Collateral Grade and Chronic Total Occlusion Outcomes

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Dec 8, 2017 **JCR 2017**

Journal of the American Heart Association
OPEN ACCESS
American Heart Association | American Stroke Association

Percutaneous Coronary Intervention Versus Optimal Medical Therapy for Chronic Total Coronary Occlusion With Well–Developed Collaterals

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J Am Heart Assoc. 2017;6:e006357; originally published September 13, 2017;
doi: 10.1161/JAHA.117.006357
The *Journal of the American Heart Association* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Online ISSN: 2047-9980

Backgrounds (1)

1. The coronary collateral circulation has been known by an alternative route of blood supply to myocardial area of distal occluded vessel.

2. Coronary collateral circulation is an important information of long-term ischemic condition and well-developed collateral may limit myocardial ischemia and symptoms in patients with CTO lesion.

Background (2)

3. Well-developed collateral flow is a positive predictive value for the possibility of myocardium viability, and it has been an important factor for a physician's decision whether or not open up for the CTO lesion, particularly in CTO patients with limited symptoms and preserved left ventricular (LV) function.

4. Well-developed collateral circulation showed clinical benefits reducing incidence of mortality and cardiovascular events in *chronic stable angina* patients.

Circulation. 2007;116:975-983

Background (3)

5. Also, it was associated with beneficial effect after *acute ischemic status* regarding reduction in infarct size and increase discharge left ventricular function.

Circulation. 1991;83:739-746

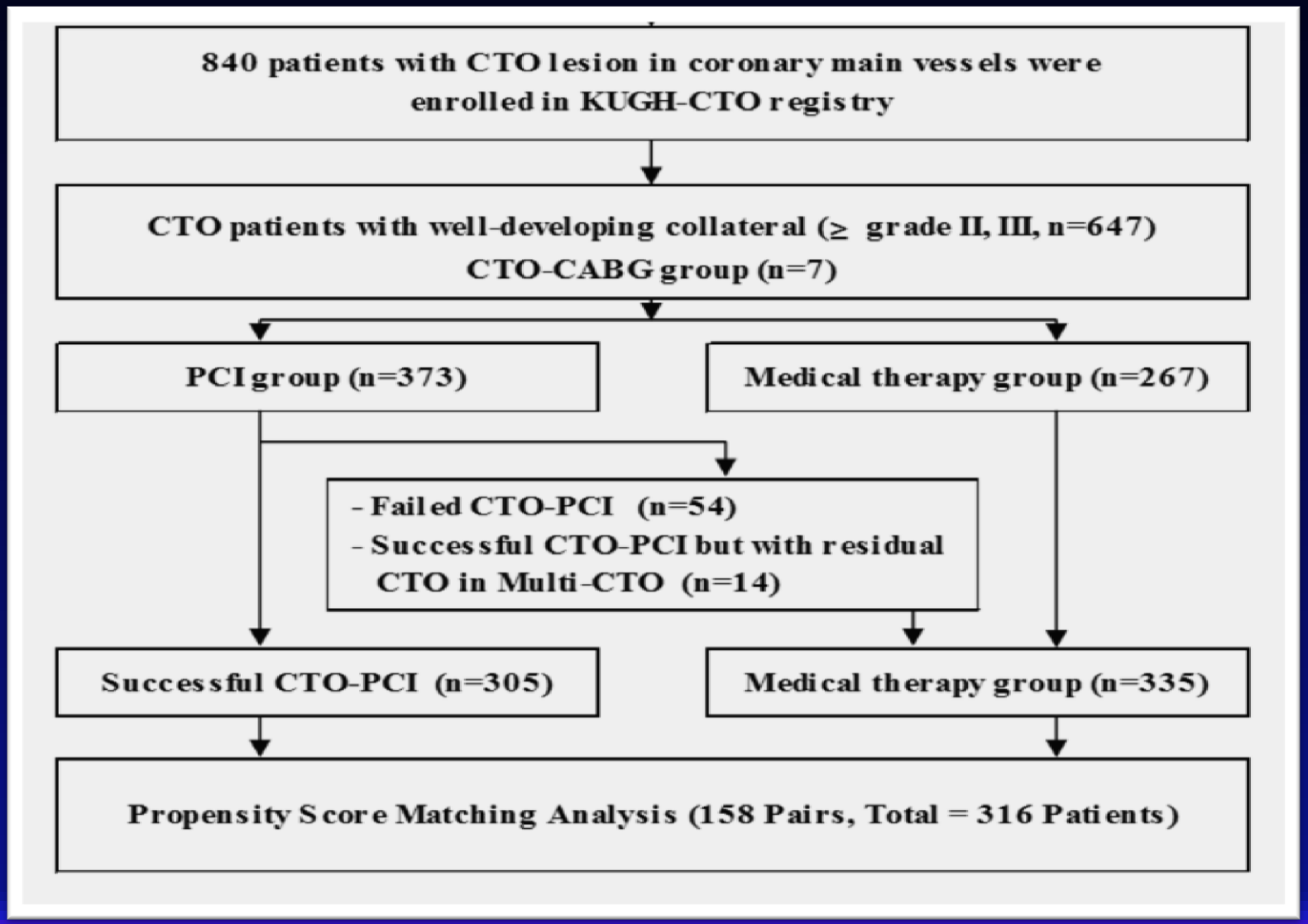
6. However, there is limited evidence of the effect of PCI in patients with CTO and abundant collateral circulation regardless of treatment strategies (medical therapy and PCI).

