Modifiable risk factors control and its relationship with 1 year outcomes after coronary artery bypass surgery: insights from the REACH registry

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Aims	To evaluate the influence of achieving secondary prevention target treatment goals for cardiovascular (CV) risk factors on clinical outcomes in patients with prior coronary artery bypass surgery (CABG).
Methods and results	Accordingly, we analysed treatment to target goals in patients with prior CABG and atherothrombotic disease or known risk factors (diabetes, hypertension, hypercholesterolaemia, smoking, obesity) enrolled in the global REduction in Atherothrombosis for Continued Health (REACH) Registry, and their association with 1 year outcomes. A total of 13 907 of 68 236 patients (20.4%) in REACH had a history of prior CABG, and 1 year outcomes data were available for 13 207 of these. At baseline <25, 25–<50, 50–<75, and ≥75% risk factors were at goal in 3.7, 12.9, 31.7, and 51.7% of patients, respectively. One-year composite rates of CV death, non-fatal MI, non-fatal stroke were inversely related to the proportion of risk factors at goal at baseline (age, gender, and region adjusted rates 6.1, 5.6, 5.2, and 4.3% of patients with <25, 25–<50, 50–<75, and >75% risk factors at goal, respectively; P for trend 0.059).
Conclusion	Risk-factor control varied greatly in CABG patients. Although CABG patients are frequently treated with appropriate therapies, these treatments fail to achieve an adequate level of prevention in many. This failure was associated with a trend for worse age-, gender-, and region-adjusted clinical outcomes. Thus, perhaps secondary prevention after CABG needs to focus on more comprehensive modification of risk factors to target goals in the hope of preventing subsequent CV events, and represents an opportunity to improve CV health.
Keywords	Coronary disease • Bypass • Revascularization • Stroke • Risk factors

Introduction

Coronary artery bypass surgery (CABG) remains an important method for coronary revascularization in patients with CAD, accounting for more than 300 000 procedures in United States per year, and even more on a global scale.[1] Recurrent ischaemic events occur frequently in these patients due to graft attrition as well as progression of native CAD.[2–5] The role of secondary prevention measures and risk-factor control in reducing recurrent ischaemic events is well established[6–10] and is reiterated in practice guidelines for both the American College of Cardiology/American Heart Association[11] and the European Society of Cardiology.[12] Despite unequivocal evidence favouring the use of secondary prevention measures and risk factor control in patients

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with advanced CAD, poor compliance with these guideline-based therapies after CABG has been reported.[13] Additionally, even among patients receiving evidence-based treatments, not all achieve the target goals of secondary prevention. However, the proportion of patients achieving recommended goals while on appropriate treatment and the implications of not achieving such targets in patients who have had CABG remain less well known.

The main purpose of the current investigation was to analyse information on patients with a history of CABG enrolled in the REACH Registry[14,15] and to evaluate the variation in the proportion of patients that fail to attain their target goals for secondary prevention at baseline (i.e. control of hypertension, diabetes, increased cholesterol, smoking cessation, and attainment of BMI in the normal range) and their 1 year outcomes.

Methods

Patient population

A total of 68 236 patients were initially enrolled in the REACH Registry with data on baseline risk factors collected in 2003–2004. In brief, the Registry recruited outpatients in 44 countries across six major regions (Latin America, North America, Europe, Asia, the Middle East, and Australia) from >5000 physician outpatient practices. Patients aged ≥45 years with already existing at least three atherothrombotic risk factors or documented cardiovascular disease, CAD (that included patients with prior CABG), or PAD were enrolled.[14,15] To ensure representative inclusion of the overall population in each practice setting it was attempted to recruit consecutively at each site; however, because of the large number of potential study candidates at sites, no enrolment logs were maintained as part of this study. A limited time period was set for the duration of enrolment at each practice setting—approximately 5 days from the first to the last patient enrolled—suggesting near, if not consecutive, patient enrolment. Enrolment occurred worldwide between December 2003 and June 2004; because of regulatory requirements in Japan, the enrolment in that country was delayed and occurred between August 2004 and December 2004.[14,15]

We focused on 13 907 patients with prior CABG enrolled in REACH. For the current study, we included 13 207 (95%) patients with CABG who had complete information available on 1 year outcomes. All other information was complete in these 13 207 patients with the exception of age and/or gender in minority [$n = 57$ (0.4%)]. These patients were not excluded from the analysis.

