Documented coronary atherothrombosis as the cause of death in post-discharge patients after coronary revascularization

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ABSTRACT

Background: The contemporary medications for secondary prevention like statins and antithrombotic agents are targeting to delay the progression of atherothrombosis. However, there is limited data on the relation between death and progressive coronary atherothrombosis. This study sought to evaluate what proportion of death after coronary revascularization is related to documented progressive coronary atherothrombosis.
Methods: We reviewed the detailed causes of death among 15,231 patients receiving their first coronary revascularization enrolled in the CREDO-Kyoto PCI/CABG registry cohort-2, dividing into two groups; 13,839 patients with clinical success and without major complication (uncomplicated) and the other 1392 patients (complicated). Documented progressive coronary atherothrombosis as the cause of death was defined as preceding coronary revascularization within 30 days before death or irreversible brain damage and/or proof of coronary thrombus by autopsy.
Results: During the median follow-up of 5.4 years, 2837 patients died with cumulative 5-year incidence of 17.5%. The proportions of cardiac/non-cardiovascular death among all-cause death in uncomplicated patients and complicated patients were 36.6%/51.5% and 74.2%/17.4%, respectively. The numbers of patients died with documented progressive coronary atherothrombosis were 41 (1.9% of all-cause death) and 304 (47.3%). The number was only 51 (2.1%) among all post-discharge patients. Dominant causes of cardiac death in post-discharge patients included heart failure (10.0%) and sudden cardiac death (9.1%), both without apparent relation with progressive atherothrombosis.
Conclusions: Only about one-third of deaths were cardiac in origin during 5-year follow-up in post-discharge patients after coronary revascularization. Cardiac death after discharge was very infrequently related to documented progressive coronary atherothrombosis.

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1. Introduction

Coronary artery disease (CAD) and cerebral vascular disease (CVD) are the two leading causes of death all over the world. CAD, CVD and peripheral artery disease (PAD) are caused primarily by atherosclerosis and thrombosis and commonly referred as "atherothrombosis" [1]. Pharmacologic interventions such as aspirin and statins to prevent progression of atherothrombosis have been successful in reducing

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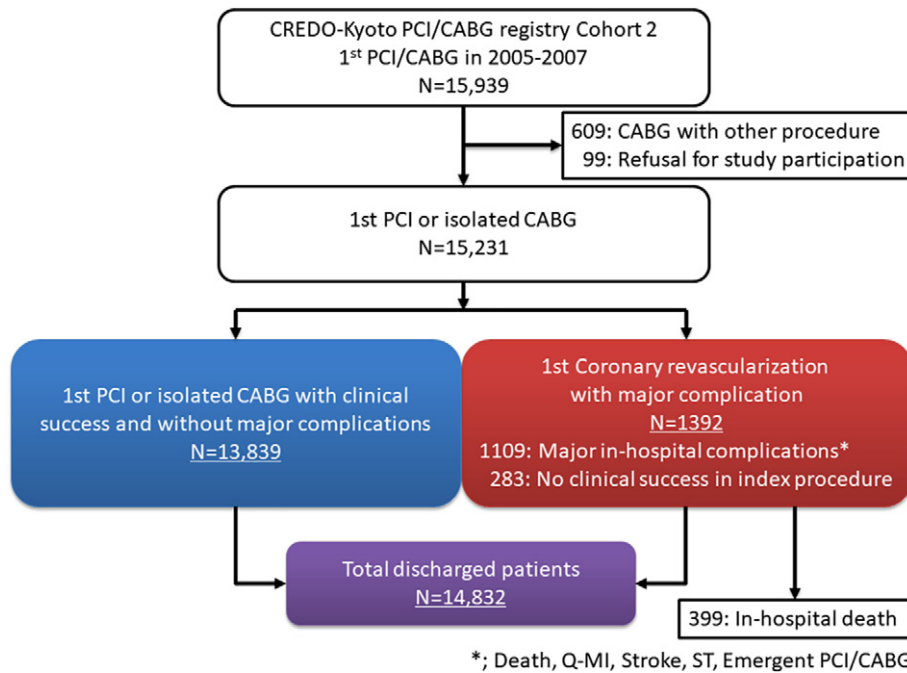
Fig. 1. Study flow. *Major in-hospital complications included death, Q-wave myocardial infarction, stent thrombosis, and emergent PCI/CABG. CREDO-Kyoto = The Coronary REvascularization Demonstrating Outcome study in Kyoto, PCI = percutaneous coronary intervention, and CABG = coronary artery bypass grafting.