Purpose

This study purposed to identify the impact of PCI on long-term clinical outcomes in patients with CTO lesion and well-developed collateral flow compared with optimal medical therapy (OMT) alone.

Methods

1. Study Population



Methods

2. Antiplatelet Regimen

1) All pts received Aspirin; 100 mg orally.
2) All pts received Clopidogrel (Plavix®) preloaded 300-600 mg before PCI, followed by daily administration of 75 mg and encouraged to continue at least for 1 year.
3) Usage of adjunctive Cilostazol to dual antiplatelet regimen (asprin + clopidogrel) was depending on physician's discretion. Cilostazol was administered by 200mg post-loading and then 100mg bid for at least one month

Methods

3. Antithrombotic therapy used for PCI

1) Enoxaparin (Clexane®); 60mg bid before PCI and after PCI during the hospital stay (within 7 days).
2) Unfractionated Heparin; a bolus of 50 U/kg prior to PCI for 1st one hour.
3) GP IIbIIIa blocker (Reopro®); depend on physician's discretion.

Methods

4. PCI Procedure

1) A variety of atheroablative devices were not utilized and mostly simple predilation or was performed to get an adequate luminal diameter which was necessary to accommodate the unexpanded DES and their delivery system.
2) Thrombus aspiration or mechanical thrombectomy were performed if clinically indicated.

5. Study Endpoints

; The clinical outcomes were compared between the two groups up to 5 years.

Statistics

1. All statistical analyses were performed using SPSS 20.0.
2. Continuous variables were expressed as means ± standard deviation and were compared using Student's t-test.
3. Categorical data were expressed as percentages and were compared using chi-square statistics or Fisher's exact test.
4. A P-value of 0.05 was considered statistically significant.
5. To adjust for any potential confounders, propensity score matching (PSM) analysis was performed using the logistic regression model.

Statistics

6. We tested all available variables that could be of potential relevance: age, male, cardiovascular risk factors (hypertension, diabetes, dyslipidemia, cerebrovascular disease peripheral artery disease, chronic kidney disease, heart failure and smoking), and angiographic and procedural characteristics (significant coronary lesion artery, CTO lesion artery, lesion locations).
7. Matching was performed via 1:1 matching protocol using the nearest neighbor matching algorithm, with a caliper width equal to 0.05 of the standard deviation of the propensity score, yielding 158 well-matched pairs.
8. Various clinical outcomes up to 5 years were estimated by the Kaplan-Meier analysis, and differences between the groups were compared with the log-rank test before and after PSM.
9. Proportional hazard models were used to assess the hazard ratio (HR) of the PCI group compared with the OMT group among the matched population.