Evaluations

Medical history, risk factors, demographic information, and management were collected at baseline, and clinical events that occurred during the follow-up period [of up to 4 years: 1 year (12 ± 3 months), 2 year (21 ± 3 months), 3 year (33 ± 3 months), 4 year (45 ± 3 months)] are recorded. For this current study, we restricted our analysis to those patients who had a documented history of prior CABG and had 1 year of follow-up data.[14,15]

Risk factors

The risk factors consisted of those that were documented in the medical record or for which patients were receiving treatment at the time of study enrolment. Similarly, whether risk factors were at goal or not were defined based on their value at baseline visit and risk factors assessment was not performed at follow-up. Five risk factors were analysed: a history of diabetes, hypertension, hyperlipidaemia, smoking status, and BMI. Uncontrolled risk factors at baseline were defined as blood sugar >126 mg/dL, BP >140/90 mmHg (except among people with diabetes in whom this was defined as BP >130/80 mmHg), total cholesterol >200 mg/dL, continued smoking (≥5 cigarettes per day), and obesity (BMI >30 kg/m^2).

The proportion of risk factors at goal was calculated for each patient as follows: Number of risk factors at goal in a given individual/total number of risk factors in that individual × 100. Then as five risk factors were taken into account <25% risk factor at goal=0 or 1 among 5, or 0 among 4, 3, 2 or 1; 25 to <50% = 2 among 5, and 1 among 4 or 3; 50 to <75% = 3 among 5 or 2 among 4 or 3, or 1 among 2; and ≥75% = 4 or 5 among 5, 3 or 4 among 4, 3 among 3, 2 among 2, and 1 among 1.

Study outcomes

For the present analysis, the outcomes of interest included the following events at 1 year: (1) combined end-point of cardiovascular death (including fatal stroke, fatal MI, and other cardiovascular death), non-fatal stroke (ischaemic or haemorrhagic), non-fatal MI, and hospitalizations for atherothrombotic events (transient ischaemic attack, unstable angina, and other ischaemic arterial event including worsening of PAD); (2) combination of non-fatal stroke, non-fatal MI, or cardiovascular death; (3) cardiovascular death; and (4) all-cause death. The association of the proportion of risk factors at goal at baseline was then evaluated with 1 year outcome.

Study setting and site selection

Site selection was undertaken to reflect different practices of management of patients with atherothrombotic diseases around the world. Physicians (family and general practitioners, cardiologists, neurologists, angiologists, vascular surgeons, and endocrinologists) were selected at a country level, based on available data. The studies had to be published, population-based, and endorsed by national or international scientific societies. Physician selection was designed to provide a distribution across regions and locations; i.e. urban, suburban, or rural areas. Because the physician selection was done at a national level, rationale and guidelines for physician selection were set and disseminated to National Coordinators and local project managers. Feedback from each participating country was centralized to check the quality and the homogeneity of the physician selection between countries, and the Steering Committee validated physician selection before the start of the inclusion period, and the local National Coordinators served as the final arbitrators of sites and distribution of patient population based on the above general criteria described. Each physician recruited a maximum of 15 patients (up to 20 patients in the US).[14,15]

Statistical analysis

Data are summarized as mean and standard deviation for continuous variables and as counts and percentages for categorical variables. No imputation was done for missing variables and denominators reflect cases reported. Univariate comparisons were made using Student's t-test for continuous variables and χ^2 test for the categorical variables. All event rates are calculated with a Cox Model after adjustment for age, sex, and region as proportions [rate = $(1 - \text{survival}) \times 100$]. The Cochran–Mantel–Haenszel test was used to calculate the P-values for trends of adjusted outcomes. All statistical analyses were performed using SAS version 9.1.3 (SAS Institute, CARY, NC) and were considered significant at the 95% confidence limit using two-sided tests or two-sided confidence intervals.

