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Unprotected left main revascularization in patients with acute coronary syndromes

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Aims In acute coronary syndromes (ACS), the optimal revascularization strategy for unprotected left main coronary disease (ULMCD) has been little studied. The objectives of the present study were to describe the practice of ULMCD revascularization in ACS patients and its evolution over an 8-year period, analyse the prognosis of this population and determine the effect of revascularization on outcome.

Methods and results Of 43 018 patients enrolled in the Global Registry of Acute Coronary Events (GRACE) between 2000 and 2007, 1799 had significant ULMCD and underwent percutaneous coronary intervention (PCI) alone ($n = 514$), coronary artery bypass graft (CABG) alone ($n = 612$), or no revascularization ($n = 673$). Mortality was 7.7% in hospital and 14% at 6 months. Over the 8-year study, the GRACE risk score remained constant, but there was a steady shift to more PCI than CABG over time. Patients undergoing PCI presented more frequently with ST-segment elevation myocardial infarction (STEMI), after cardiac arrest, or in cardiogenic shock; 48% of PCI patients underwent revascularization on the day of admission vs. 5.1% in the CABG group. After adjustment, revascularization was associated with an early hazard of hospital death vs. no revascularization, significant for PCI (hazard ratio (HR) 2.60, 95% confidence interval (CI) 1.62–4.18) but not for CABG (1.26, 0.72–2.22). From discharge to 6 months, both PCI (HR 0.45, 95% CI 0.23–0.85) and CABG (0.11, 0.04–0.28) were significantly associated with improved survival in comparison with an initial strategy of no revascularization. Coronary artery bypass graft revascularization was associated with a five-fold increase in stroke compared with the other two groups.

Conclusion Unprotected left main coronary disease in ACS is associated with high mortality, especially in patients with STEMI and/or haemodynamic or arrhythmic instability. Percutaneous coronary intervention is now the most common revascularization strategy and preferred in higher risk patients. Coronary artery bypass graft is often delayed and performed in lower risk patients, leading to good 6-month survival. The two approaches therefore appear complementary.

Keywords Left main disease • Acute coronary syndrome

Introduction

The optimal revascularization strategy for unprotected left main coronary disease (ULMCD) is the subject of ongoing debate. In theory, it is one of the best indications for coronary artery bypass graft (CABG) surgery, mainly because randomized studies performed decades ago demonstrated a reduction in mortality with CABG vs. conservative medical treatment.[1,2] However,

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since then, the feasibility of unprotected left main percutaneous coronary intervention (PCI) with bare-metal stents has been reported[3–5] followed, more recently, by favourable outcomes with drug-eluting stents.[6–9] Data on the management of ULMCD are available from a limited number of observational studies, all of which had small sample sizes; a recent pooled analysis identified 16 of these studies, involving a total of 1278 patients with ULMCD, and showed a 2.3% hospital mortality rate in patients who underwent PCI with drug-eluting stents.[10] Propensity score matching methods have also been used and demonstrated similar outcomes for PCI and CABG revascularization in ULMCD.[11,12] Randomized comparisons of PCI vs. CABG in patients with ULMCD are limited to the left main stenting trial, in which 105 patients were randomized to either strategy,[13] and to the ULMCD subgroup in the recently presented SYNTAX (SYNergy Between PCI with TAXUS and Cardiac Surgery) study.[14]

In most of these studies, especially when randomizing or comparing matched cohorts, the highest risk patients were excluded. Indeed, acute (e.g. ST-segment elevation myocardial infarction (STEMI)) or serious (e.g. cardiogenic shock) cases, the elderly, and patients with comorbid conditions are all more likely to be treated with PCI, while those with complex anatomies or ULMCD with concomitant multivessel disease are more likely to undergo CABG. We explored the treatment strategies applied to ULMCD in unselected patients presenting with an acute coronary syndrome (ACS), a high-risk clinical situation that impacts treatment choices and clinical outcomes in a way not seen in studies that dealt mainly with stable and scheduled cases.