Results

Baseline Clinical Characteristics

Variables, N (%)	Entire population				Matched population			
	PCI (n=305)	OMT (n=335)	P value	SD	PCI (n=158)	OMT (n=158)	P value	SD
Sex, male	230 (75.4)	242 (72.2)	0.362	0.37	117 (74.1)	113 (71.5)	0.613	0.30
Age, year	62 ± 11	66 ± 11	< 0.01	-0.40	64 ± 9	64 ± 11	0.739	0.04
LV ejection Fraction, %	53 ± 11	49 ± 12	< 0.01	0.31	50 ± 12	50 ± 12	0.928	-0.01
Myocardial infartion	62 (20.3)	66 (19.7)	0.843	0.14	34 (21.5)	34 (21.5)	> 0.99	0.00
STEMI	23 (7.5)	24 (7.2)	0.855	0.14	11 (7.0)	16 (10.1)	0.314	-1.08
NSTEMI	39 (12.8)	41 (12.2)	0.834	0.16	23 (14.6)	18 (11.4)	0.403	0.88
Hypertension	196 (64.3)	227 (67.8)	0.350	-0.43	107 (67.7)	111 (70.3)	0.627	-0.31
Diabetes	136 (44.6)	149 (44.5)	0.977	0.02	78 (49.4)	72 (45.6)	0.499	0.55
Dyslipidemia	87 (28.5)	111 (33.1)	0.208	-0.83	51 (32.3)	49 (31.0)	0.809	0.23
Cerebrovascular disease	28 (9.2)	47 (14.0)	0.057	-1.42	21 (13.3)	17 (10.8)	0.489	0.73
Peripheral artery disease	24 (7.9)	40 (11.9)	0.086	-1.29	18 (11.4)	17 (10.8)	0.858	0.19
Chronic kidney disease	19 (6.2)	23 (6.9)	0.745	-0.25	14 (8.9)	13 (8.2)	0.841	0.22
Heart failure	35 (11.5)	57 (17.0)	0.046	-1.47	24 (15.2)	25 (15.8)	0.876	-0.16
Smoking	169 (55.4)	187 (55.8)	0.917	-0.06	79 (50.0)	94 (59.5)	0.090	-1.29
Current	115 (37.7)	124 (37.0)	0.857	0.11	61 (38.6)	57 (36.1)	0.642	0.42
CCS classification			< 0.01				0.619	
I	85 (27.9)	207 (61.8)		-5.08	63 (39.9)	74 (46.8)		-1.06
II	69 (22.6)	58 (17.3)		1.19	38 (24.1)	31 (19.6)		0.95
III	70 (23.0)	35 (10.4)		3.06	28 (17.7)	25 (15.8)		0.46
IV	81 (26.6)	35 (10.4)		3.75	29 (18.4)	28 (17.7)		0.15
Serum glucose, mg/dl	139 ± 58	130 ± 56	0.087	0.15	143 ± 63	131 ± 58	0.120	0.20
A1c, %	6.6 ± 1.3	6.6 ± 1.3	0.558	-0.06	6.6 ± 1.3	6.6 ± 1.3	0.967	-0.01
Total cholesterol, mg/dl	167 ± 43	167 ± 41	0.922	0.01	166 ± 43	168 ± 45	0.725	-0.04
Triglyceride, mg/dl	147 ± 92	137 ± 94	0.222	0.11	136 ± 76	138 ± 99	0.829	-0.03
HDL-cholesterol, mg/dl	42 ± 12	42 ± 12	0.993	0.00	42 ± 11	42 ± 11	0.754	0.04
LDL-cholesterol, mg/dl	106 ± 39	104 ± 36	0.657	0.04	107 ± 41	104 ± 37	0.666	0.06

Angiographic and Procedural characteristics

Variables, N (%)	Entire population				Matched population			
	PCI (n=305)	OMT (n=335)	P value	SD	PCI (n=158)	OMT (n=158)	P value	SD
PCI procedure	305 (100.0)	186 (55.5)	< 0.01	5.07	158 (100.0)	103 (65.2)	< 0.01	3.85
Muli-vessel disease	181 (59.3)	273 (81.5)	< 0.01	-2.65	104 (65.8)	117 (74.1)	0.111	-0.99
No. of vessels	1.8 ± 0.8	2.3 ± 0.8	< 0.01	-0.57	2.0 ± 0.8	2.1 ± 0.8	0.227	-0.14
Significant coronary lesion								
LAD	210 (68.9)	241 (71.9)	0.392	-0.37	109 (69.0)	108 (68.4)	0.903	0.08
LCX	162 (53.1)	233 (69.6)	< 0.01	-2.11	94 (59.5)	97 (61.4)	0.730	-0.24
RCA	178 (58.4)	268 (80.0)	< 0.01	-2.61	105 (66.5)	112 (70.9)	0.396	-0.54
LM	15 (4.9)	33 (9.9)	0.018	-1.82	10 (6.3)	16 (10.1)	0.219	-1.32
RAMUS	7 (2.3)	17 (5.1)	0.065	-1.45	4 (2.5)	9 (5.7)	0.157	-1.56
Coronary CTO lesion								
Muli-vessel CTO	22 (7.2)	61 (18.2)	< 0.01	-3.09	14 (8.9)	13 (8.2)	0.841	0.22
No. of CTO vessels	1.1 ± 0.3	1.2 ± 0.4	< 0.01	-0.32	1.1 ± 0.3	1.1 ± 0.3	0.856	0.02
LAD	119 (39.0)	90 (26.9)	0.001	2.12	52 (32.9)	49 (31)	0.717	0.34
LCX	85 (27.9)	107 (31.9)	0.262	-0.75	45 (28.5)	43 (27.2)	0.802	0.24
RCA	121 (39.7)	197 (58.8)	< 0.01	-2.73	73 (46.2)	78 (49.4)	0.573	-0.46
RAMUS	2 (0.7)	3 (0.9)	0.731	-0.27	2 (1.3)	2 (1.3)	> 0.99	0.00
CTO location			0.029				0.190	
Proximal	152 (49.8)	183 (54.6)		-0.66	80 (50.6)	83 (52.5)		-0.27
Mid	121 (39.7)	102 (30.4)		1.56	62 (39.2)	50 (31.6)		1.28
Distal	32 (10.5)	50 (14.9)		-1.24	16 (10.1)	25 (15.8)		-1.58
Failed CTO procedure	0 (0.0)	54 (16.1)	< 0.01	-5.68	0 (0.0)	32 (20.3)	< 0.01	-6.37