Results

Baseline clinical features and risk factors

Of 13 907 (20.38%) patients with a history of CABG at baseline visit, 1 year follow-up information was available in the majority (*n* = 13 207, 95%). The regional prevalence of CABG patients in the REACH population at baseline ranged from 26.79% (6964) in North America to 10.72% (1146) in Asia, with rates for Western Europe (*n* = 3075, 17.94%) and the rest of the world (*n* = 2022, 18.14%) in between that of USA and Asia. Individual risk factors treated to goal in post-CABG patients varied considerably. This was lowest for diabetes control (43.30%) and highest for smoking cessation (86.13%). The proportion of patients with BMI >30 kg/m² (69.89%), cholesterol at goal among those with high cholesterol (75.01%) and BP at goal among those with high blood pressure (76.30%) was in between that for the above two risk factors.

Failure to achieve at least 50% of simple secondary prevention goals was present in 16.58% of CABG patients (*Table 1*). This number increased to almost 50% when we considered CABG patients who failed to achieve 75% of secondary prevention goals. Patients with ≥75% of risk factors at goal were more likely to be older, Caucasian, male, have a lower BMI, and smaller waist circumference when compared with those with <25% risk factors at goal. In contrast, fewer patients with ≥75% of risk factors at goal had diabetes, hyperlipidaemia, prior MI, prior percutaneous coronary interventions, prior stroke, prior PAD, and prior cardiovascular disease. Similarly, these patients had lower systolic and diastolic BP, lower total cholesterol, and lower triglyceride levels compared with those with <25% risk factors at goal.
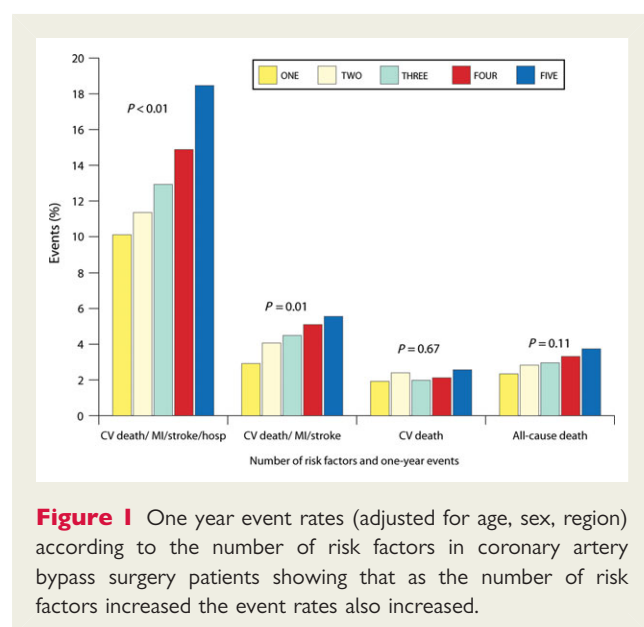
Risk factors at goal and outcomes

There was a trend for higher 1 year events as the number of risk factors increased (*Figure 1*). Risk factors at goal and outcomes are shown in *Tables 2* and *3*. Most event rates tended to be lower (either significantly or non-significantly) when patients treated for a given risk factor were at goal compared with those treated but not at goal at baseline (*Table 2*). Furthermore, a trend for an inverse relationship was observed with the percentage of risk factors at goal and 1 year event rates in CABG patients (*Table 3*, *Figure 2*) with the lower event rates among those with a greater percentage of risk factors at goal at baseline (a non-significant trend for some events). Additionally, this inverse relationship between the percentage of risk factors at goal at baseline and 1 year adverse clinical events (for some events a non-significant trend) was demonstrated among patients regardless of the number of their underlying risk factors (data not shown).

Table 1 Baseline characteristics in coronary artery bypass surgery patients among percentage of risk factors at goal