Methods

Full details of the Global Registry of Acute Coronary Events (GRACE) methods have been published.[15–17] In brief, GRACE was designed to reflect an unselected population of patients with ACS, irrespective of geographic region. A total of 14 countries in North and South America, Europe, Australia, and New Zealand have contributed data to this observational study.

Adult patients (≥18 years) admitted with a presumptive diagnosis of ACS at participating hospitals were potentially eligible for this study. Eligibility criteria were a clinical history of ACS accompanied by at least one of the following: electrocardiographic changes consistent with ACS, serial increases in biochemical markers of cardiac necrosis (CK-MB, creatine phosphokinase, or troponin), and documented coronary artery disease. Patients with non-cardiovascular causes for the clinical presentation, such as trauma, surgery, or aortic aneurism, were excluded. Patients were followed up at approximately 6 months by telephone, clinic visits, or through calls to their primary care physician to ascertain the occurrence of several long-term outcomes. Where required, study investigators received approval from their local hospital ethics or institutional review board for the conduct of this study.

To enrol an unselected population of patients with ACS, sites were encouraged to recruit the first 10 to 20 consecutive eligible patients each month. Regular audits were performed at all participating hospitals. Data were collected by trained study co-ordinators using standardized case report forms. Demographic characteristics, medical history, presenting symptoms, duration of pre-hospital delay, biochemical and electrocardiographic findings, treatment practices, and a variety of hospital outcome data were collected. Standardized definitions of all patient-related variables, clinical diagnoses, and hospital complications and outcomes were used.[15] All cases were assigned to one of the following categories: STEMI, non-STEMI, or unstable angina.

Patients were diagnosed with STEMI when they had new or presumed new ST-segment elevation ≥1 mm seen in any location, or new left bundle branch block on the index or subsequent electrocardiogram with at least one positive cardiac biochemical marker of necrosis (including troponin measurements, whether qualitative or quantitative). In cases of non-STEMI, at least one positive cardiac biochemical marker of necrosis without new ST-segment elevation seen on the index or subsequent electrocardiogram had to be present. Unstable angina was diagnosed when serum biochemical markers indicative of myocardial necrosis in each hospital's laboratory were within the normal range. The main outcome measure of the present study was mortality evaluated in-hospital and at 6 months' follow-up. Other ischaemic and haemorrhagic endpoints were evaluated at same time points. Full definitions can be found on the GRACE web site at www.outcomes.org/grace. Hospital-specific feedback regarding patient characteristics, presentation, management, and outcomes are provided to each centre on a quarterly basis in the form of written reports.

Statistical analysis

Univariate comparisons were performed using Fisher's exact test for dichotomous variables, the Cochran–Mantel–Haenszel trend test for Killip class (ordinal), and the Wilcoxon rank-sum test for continuous variables. Kaplan–Meier curves show unadjusted cumulative mortality and stroke from hospital admission to 6 months according to the revascularization group. The groups were treated as time-varying covariates, so that if a patient underwent CABG on day 4 after admission they were counted as not having revascularization performed on days 0–3, and as having had CABG surgery from day 4 onwards.

Adjusted results for mortality were calculated from multiple Cox regression models, treating PCI and CABG as time-varying covariates. The results were adjusted for the GRACE risk score variables (age, cardiac arrest at presentation, Killip class, ST deviation on presentation, initial creatinine concentration, positive initial cardiac markers, heart rate, systolic blood pressure).[17] In addition, we adjusted for significant Q-waves on presentation and mechanical ventilation. The Cox model included a time-varying indicator variable of whether an observation for a patient on day t occurs in hospital or after discharge. We then formed an interaction between this variable and revascularization to estimate distinct hazard ratios (HRs) for revascularization with in-hospital and post-discharge mortality.[18] We ran all analyses using SAS version 9.1 (SAS Institute Inc., Cary, NC).