Clinical outcomes up to 5 years

	No. of Events up to 5 years (%)				
Outcomes	**PCI Group**	**OMT Group**	**Log Rank**	**Hazard Ratio (95% CI)**	**P-value**
Entire Population					
Total death	5 (1.9)	28 (8.9)	< 0.01	0.451 [0.147 - 1.381]	0.163
Cardiac death	3 (1.1)	13 (4.2)	0.025	0.502 [0.111 - 2.261]	0.370
Myocardial infarction	2 (0.7)	17 (5.9)	0.002	0.177 [0.034 - 0.913]	0.039
Revascularization	51 (19.6)	38 (13.0)	0.024	1.687 [0.985 - 2.889]	0.056
Target lesion (CTO vessel)	28 (10.7)	9 (3.0)	< 0.01	3.942 [1.584 - 9.810]	0.003
Target vessel (CTO vessel)	35 (13.3)	11 (3.7)	< 0.01	4.218 [1.854 - 9.597]	0.001
Non-target vessel (Non-CTO vessel)	24 (9.2)	34 (11.7)	0.428	0.761 [0.394 - 1.470]	0.416
Stroke	3 (1.1)	5 (1.6)	0.613	0.892 [0.147 - 5.405]	0.901
Total MACE	55 (20.8)	65 (20.9)	0.932	1.305 [0.822 - 2.073]	0.258
Total death or myocardial infarction	6 (2.3)	39 (12.6)	< 0.01	0.298 [0.110 - 0.802]	0.017
Propensity-Matched Population					
Total death	3 (2.0)	11 (7.9)	0.028	0.305 [0.084 - 1.102]	0.070
Cardiac death	2 (1.4)	5 (3.6)	0.242	0.408 [0.078 - 2.124]	0.287
Myocardial infarction	2 (1.4)	7 (5.6)	0.084	0.276 [0.057 - 1.337]	0.110
Revascularization	30 (22.0)	20 (14.9)	0.139	1.543 [0.873 - 2.730]	0.135
Target lesion (CTO vessel)	17 (12.5)	6 (4.3)	0.021	2.868 [1.125 - 7.308]	0.027
Target vessel (CTO vessel)	20 (14.5)	8 (5.8)	0.021	2.615 [1.146 - 5.965]	0.022
Non-target vessel (Non-CTO vessel)	14 (10.1)	19 (14.5)	0.312	0.711 [0.355 - 1.424]	0.337
Stroke	2 (1.5)	2 (1.3)	0.974	0.946 [0.132 - 6.761]	0.956
Total MACE	33 (23.8)	30 (21.3)	0.661	1.165 [0.708 - 1.917]	0.547
Total death or myocardial infarction	4 (2.8)	16 (11.9)	0.005	0.263 [0.087 - 0.790]	0.017