| | Percentage of risk factors at goal | | | | | |
	Total	<25%	25–50%	50–<75%	≥75%	*P*-value
n (%)	13 207 (100)	489 (3.70)	1701 (12.88)	4188 (31.71)	6829 (51.71)	
Age, years, mean ± SD	69.6 ± 9.5	65.2 ± 9.4	66.7 ± 9.2	69.1 ± 9.4	70.9 ± 9.3	<0.0001
Male, *n* (%)	10 163 (77.00)	328 (67.91)	1219 (71.66)	3159 (75.45)	5457 (79.92)	<0.0001
Caucasian, *n* (%)	9564 (77.02)	343 (74.73)	1229 (76.67)	3012 (76.56)	4980 (77.56)	0.3934
BMI > 30 kg/m², *n* (%)	3922 (30.11)	444 (94.07)	1064 (63.30)	1673 (40.64)	741 (10.97)	<0.0001
Waist circumference, cm, mean ± SD	99.2 ± 15.0	109.2 ± 12.6	105.2 ± 15.8	100.7 ± 15.1	96.0 ± 13.9	<0.0001
Hypertension, *n* (%)	10 643 (80.60)	402 (82.38)	1424 (83.72)	3258 (77.81)	5559 (81.40)	<0.0001
Diabetes mellitus, *n* (%)	5467 (41.40)	359 (73.42)	1137 (66.84)	1864 (44.52)	2107 (30.85)	<0.0001
Hyperlipidaemia, *n* (%)	10 912 (82.70)	398 (81.56)	1471 (86.58)	3471 (82.94)	5572 (81.68)	<0.0001
Current smoker, *n* (%)	1119 (8.74)	140 (29.79)	335 (20.64)	468 (11.58)	176 (2.64)	<0.0001
Prior myocardial infarction, *n* (%)	7195 (55.57)	294 (61.25)	972 (58.66)	2261 (55.09)	3668 (54.69)	0.0017
Prior heart failure, *n* (%)	2951 (22.82)	128 (27.35)	432 (25.91)	902 (21.98)	1489 (22.25)	0.0006
Prior percutaneous coronary interventions, *n* (%)	4032 (30.96)	184 (38.17)	517 (30.98)	1265 (30.67)	2066 (30.62)	0.0066
Prior stroke, *n* (%)	1417 (10.89)	87 (18.05)	226 (13.50)	440 (10.67)	664 (9.86)	<0.0001
Prior cerebrovascular disease, *n* (%)	2119 (16.04)	110 (22.49)	313 (18.40)	667 (15.93	1029 (15.07)	<0.0001
Prior peripheral arterial disease, *n* (%)	1773 (13.42)	86 (17.59)	274 (16.11)	596 (14.23)	817 (11.96)	<0.0001
Diastolic BP, mmHg, mean ± SD	75.7 ± 10.9	85.7 ± 10.4	81.3 ± 11.8	76.3 ± 10.9	73.3 ± 9.6	<0.0001
Systolic BP, mmHg, mean ± SD	133.6 ± 18.8	147.2 ± 19.9	141.3 ± 20.5	134.2 ± 18.8	130.4 ± 17.2	<0.0001
Serum creatinine, mg/dL, mean ± SD	1.2 ± 0.7	1.2 ± 0.8	1.2 ± 0.8	1.2 ± 0.7	1.2 ± 0.7	0.8072
Total cholesterol, mg/dL, mean ± SD	178.9 ± 42.6	228.2 ± 45.3	207.2 ± 50.7	188.5 ± 44.5	166.2 ± 33.1	<0.0001
Triglycerides, mg/dL, mean ± SD	157.4 ± 92.0	222.6 ± 125.1	199.9 ± 108.9	171.5 ± 100.3	139.0 ± 75.4	<0.0001
Ankle brachial index, mean ± SD	0.9 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	0.4484
Carotid medial thickness, mm, mean ± SD	1.3 ± 0.7	1.3 ± 0.7	1.3 ± 0.7	1.4 ± 0.7	1.3 ± 0.7	0.7831
Microalbuminuria, mean ± SD	106.7 ± 431.9	153.5 ± 404.6	158.3 ± 522.7	110.2 ± 556.3	83.071 ± 279.6	0.0545

BMI, body mass index; BP, blood pressure.

Figure 1 One year event rates (adjusted for age, sex, region) according to the number of risk factors in coronary artery bypass surgery patients showing that as the number of risk factors increased the event rates also increased.

Global variations in prevalence and proportion of risk factors at goal and outcomes

Table 4 shows that risk factors at goal and outcomes demonstrated geographical variations among patients with CABG. Prevalence of risk factors in patients with prior CABG was in general higher among North American patients. Achievement of target goals for risk factors also varied according to the region and was worse for almost all risk factors for the rest of the world compared with US, Western Europe, and Asia. All adverse event rates were higher among patients in the rest of the world compared with other cohort.