Results

Patient population

This analysis is based on 43 018 patients who presented to 106 hospitals with an ACS between 2000 and 2007, had complete 6-month follow-up data available, and underwent cardiac catheterization. Of these patients, 2783 had significant (>50% stenosis) left main disease identified on the coronary angiogram. To exclude patients with protected left main disease, all individuals with a history of CABG were excluded ($n = 921$, *Figure 1*). Patients with missing information on revascularization and those who underwent both types of revascularization during the index admission were also excluded. A total of 1799 patients with left main disease were therefore included in the analysis, and were

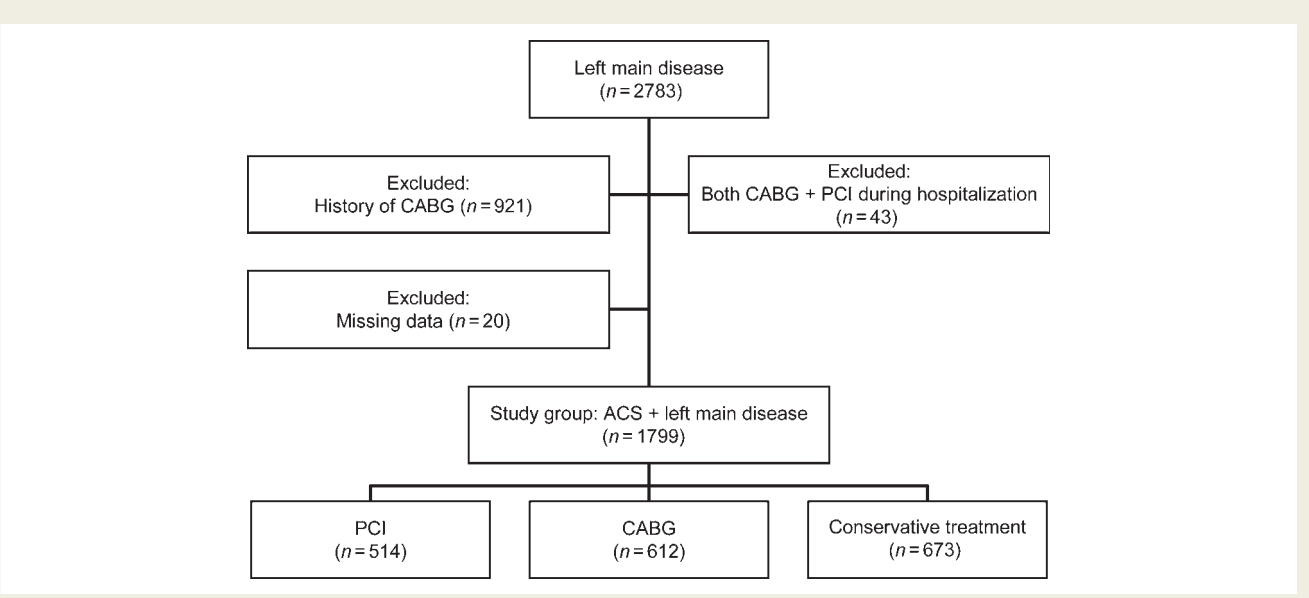

Figure 1 Study flow diagram.

categorized according to the initial treatment strategy as follows: PCI alone ($n = 514$), CABG alone ($n = 612$), or no revascularization during hospitalization ($n = 673$).

Baseline demographics

The median age of the population was 70 (inter-quartile range 60–78) years and 498 (28%) were women. The population was generally high risk, with 603 (40%) being above 75 years, 472 (26%) with a history of myocardial infarction, 158 (8.9%) with prior stroke, and 168 (9.4%) with renal insufficiency. The most severe patients presented with ongoing STEMI ($n = 627$, 35%, had new ST elevation or left bundle branch block), heart failure ($n = 404$, 23% had Killip class >I), and/or cardiac arrest or cardiogenic shock (59, 3.4%). Most ($n = 1688$, 94%) patients had coronary lesions in addition to left main disease (*Table 1*). The median GRACE risk score[17] was 141 (inter-quartile range 117–169) (equivalent to an approximate 3% risk of in-hospital death).