Kaplan–Meier Survival Curves

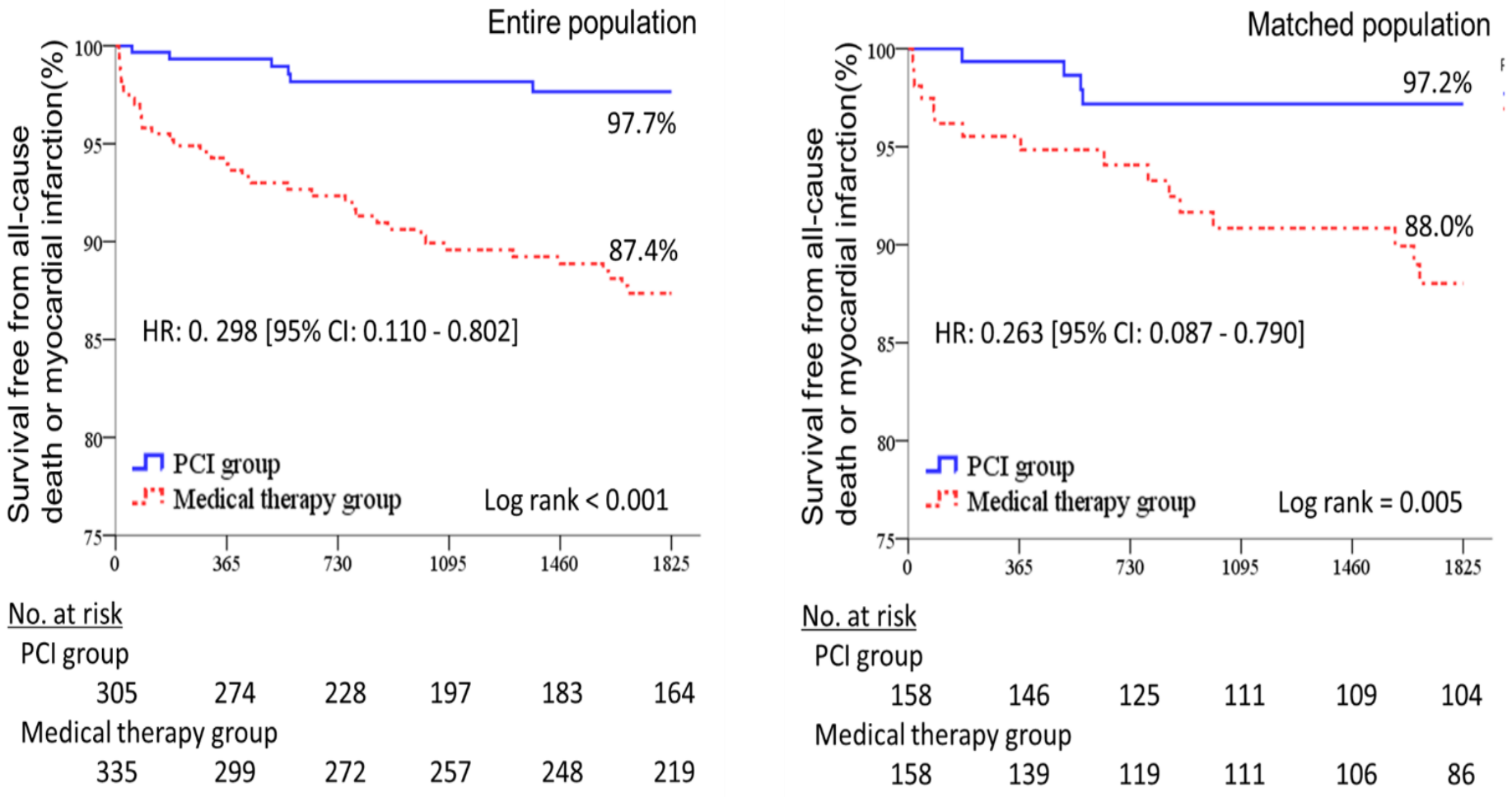
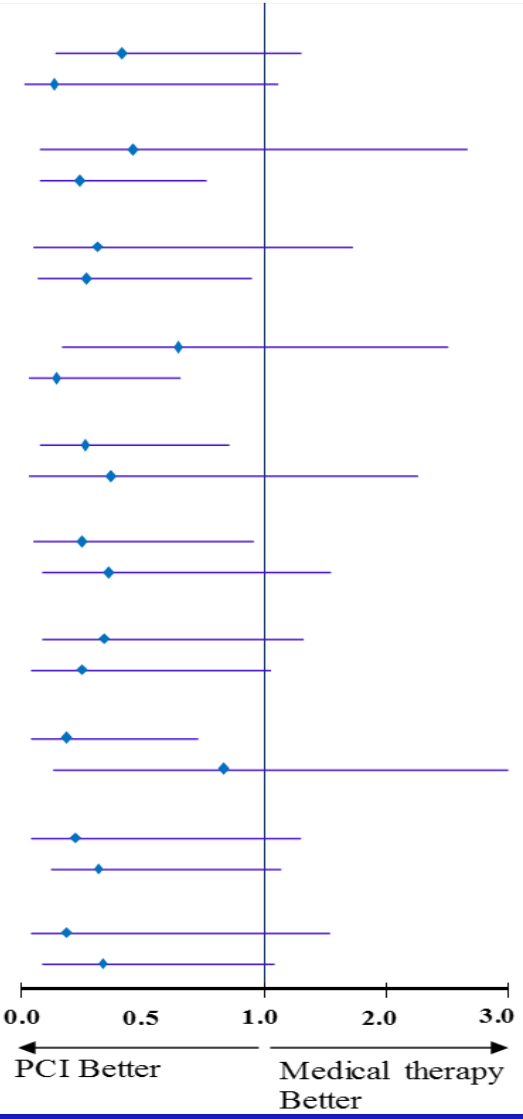