Discussion

Our study findings

The major finding of this study in patients with a history of CABG was that the failure to achieve target goals varied widely across various participating sites, among different risk factors and across different regions. There was a suggestion that this variation in risk factor control among CABG patients was associated with variation in outcomes. Thus, a failure to achieve target goal for different risk factors was associated with a trend (for some event non-significant) towards increase in 1 year adverse cardiovascular event rates. This relationship also showed a trend for dose–response linkage with higher clinical adverse event rates among patients who had a lower proportion of risk factors that were at goal. Additionally, risk factors at target goal for that risk factor were associated with a trend (non-significant for some events) for better outcomes than those just treated but not at goal. Thus, perhaps achieving target goals for risk factors appeared to be more important than merely treating patients without reaching this goal. Furthermore, the trend for inverse relationship between risk factors at goal and 1 year outcomes was observed for all

patients irrespective of the number of the underlying risk factors that they had (even in those with four or five risk factors). This suggests that reducing the variability and increasing the modulation of risk factors to their target goal is important for all CABG patients, who are at high atherothrombotic risk, and may have the potential to decrease their long-term adverse event rates.

Our study suggests that in patients who had previous CABG, the vast majority had a clustering of atherothrombotic risk factors, i.e. diabetes, hypertension, high cholesterol, BMI $> 30 \, \text{kg/m}^2$, and smoking, with 95.3% having one or more of these factors. A trend towards higher 1 year adverse clinical events rates of cardiovascular mortality; all-cause death; composite of death, non-fatal stroke, and non-fatal MI; and this composite combined with repeat hospitalization, were noted as the number of risk factors increased. Despite the ubiquitous presence of risk factors among CABG patients and a suggestion of a link between risk factors and adverse events at 1 year, our data indicate that there is a wide variation in treatments to goal of these risk factors. Particularly, in such a population with advanced atherothrombosis at high risk for subsequent event, only 50% of patients had $\geq 75\%$ of their risk factors at treatment goal.

Consistent with that reported previously for the overall patients enrolled in REACH,[15] we also found striking global differences in the prevalence of risk factors and treatments of these risk factors to achieve target goals among patients with prior CABG. Consistent with the overall findings of this investigation, the region with the highest proportion of individual patient risk factors not at goal had also a trend for the worst 1 year adverse event rates. These data suggest that targeting various regions for not only improving treatments of risk factors, but also perhaps to strive and attain target goals to minimize variability in control of risk factors, may have the potential for reducing the geographical variations in adverse outcomes.

Findings of previous studies

Previous observational studies have reported significant variability in guideline-based care for CABG patients.[13,16–18] This variability and lack of adherence to appropriate treatments has been much greater for patients with CABG than those without CABG. Additionally, the PREVENT-IV trial investigators demonstrated a dose-dependent relationship between adherence to guidelines and outcomes among patients undergoing CABG.[16] In PREVENT IV, the 2 year composite event of death or MI increased from 4.2% in patients taking all their indicated medications to 8.2% in those taking less than half their medications [adjusted HR 1.69 (95% CI 1.12–2.55)].[16]

Similarly, Vanasse *et al.*[17] examined a population of patients ≥ 65 years of age in Quebec, Canada who survived their MI and demonstrated that 2 year cardiovascular death rates increased from 4.5 to 15.5%, and non-cardiovascular death rates increased from 6.4 to 14.9% when medication use (aspirin, beta-blockers, angiotensin converting enzyme inhibitors, statins) decreased from 4 to 0 in patients undergoing CABG or percutaneous coronary intervention. These findings are consistent with studies that have examined the overall CAD population as well as those with congestive heart failure, which have shown that performance measures have a major influence on cardiovascular outcomes.[19]

Table 2 Risk factors and 1 year outcomes in coronary artery bypass surgery patients according to individual risk factors adjusted for age, sex, and region