The baseline characteristics of patients differed significantly between the three strategies. The most severe patient characteristics were found in the group who did not undergo revascularization. The most severe presentation of the index ACS was found in the PCI group. Compared with the other two groups, patients undergoing PCI presented more frequently with an acute myocardial infarction (as opposed to unstable angina), after a cardiac arrest, or in cardiogenic shock, more frequently had a low ejection fraction (median 46%, inter-quartile range 35–57 vs. 50%, 35–60 in the other two groups, $P < 0.05$) or a recent history of major surgery or trauma (*Table 1*). They were also older (median of 71, IQR [60–79]) than patients undergoing CABG (median of 69, IQR [60–75]), but younger than those that did not undergo revascularization during the index hospitalization (median of 72, IQR [61–79]). The median GRACE risk score[17] was 151 (equivalent to a 4% risk of in-hospital death) in PCI patients, 134 (≅2.4%) in CABG patients, and 143 (≅3.2%) in non-revascularized patients ($P < 0.001$ for linear trend).

Time to revascularization varied greatly between the PCI and CABG groups: in the PCI group, 48% of patients underwent revascularization on the day of admission vs. 5.1% in the CABG group. At 48 h, 69% of the PCI patients vs. 25% of the CABG patients were revascularized, the median delay to revascularization being 4.5 days for CABG. In revascularized patients, on average one or two stents were used in 79% ($n = 376$) of PCI patients, with the majority ($n = 121$, 70%) being bare-metal stents, whereas one to three grafts were placed in 88% ($n = 510$) of the CABG patients, with the majority ($n = 426$, 73%) receiving both venous and arterial grafts (*Table 2*). In PCI patients, there was a steady increase in the use of drug eluting stents over time, reaching 49% of stents implanted in 2007 ($P < 0.001$ for linear trend).

Trends in left main revascularization over 8 years

The median GRACE risk score remained constant over the 8-year study period, with a stable 20-point difference between PCI and CABG groups from 2000 to 2007 (*Figure 2A*).

In 2000, the rate of CABG was 2.5-fold higher than the rate of PCI. There was a steady shift to more PCIs over time despite the same difference in risk score between CABG and PCI over this period (*Figure 2B*). In 2007, the PCI rate was 40% while the CABG rate was 25%. The proportion of patients who did not undergo revascularization remained stable over the study period (39% in 2000; 35% in 2007).

Clinical outcomes

Hospital mortality was 7.7% ($n = 139$) in the whole population, 11% ($n = 69$) in those with new ST elevation or left bundle branch block on the index ECG, and 34% ($n = 20$) in patients who presented with cardiogenic shock and/or after a cardiac