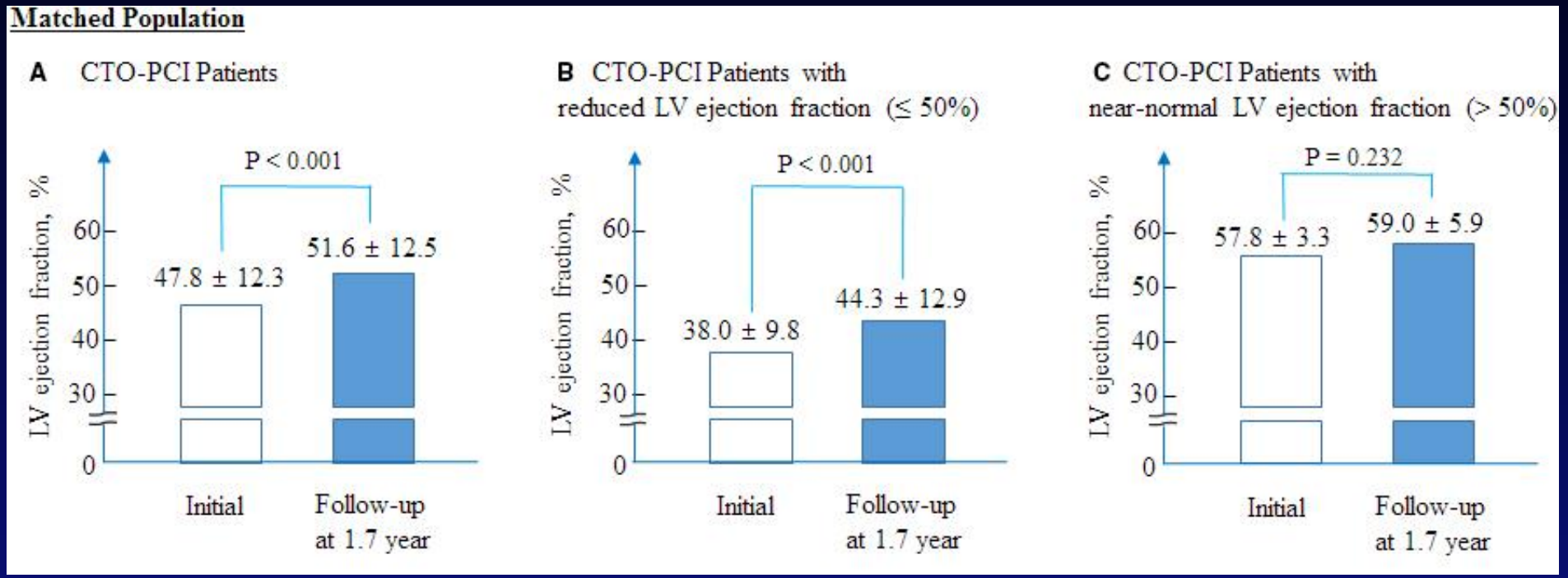
Figure 3. The composite total death and myocardial infarction free survival by Kaplan–Meier curves. CI indicates confidence interval; HR, hazard ratio; OMT, optimal medical therapy; PCI, percutaneous coronary intervention.