Risk factor	N	Cardiovascular death/MI/stroke			Cardiovascular death			All-cause death			Cardiovascular death/MI/stroke or hospitalization		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
No diabetes	7739	278	3.87	[2.92; 4.80]	116	1.59	[1.01; 2.17]	174	2.43	[1.72; 3.13]	963	12.42	[10.85; 13.95]
Diabetes-overall	5467	304	6.28	[4.79; 7.75]	143	3.05	[1.98; 4.10]	210	4.38	[3.14; 5.59]	952	17.57	[15.41; 19.66]
Diabetes-not treated[a]	591	28	4.95	[2.56; 7.26]	13	2.34	[0.75; 3.96]	23	3.90	[1.77; 5.98]	86	15.10	[11.14; 18.87]
Diabetes-treated[a]	4860	276	6.55	[4.49; 8.53]	130	3.28	[1.85; 4.72]	187	4.61	[2.95; 6.25]	861	17.84	[14.84; 20.71]
Diabetes-treated not at goal[a]	2411	134	6.26	[3.86; 8.65]	58	2.73	[1.45; 4.03]	87	4.09	[2.45; 5.72]	424	17.68	[13.91; 21.25]
Diabetes-treated at goal[a]	1661	87	5.66	[3.35; 7.97]	45	2.97	[1.51; 4.45]	65	4.17	[2.42; 5.91]	275	16.52	[12.78; 20.06]
No hypertension	2562	94	4.22	[2.96; 5.47]	54	2.54	[1.48; 3.60]	71	3.24	[2.10; 4.36]	302	12.28	[10.34; 14.17]
Hypertension-overall	10 643	488	4.99	[3.86; 6.10]	205	2.09	[1.39; 2.79]	313	3.20	[2.34; 4.05]	1612	15.07	[13.31; 16.80]
Hypertension-treated[a]	10 550	486	5.03	[3.78; 5.03]	205	2.13	[1.32; 2.92]	312	3.24	[2.27; 4.19]	1603	15.93	[14.78; 17.06]
Hypertension-not treated[a]	90	2	2.26	[0.00; 5.35]	0	NE[b]	NE[b]	1	1.04	[0.00; 3.05]	8	9.49	[2.86; 15.66]
Hypertension-treated not at goal[a]	2497	128	5.78	[4.04; 7.48]	45	2.31	[1.20; 3.41]	67	3.50	[2.15; 4.82]	427	16.79	[14.22; 19.27]
Hypertension-treated at goal[a]	8031	358	4.81	[3.58; 6.02]	160	2.08	[1.28; 2.87]	245	3.18	[2.21; 4.14]	1174	14.55	[12.65; 16.41]
No hyperlipidaemia	2282	144	6.78	[4.95; 8.56]	78	3.65	[2.24; 5.02]	112	5.16	[3.55; 6.74]	355	16.58	[14.11; 18.97]
Hyperlipidaemia-overall	10 912	437	4.42	[3.41; 5.40]	181	1.86	[1.24; 2.47]	272	2.78	[2.03; 3.53]	1558	14.16	[12.50; 15.78]
Hyperlipidaemia-not treated[a]	99	5	5.64	[0.29; 10.74]	4	4.28	[0.00; 8.80]	4	4.25	[0.00; 8.64]	14	13.45	[6.36; 19.99]
Hyperlipidaemia-treated[a]	10 805	430	4.36	[3.22; 5.49]	176	1.80	[1.12; 2.51]	267	2.75	[1.88; 3.62]	1540	14.11	[12.26; 15.92]
Hyperlipidaemia-treated not at goal[a]	2235	94	4.85	[3.11; 6.54]	29	1.68	[0.72; 2.67]	48	2.79	[1.51; 4.08]	366	15.96	[13.19; 18.64]
Hyperlipidaemia-treated at goal[a]	6770	253	4.08	[2.83; 5.08]	101	1.57	[0.85; 2.32]	156	2.42	[1.52; 3.33]	906	13.27	[11.26; 15.23]
Non-smoker ever	4741	211	4.59	[3.40; 5.75]	96	2.11	[1.30; 2.90]	129	2.82	[1.93; 3.69]	622	12.74	[10.98; 14.46]
Smoker-former or current	8069	354	5.03	[3.84; 6.21]	157	2.25	[1.46; 3.04]	246	3.50	[2.52; 4.47]	1223	15.53	[13.63; 17.38]
Smoker-current	1119	63	7.44	[4.58; 10.18]	22	2.79	[1.10; 4.47]	39	5.07	[2.70; 7.36]	208	19.23	[15.49; 22.79]
Smoker-former	6950	291	4.60	[3.87; 5.33]	135	2.16	[120; 3.12]	207	3.30	[2.15; 4.44]	1015	14.99	[12.69; 17.20]
BMI $>$30 kg/m^2	3922	149	4.46	[3.26; 5.65]	66	2.10	[1.28; 2.93]	97	3.08	[2.08; 4.07]	591'	14.65	[12.68; 16.58]
BMI $\leq$30 kg/m^2	9105	426	5.00	[3.84; 6.14]	192	2.24	[1.48; 2.99]	282	3.26	[2.36; 4.14]	1304	14.57	[12.80; 16.29]

MI, myocardial infarction; BMI, body mass index; N, number of patients at risk; n, number of events; (%), percentage of 'at risk' patients who experienced an event.
[a]Numbers do not add up due to missing variables.
[b]NE, the number of events is $<$5, so the event rates are non-estimable.