Table 1 Patient baseline characteristics and clinical presentation

	Total population			PCI (n = 514)			CABG (n = 612)			Neither (n = 673)			P^*
	n	N	%	n	N	%	n	N	%	n	N	%	
Demographic													
Women	498	1795	28	140	511	27	160	612	26	198	672	30	0.64
Age >75 years	603	1786	40	181	510	36	157	608	26	265	668	40	<0.001
Medical history													
Angina	925	1794	52	217	514	42	340	611	56	368	669	55	<0.001
Myocardial infarction	472	1791	26	128	511	25	160	611	26	184	669	28	0.68
Heart failure	163	1797	9.1	31	510	6.1	46	609	7.6	86	668	13	0.35
PCI	229	1790	13	81	512	16	70	609	12	78	669	12	0.04
Peripheral arterial disease	234	1785	13	59	509	12	77	607	13	98	669	15	0.65
Atrial fibrillation	100	1781	5.6	30	507	5.9	22	610	3.6	48	664	7.2	0.09
TIA/stroke	158	1782	8.9	37	508	7.3	56	610	9.2	65	664	9.8	0.28
Renal insufficiency	168	1793	9.4	44	512	8.6	48	610	7.9	76	671	11	0.66
Recent† major surgery/ trauma	108	1793	6.0	52	512	10	29	610	4.8	27	671	4.0	<0.001
Risk factors/medications													
Hypertension	1215	1789	68	321	507	63	430	612	70	464	670	69	0.02
Hyperlipidemia	916	1790	51	233	508	46	351	609	58	332	673	49	<0.001
Smoking (current/former)	1022	1793	57	271	512	53	370	612	61	381	669	57	0.01
Diabetes	524	1793	29	140	512	27	169	610	28	215	671	32	0.95
Aspirin	718	1799	40	177	514	34	266	612	44	275	673	41	0.002
Warfarin	78	1764	4.4	18	500	3.6	30	599	5.0	30	665	4.5	0.30
Thienopyridine	125	1771	7.1	39	500	7.8	31	604	5.1	55	667	8.2	0.08
ACE inhibitor	524	1786	29	123	510	24	169	607	28	232	669	35	0.17
Statin	506	1784	28	118	508	23	183	607	30	205	669	31	0.01
Clinical presentation													
New STE/LBBB	627	1799	35	293	514	57	139	612	23	195	673	29	<0.001
ST depression	771	1799	43	229	514	45	223	612	36	319	673	47	0.01
T-wave inversion	486	1799	27	117	514	23	177	612	29	192	673	29	0.02
Q wave	341	1799	19	119	514	23	110	612	18	112	673	17	0.04
LVEF <40%	311	1113	28	95	336	28	110	420	26	106	357	30	0.56
Killip class													
I	1344	1748	77	379	497	76	471	594	79	494	657	75	0.08
II	270	1748	16	72	497	15	89	594	15	109	657	17	
III	103	1748	5.9	32	497	6.4	28	594	4.7	43	657	6.5	
IV	31	1748	1.8	14	497	2.8	6	594	1.0	11	657	1.7	
Cardiac arrest and/or cardiogenic shock	59	1735	3.4	25	491	5.1	10	589	1.7	24	655	3.7	0.003
Left main alone (vs. left main with other territory)	111	1799	5.6	41	514	8.0	32	612	5.2	38	673	5.6	0.07

*PCI vs. CABG.
†Within previous 2 weeks.
ACE, angiotensin-converting enzyme; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TIA, transient ischaemic attack.

arrest (*Table 3*). The cumulative mortality rate from hospitalization to 6 months post-discharge in the ACS cohort with left main disease was 14%. As expected based on composite GRACE risk scores and percutaneous revascularization of the most acute cases, both in-hospital and 6-month mortality rates were higher in the PCI group (*Table 3*). The lowest mortality both in hospital and after discharge was in patients who had initially undergone a surgical revascularization strategy (*Figure 3A*). After discharge, patients who did not undergo hospital revascularization had the highest mortality rate at 6 months (n = 46, 10% vs. n = 17, 5.4% in the PCI group and n = 7, 1.6% in the CABG group) (*Table 3*). The initially non-revascularized patients had a 43% (n = 179) rate of surgical revascularization during the 6-month follow-up period. Ninety-two per cent of the 43% revascularized after

Table 2 Hospital management

	Total population			PCI			CABG			Neither			P*
	n	N	%	n	N	%	n	N	%	n	N	%	
Medication													
Aspirin	1697	1799	94	486	514	95	577	612	94	634	673	94	0.90
Warfarin	124	1764	7.0	20	500	4.0	63	599	11	41	665	6.2	<0.001
Thienopyridine	1040	1787	58	446	511	87	248	609	41	346	667	52	<0.001
Unfractionated heparin	1011	1781	57	292	509	57	432	606	71	287	666	43	<0.001
LMWH	1100	1787	62	299	508	59	342	609	56	459	670	69	0.40
GP IIb/IIIa inhibitor	545	1778	31	286	509	56	150	601	25	109	668	16	<0.001
ACE inhibitor	1259	1786	71	373	510	73	433	607	71	453	669	68	0.55
Beta-blocker	1537	1789	86	423	511	83	550	606	91	564	672	84	<0.001
Calcium antagonist	447	1779	25	85	507	17	184	608	30	178	664	27	<0.001
Diuretic	941	1784	53	201	507	40	454	610	74	286	667	43	<0.001
IV inotropic drugs	416	1771	24	105	505	21	254	600	42	57	666	8.6	<0.001
Statin	1329	1784	75	391	508	77	439	607	72	499	669	75	0.08
Revascularization													
Stents per patient													
0	–	–	–	30	482	6.2	–	–	–	–	–	–	n/a
1	–	–	–	246	482	51	–	–	–	–	–	–	
2	–	–	–	136	482	28	–	–	–	–	–	–	
≥3	–	–	–	70	482	15	–	–	–	–	–	–	
Drug-eluting stent	–	–	–	121	409	30	–	–	–	–	–	–	n/a
Grafts per patient													
0	–	–	–	–	–	–	14	578	2.4	–	–	–	n/a
1	–	–	–	–	–	–	117	578	20	–	–	–	
2	–	–	–	–	–	–	255	578	44	–	–	–	
3	–	–	–	–	–	–	138	578	24	–	–	–	
≥4	–	–	–	–	–	–	54	578	9.3	–	–	–	
Type of graft													
Venous	–	–	–	–	–	–	97	582	17	–	–	–	n/a
Arterial	–	–	–	–	–	–	59	582	10	–	–	–	
Both	–	–	–	–	–	–	426	582	73	–	–	–	
IABP	271	1752	16	99	501	20	143	593	24	29	658	4.4	0.009

