (49.9)	128 (40.8)	0.011	-1.34	96 (48.7)	87 (43.2)	0.276	-0.80
Anterior tibial artery	254 (46.6)	156 (49.8)	0.361	0.47	98 (49.7)	106 (52.7)	0.551	0.42
Posterior tibial artery	210 (38.5)	111 (35.4)	0.371	-0.51	69 (35.0)	72 (35.8)	0.868	0.13
Peroneal artery	105 (19.2)	56 (17.8)	0.620	-0.32	40 (20.3)	41 (20.3)	0.982	0.02

Data are presented as N (%) or mean ± standard deviation. CAD, coronary artery disease; S.diff, standardized difference; CABG, coronary artery bypass graft surgery; PCI, percutaneous coronary intervention; PTA, percutaneous transluminal angioplasty

Results (3)

Table. Post-procedural medications..

Variable, N (%)	All patients				Matched patients			
	CAD (n=413 Pts)	Non-CAD (n=261 Pts)	P value	S.diff	CAD (n=160 Pts)	Non-CAD (n=160 Pts)	P value	S.diff
In-hospital complications								
Acute limb ischemia	5 (1.2)	7 (2.6)	0.230	1.05	1 (0.6)	3 (1.8)	0.623	1.12
Acute renal failure	9 (2.1)	3 (1.1)	0.386	-0.80	3 (1.8)	3 (1.8)	> 0.99	0.00
Congestive heart failure	3 (0.7)	0 (0.0)	0.287	-1.21	-	-	-	
Strokes	1 (0.2)	3 (1.1)	0.304	1.09	0 (0.0)	2 (1.2)	0.498	1.58
Hemorrhagic	0 (0.0)	1 (0.3)	0.387	0.88	0 (0.0)	1 (0.6)	> 0.99	1.12
Ischemic	1 (0.2)	2 (0.7)	0.563	0.74	0 (0.0)	1 (0.6)	> 0.99	1.12
Post-procedural medications								
Aspirin	405 (98.0)	254 (97.3)	0.523	-0.08	155 (96.8)	155 (96.8)	> 0.99	0.00
Clopidogrel	379 (91.7)	224 (85.8)	0.014	-0.63	142 (88.7)	142 (88.7)	> 0.99	0.00
Cilostazol	179 (43.3)	118 (45.2)	0.634	0.28	62 (38.7)	69 (43.1)	0.426	0.69
Ticlopidine	3 (0.7)	0 (0.0)	0.287	-1.21	-	-	-	
Anplag	100 (24.2)	51 (19.5)	0.156	-1.00	25 (15.6)	33 (20.6)	0.246	1.18
ARBs	176 (42.6)	106 (40.6)	0.608	-0.31	72 (45.0)	65 (40.6)	0.429	-0.67
ACEIs	86 (20.8)	19 (7.2)	< 0.001	-3.62	15 (9.3)	16 (10.0)	0.850	0.20
Calcium channel blocker	182 (44.0)	106 (40.6)	0.377	-0.53	60 (37.5)	69 (43.1)	0.305	0.89
β-blocker	143 (34.6)	54 (20.6)	< 0.001	-2.65	38 (23.7)	41 (25.6)	0.697	0.38
Diuretic	116 (28.0)	58 (22.2)	0.090	-1.17	39 (24.3)	39 (24.3)	> 0.99	0.00

Results (4)

Table. Kaplan–Meier curve analysis of clinical outcomes and log-rank test results

Variables, N (%)	All patients			Matched Patients		
	CAD (n=413 Pts)	Non-CAD (n=261 Pts)	Log Rank	CAD (n=160 Pts)	Non-CAD (n=160 Pts)	Log Rank
Five-year clinical outcomes						
Total death	51 (12.3)	25 (9.5)	0.266	13 (8.1)	21 (13.1)	0.153
Cardiac death	12 (2.9)	2 (0.7)	0.058	5 (3.1)	2 (1.3)	0.263
Myocardial infarction	12 (3)	3 (1.1)	0.130	2 (1.2)	2 (0.6)	0.989
STEMI	5 (1.2)	1 (0.3)	0.263	1 (0.6)	1 (0.6)	0.998
Coronary revascularization	36 (9.3)	2 (0.8)	< 0.001	13 (8.5)	0 (0.0)	< 0.001
Stroke	17 (4.4)	15 (5.9)	0.345	8 (5.2)	10 (6.5)	0.587
MACCE	88 (21.3)	39 (14.9)	0.042	28 (17.5)	29 (18.1)	0.874
Variables, N (%)	CAD (n=545 Limb)	Non-CAD (n=313 Limb)	Log Rank	CAD (n=197 Limb)	Non-CAD (n=201 Limb)	Log Rank
Peripheral revascularization						
Target lesion	80 (15.6)	57 (19.3)	0.221	33 (17.3)	37 (19.7)	0.593
Target extremity	86 (16.8)	62 (21.0)	0.168	36 (18.9)	41 (21.7)	0.491
Target extremity surgery						
Above the knee amputations	1 (0.1)	3 (1.0)	0.111	0 (0.0)	2 (1.0)	0.157
Above the ankle amputations	23 (4.4)	15 (4.9)	0.704	5 (2.6)	10 (5.1)	0.187
Below the ankle amputations	102 (19.2)	47 (15.4)	0.150	44 (22.5)	32 (16.4)	0.121
Major adverse limb events	161 (30.6)	93 (30.6)	0.813	65 (33.3)	62 (32)	0.705

Data are presented as incidence (%). CAD, coronary artery disease; STEMI; ST-segment elevation myocardial infarction; MACCE, major adverse cerebrovascular and cardiac events

Summary

- The main finding of this study is that routine CAG and subsequent PCI for significant CAD is safe and resulted in similar long-term survival in PAD patients without CAD who underwent PTA at long-term follow-up.

- Not surprisingly, repeat PCI was performed more frequently in PAD patients with CAD at long-term follow-up.

Limitations

- First, we analyzed data retrospectively, and PSM analysis was performed to minimize confounding factors, which could have affected our results. The registry was also designed as an all-comers prospective registry from 2006. However, we could not adjust for all limiting factors not shown in medical records or collected through telephone contact.

- Second, all subjects in this study underwent CAG, and therefore our results are not generalizable to patients who do not receive CAG.

- Third, all the PAD patients with significant CAD patients did not undergone PCI due to some reasons (cost, less symptoms and so on).

Conclusion

- Our results highlight the importance for evaluation for CAD in patients with PAD.

- A randomized trial comparing aggressive revascularization versus optimal medical therapy is needed to evaluate the clinical benefit of this strategy.

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