Table 3 One-year event rates according to percentage and number of risk factors at goal (adjusted for age, sex, and region)

Percent of risk factors at goal	N	Cardiovascular death/MI/stroke-adjusted			Cardiovascular death-adjusted			All cause death-adjusted			Cardiovascular death/MI/stroke or hospitalization		
		n	(%)	95% CI	n	(%)	95% CI	n	(%)	95% CI	n	(%)	95% CI
<25%	489	22	6.06	[3.15; 8.87]	10	3.22	[0.90; 5.47]	15	4.67	[1.95; 7.29]	82	16.47	[12.57; 20.19]
25–<50%	1701	81	5.61	[3.85; 7.33]	28	2.14	[1.07; 3.20]	45	3.57	[2.14; 4.97]	293	16.97	[14.33; 19.52]
50–<75%	4188	190	5.15	[3.83; 6.45]	92	2.60	[1.62; 3.56]	126	3.52	[2.44; 4.59]	634	15.31	[13.29; 17.27]
≥75%	6829	289	4.43	[3.37; 5.47]	129	1.90	[1.23; 2.56]	198	2.90	[2.08; 3.72]	906	13.35	[11.67; 14.99]
Total	13 207	—	4.84	[3.76; 5.91]	—	2.18	[1.46; 2.88]	—	3.21	[2.36; 4.05]	—	14.56	[12.88; 16.20]
P-value for trend		—	0.0585	—	—	0.1549	—	—	0.0971	—	—	<0.0001	—

MI, myocardial infarction; N, number of patients at risk; n, number of events; (%), percentage of 'at risk' patients who experienced an event.
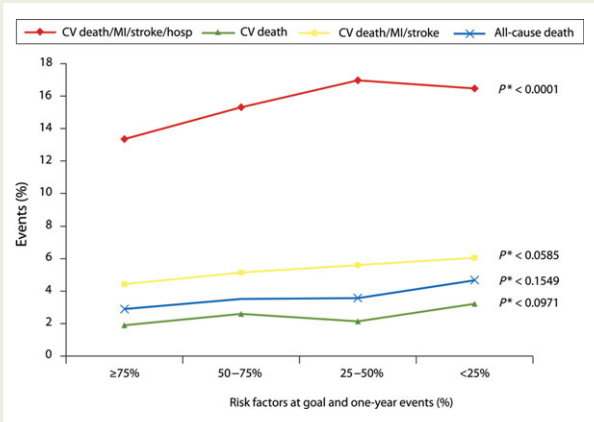
Figure 2 One year event rates (adjusted for age, sex, and region) according to the percentage of risk factors at goal among coronary artery bypass surgery patients. Note the inverse relationship between the percent of risk factors at goal and outcomes. *P-value for trend.

Almost all these studies have focused on the use of evidence-based medications and life-style modification goals and their relationship with patient outcomes.[13,16–18] No prior study has focused on the association of achieving target goals with these therapies with patient outcomes. Thus, the present study adds to this existing knowledge by demonstrating that beyond mere use of evidence-based treatment, there is wide variation in the use of treatments to achieve target goals that may be associated with variation in clinical outcomes in patients with CABG. The widely used performance systems for assessing quality are based on the concept that more consistent use of selected guideline-based therapies leads to better outcomes. Even quality improvement initiatives have focused primarily on improving the use of these therapies.[20] Our data suggest that perhaps guideline-based care should not be limited to mere adherence to these process measures, but should aim for their use to achieve target goals to have the maximum impact on patients' outcomes.

Clinical implications

Our study findings have clinical implications for patients with CABG and CAD in general. Coronary heart disease remains the leading cause of morbidity and mortality in both developed and developing countries.[1,21] While new therapies are continuously evolving to meet the challenge of this global health care burden, better application of available therapy specifically to targeted goals may represent the most cost-effective option for saving lives and improving outcomes. While a modest increase in the use of evidence-based medicine has been shown to result in saving 50 000 or more lives per year,[19] our data suggest a potential for saving even more lives if the wide variability in the use of therapies to targeted goals for secondary prevention is minimized.