*PCI vs. CABG.
ACE, angiotensin-converting enzyme; GP, glycoprotein; IABP, intra-aortic balloon pump; IV, intravenous; LMWH, low-molecular-weight heparin; n/a, not applicable.

discharge were scheduled for post-discharge revascularization in the hospital.

The two most frequent in-hospital complications in our ACS population with left main disease were episodes of recurrent ischaemia ($n = 503$, 28%) and heart failure ($n = 389$, 22%), which often may have prompted revascularization. Nine per cent ($n = 162$) of patients developed cardiogenic shock during hospitalization and significantly more of these had PCI ($n = 70$, 14%) than CABG ($n = 45$, 7.4%; *Table 3*). CABG revascularization was associated with a five-fold increase in stroke in comparison with the other two groups (*Table 3*, *Figure 3B*). There was no between-group difference for stroke after discharge up to 6 months (*Table 3*). Finally, there was no difference between groups for the triple ischaemic endpoint of death, re-infarction, or stroke (*Table 3*).

Cox regression model for death

The covariates (HR, 95% confidence interval (CI)) were cardiac arrest at presentation (0.74, 0.29–1.86), Killip class I–IV (1.27, 1.06–1.53), ST elevation (1.45, 1.01–2.06), ST depression (1.80, 1.30–2.49), Creatinine, per 1 mg (1.19, 1.09–1.32), positive initial enzymes (1.15, 0.81–1.64), age per 10 years (1.63, 1.39–1.91), pulse per 30 b.p.m. (1.20, 0.98–1.48), systolic BP per 20 mm hg decrease (1.20, 1.08–1.33), Q wave (1.12, 0.77–1.63), mechanical ventilator (3.04, 2.10–4.39). After adjustment for these covariates and considering PCI and CABG as time-varying covariates, revascularization was associated with an early hazard of hospital death compared with no revascularization that was significant for PCI (HR 2.60, 95% CI 1.62–4.18) but not for CABG (HR 1.26, 95% CI 0.72–2.22). From discharge to 6 months, both PCI (HR 0.45,