cardiovascular (CV) events [2–7]. Moreover, recent studies reported there remains a residual risk for CV events even after aggressive lipid lowering with intensive statins therapy in conjunction with other contemporary evidence-based medications to prevent CV events [7,8]. Therefore, various novel pharmacologic anti-atherothrombotic interventions to further reduce CV events have been explored extensively [9–13]. However, there seem to be many CV events actually not related to the progression of atherothrombosis. Anti-atherothrombotic agents could at least theoretically prevent death caused by progression of atherothrombosis, but most likely could not prevent death unrelated to it. Currently, there is a paucity of information regarding the relation between progressive atherothrombosis and mortality. Therefore, we sought to explore the actual causes of death and their relation with progressive coronary atherothrombosis documented by coronary

Table 1
Baseline clinical characteristics.

	All patients	Uncomplicated patients	Complicated patients	P value
	N = 15,231	N = 13,839 (90.9%)	N = 1392 (9.1%)	
Age (years)	68.2 ± 10.8	68.0 ± 10.7	71.0 ± 11.2	<0.001
Age ≥75 years	4699 (31%)	4108 (30%)	591 (42%)	<0.001
Male	11,009 (72%)	10,061 (73%)	948 (68%)	<0.001
BMI (kg/m^2)	23.7 ± 3.4	23.7 ± 3.4	23.2 ± 3.7	<0.001
BMI <25.0 kg/m^2	10,493 (69%)	9439 (68%)	1054 (75%)	<0.001
Acute myocardial infarction	4892 (32%)	4318 (31%)	574 (41%)	<0.001
Hyperlipidemia	10,507 (69%)	9626 (70%)	881 (63%)	<0.001
Hypertension	12,512 (82%)	11,414 (82%)	1098 (79%)	0.001
Diabetes mellitus	5999 (39%)	5459 (39%)	540 (39%)	0.63
Insulin therapy	1353 (9%)	1232 (9%)	121 (9%)	0.79
Current smoking	4709 (31%)	4333 (31%)	376 (27%)	<0.001
Heart failure	3134 (21%)	2561 (19%)	573 (41%)	<0.001
Shock at presentation	840 (6%)	558 (4%)	282 (20%)	<0.001
Multivessel disease	9191 (60%)	8225 (59%)	966 (69%)	<0.001
LMCA disease	1290 (8%)	1087 (8%)	203 (15%)	<0.001
Mitral regurgitation grade 3/4	591 (4%)	506 (4%)	85 (6%)	<0.001
LVEF (%)	58.4 ± 13.4	58.7 ± 13.0	54.2 ± 16.3	<0.001
LVEF ≤40%	1419 (11%)	1191 (10%)	228 (30%)	<0.001
Prior myocardial infarction	1817 (12%)	1610 (12%)	207 (15%)	<0.001
Prior stroke	1688 (11%)	1491 (11%)	197 (14%)	<0.001
Peripheral artery disease	1225 (8%)	1108 (8%)	117 (8%)	0.6
ESRD (eGFR <30 mL/min/1.73 m^2) not on dialysis	682 (4%)	560 (4%)	122 (9%)	<0.001
Dialysis	600 (4%)	510 (4%)	90 (6%)	<0.001
Atrial fibrillation	1493 (10%)	1306 (9%)	187 (13%)	<0.001
Anemia (hemoglobin <11 g/dL)	1927 (13%)	1676 (12%)	251 (18%)	<0.001
Thrombocytopenia (platelets <10^11/L)	247 (2%)	192 (1%)	55 (4%)	<0.001
Chronic obstructive pulmonary disease	529 (3%)	473 (3%)	56 (4%)	0.25
Liver cirrhosis	404 (3%)	369 (3%)	35 (3%)	0.73
Malignancy	1402 (9%)	1275 (9%)	127 (9%)	0.91

BMI = body mass index, eGFR = estimated glomerular filtration rate, ESRD = end-stage renal disease, LMCA = left main coronary artery, and LVEF = left ventricular ejection fraction.