Limitations

Our study has limitations. First, it is observational and non-randomized, therefore causality should be inferred with caution. We cannot account for the influence of unmeasured confounders

Table 4 Risk factors and 1 year outcomes according to regions among coronary artery bypass surgery patients

	North America	Western Europe	Asia	Rest of World
n	6964	3075	1146	2022
Diabetes mellitus, *n* (%)	3192 (45.84)	1082 (35.19)	551 (48.08)	642 (31.75)
Diabetes not at goal (in diabetic patients), *n* (%)	1552 (55.07)	498 (58.45)	263 (58.57)	293 (61.43)
Hypertension, *n* (%)	5875 (84.37)	2368 (77.03)	836 (72.95)	1564 (77.35)
Blood pressure not at goal (in hypertensive patients), *n* (%)	951 (16.22)	795 (33.69)	245 (29.38)	526 (33.67)
Hyperlipidaemia, *n* (%)	6032 (86.75)	2561 (83.34)	703 (61.34)	1616 (79.92)
Cholesterol not at goal in patients with history of high cholesterol, *n* (%)	950 (18.10)	685 (33.59)	189 (33.22)	450 (36.23)
Never smoker, *n* (%)	2471 (36.37)	1009 (34.66)	465 (42.01)	796 (39.84)
Former or current smoker, *n* (%)	4323 (63.63)	1902 (65.34)	642 (57.99)	1202 (60.16)
Current smoker among former or current smoker, *n* (%)	618 (14.30)	258 (13.56)	94 (14.64)	149 (12.40)
BMI > 30 kg/m^2, *n* (%)	2546 (37.26)	756 (24.80)	81 (7.10)	539 (26.88)
Outcomes				
Mortality (cardiovascular death); *n*, [% − (95% CI)]	160, [2.24 − (1.73; 2.74)]	59, [2.18 − (1.49; 2.86)]	5, [1.29 − (0.51; 2.06)]	49, [2.48 − (1.56; 3.39)]
Cardiovascular death/MI/ stroke; *n*, [% − (95% CI)]	323, [4.46 − (3.77; 5.15)]	147, [5.30 − (4.24; 6.35)]	19, [4.24 − (2.72; 5.74)]	125, [5.53 − (4.26; 6.79)]
Cardiovascular death/MI/ stroke/hospitalization; *n*, [% − (95% CI)]	1017, [15.18 − (14.00; 16.35)]	485, [16.64 − (15.12; 18.14)]	43, [7.58 − (6.00; 9.13)]	370, [16.91 − (15.14; 18.65)]

BMI, body mass index; MI, myocardial infarction.

on treatment and outcomes, particularly patient and physician preferences for treatments. We evaluated patients at baseline to see if they were at target goals and did not examine whether these goals changed over 1 year—a time-frame used for clinical events. Changes in target goals for better or worse may have had an influence on outcomes. We are unable to adjust for the time between CABG and enrolment in REACH that could have potential impact on adverse events as we do not have the date of previous CABG. Although we define obesity as >30 kg/m^2 for uniformity, this cutoff may differ among patients in different parts of the world. Finally, there may be a selection bias as we examined patients enrolled in the REACH Registry that were enrolled at motivated outpatient practices and failure to achieve target goals may be even higher in the community than that observed in the REACH Registry. We acknowledge that risk factors control and outcomes are likely to vary across sites, countries, and continents in this large, international, multi-centre study. Thus our findings need to be confirmed and validated over a more global population before generalizing them.

Conclusions

Patients remain at high risk of subsequent major cardiovascular events after CABG. Despite this, there is wide variation in post-CABG secondary prevention care around the world. Although patients are frequently treated after CABG with appropriate therapies, these treatments fail to achieve an adequate level of prevention in many. This failure was associated with a trend towards worse age, gender, and region adjusted clinical outcomes at 1 year. Thus, secondary prevention after CABG may have to be focused on more comprehensive risk factor modifications to bring patients to target goals and reduce the existing variability in risk factor control. This strategy may have the potential to prevent further cardiovascular events, and perhaps represents an opportunity to save many lives and improve cardiovascular health.

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