Subgroup Analysis for the Composite Total Death or Myocardial Infarction

Variables	No. of Patients	Hazard Ratio (95% CI)	Hazard Ratio (95% CI)	P-value
Sex				
Male	363		0.413 [0.131 - 1.295]	0.129
Female	137		0.126 [0.014 - 1.124]	0.064
Age				
≤ 65 yr	278		0.473 [0.084 - 2.636]	0.393
> 65 yr	222		0.224 [0.065 - 0.768]	0.017
Myocardial infarction				
Yes	66		0.309 [0.055 - 1.725]	0.181
No	434		0.286 [0.085 - 0.958]	0.042
LV ejection fraction				
≥ 50%			0.658 [0.178 - 2.430]	0.531
< 50%			0.134 [0.027 - 0.657]	0.013
Hypertension				
Yes	339		0.265 [0.079 - 0.884]	0.031
No	161		0.384 [0.066 - 2.219]	0.285
Diabetes				
Yes	221		0.243 [0.061 - 0.958]	0.043
No	279		0.380 [0.090 - 1.594]	0.186
Smoking				
Yes	273		0.336 [0.083 - 1.359]	0.126
No	227		0.253 [0.061 - 1.041]	0.057
Muli-vessel disease				
Yes	332		0.197 [0.054 - 0.715]	0.014
No	168		0.819 [0.153 - 4.382]	0.816
CTO at LAD				
Yes	151		0.203 [0.032 - 1.278]	0.089
No	341		0.331 [0.103 - 1.062]	0.063
CCS				
0 or 1	198		0.197 [0.024 - 1.598]	0.128
II or III	302		0.318 [0.096 - 1.048]	0.060



Changes of LVEF using paired t test analysis in the first 1.7 years after revascularization.



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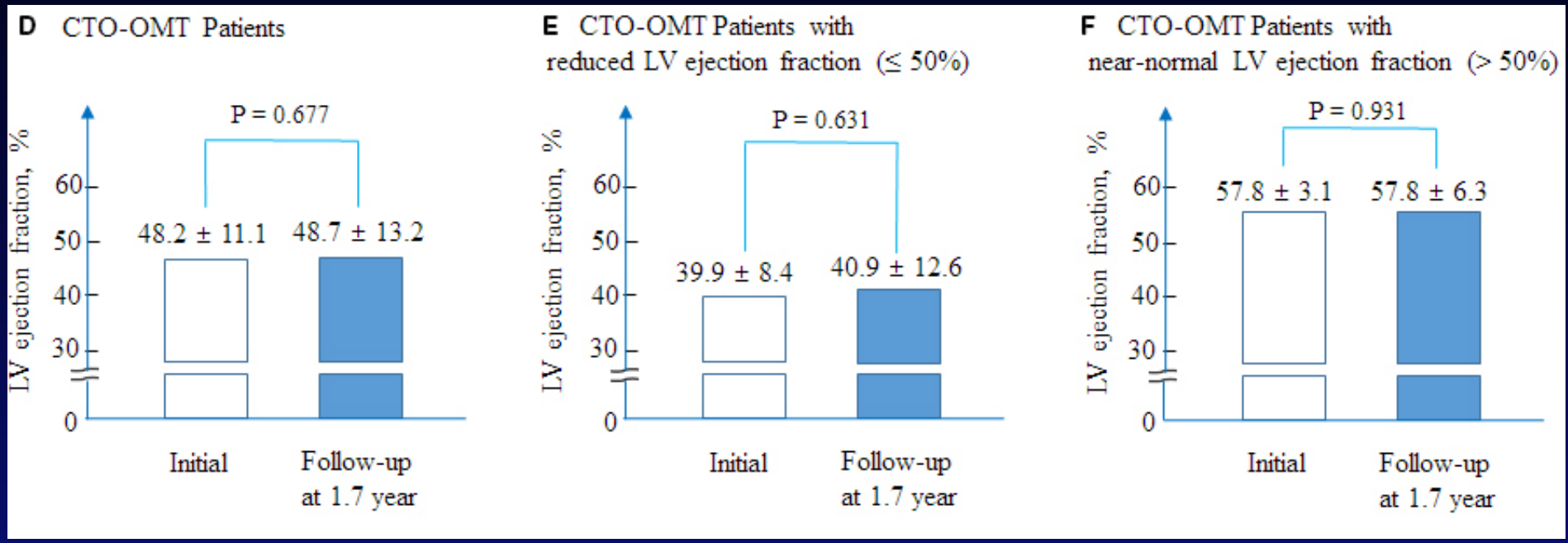

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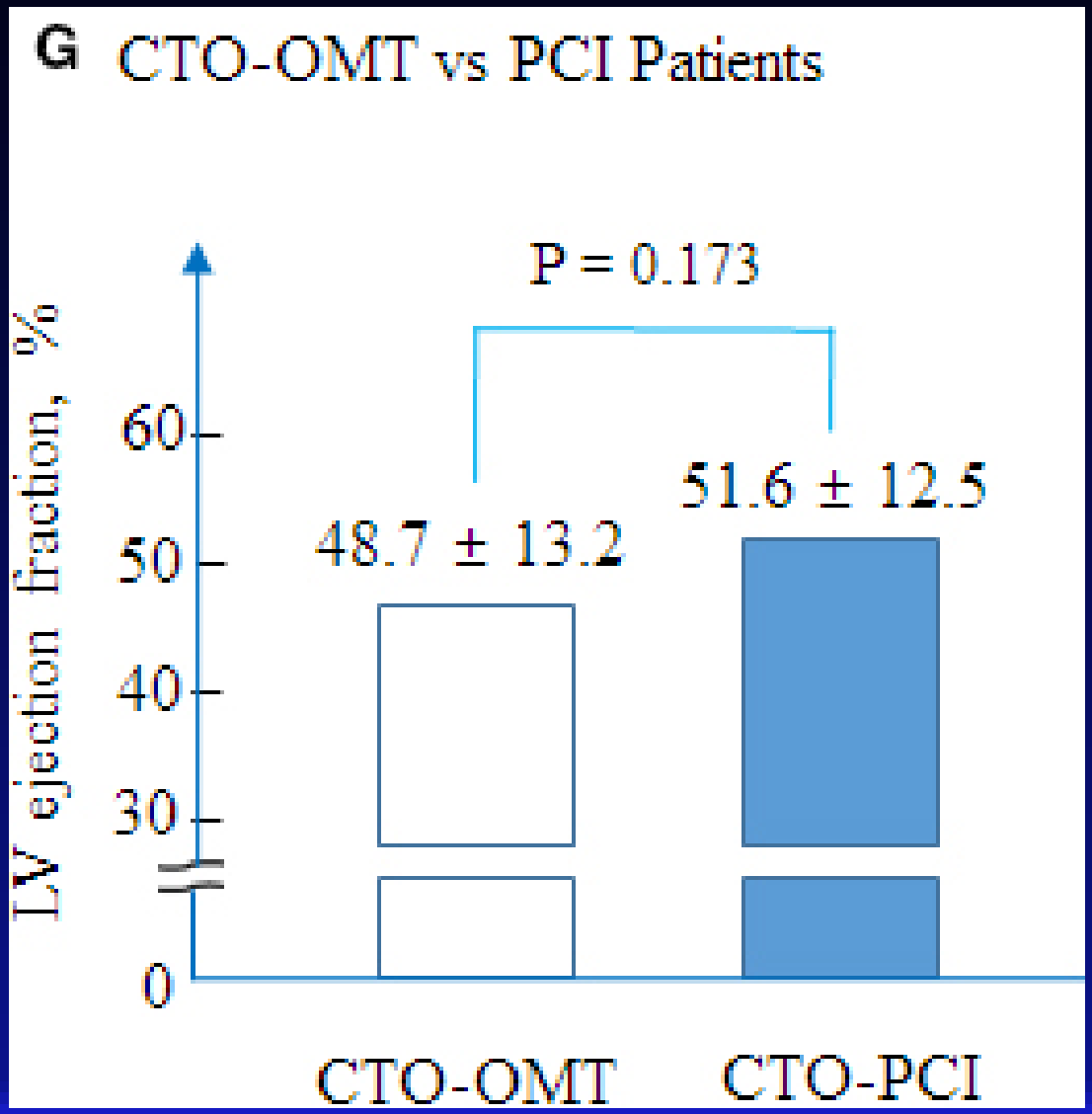

Summary (1)

1. After propensity score matching, the baseline clinical characteristics were balanced between the two groups.

2. The PCI group demonstrated the lower incidence of total death and the composite of total death or MI than the OMT group, whereas the incidence of TLR and TVR was lower in the OMT group.

Summary (2)

3. In a subgroup analysis, the PCI group was associated with favorable outcomes in patients with older age (>65 years), non-MI, reduced LVEF level (≤50%), hypertension, diabetes, and multi-vessel disease subgroups.

Conclusion

In our study, mechanical revascularization by PCI for CTO lesions in pts with well-developed collaterals reduced the incidence of the *composite of mortality or MI but increase revascularization.*

Clinical Implication

When physicians decide the treatment strategy for a chronic total occlusion, our results suggest that chronic total occlusion *percutaneous coronary intervention is a more appropriate treatment strategy* for patients with *good collateral circulation* in whom coronary steal and myocardial viability are likely to exist and cardiac function likely to improve.

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