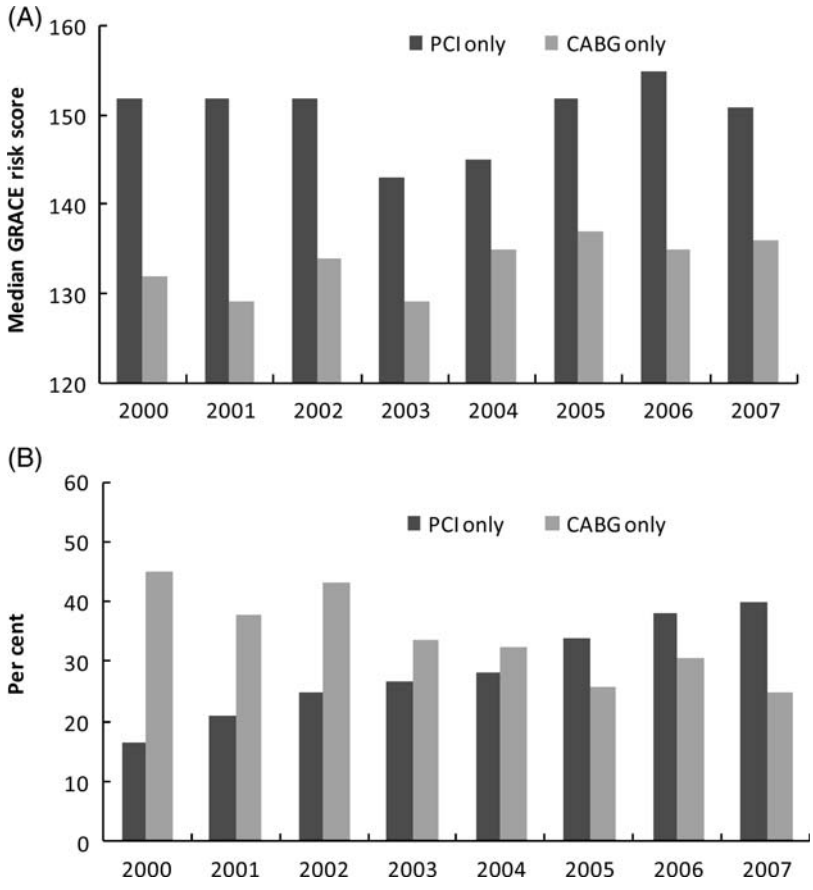

Figure 2 Temporal trends in acute coronary syndrome (*A*) score severity and (*B*) type of revascularization in left main disease.

95% CI 0.23–0.85) and CABG (HR 0.11, 95% CI 0.04–0.28) were significantly associated with improved survival in comparison with an initial strategy of no revascularization.

Discussion

To our knowledge, this study presents one of the largest data sets of ULMCD and certainly the largest experience in ACS. The incidence of ULMCD in patients with an ACS is not known precisely and we report here an incidence of 4% (1799 of 43 018), which may be an underestimate as many patients may have died early before enrolment and, cardiac catheterization was performed in only 62% of the patients enrolled in the registry. An important finding from this 8-year study is that PCI has become the preferred mode of revascularization for ULMCD and is used in the highest risk patients, but is associated with frequent repeat revascularizations in the following 6 months. In contrast, surgery is performed in lower risk patients and is associated with better survival but with more frequent acute strokes. After adjustment for baseline characteristics, both types of revascularization improved 6-month survival in comparison with an initial conservative medical strategy.

Although still debated, the use of percutaneous revascularization in ULMCD has increased in frequency, with improvements and standardization of techniques, including T-stenting, high pressure inflation, optimization of stenting with intravascular ultrasounds, the kissing-balloon technique, and restenosis reduction with drug-eluting stents. Our study confirms this impression in unselected patients presenting with an ACS, recruited in more than 100 multinational centres, and in whom PCI was the preferred revascularization strategy in the last 3 years of the study. There may be an early hazard for this approach in ACS patients, with an in-hospital mortality rate two- to four-fold higher than the rates usually reported for scheduled percutaneous revascularization of ULMCD.[10,14,19,20] This is explained largely by the patients' high-risk characteristics, due to the absence of exclusion criteria in GRACE, and, when ACS is complicated by cardiogenic shock and/or resuscitated cardiac arrest, in-hospital mortality reached 40% in the PCI group. Whether CABG would be a better option in shock patients is still discussed.[21]

Despite the trend over time to more frequent percutaneous revascularization, the group who underwent CABG was as large as the PCI and non-revascularization groups, and had the lowest non-adjusted mortality rate at hospital discharge and at 6 months. The GRACE risk score, which evaluates risk of in-hospital mortality in ACS patients,[17] was significantly lower in CABG patients than in PCI patients, reflecting the selection of patients for CABG surgery. A similar observation was reported with the EuroScore and Parsonnet revascularization scores,

Table 3 Clinical outcomes

	Total population			PCI			CABG			Neither			P*
	n	N	%	n	N	%	n	N	%	n	N	%	
Hospital outcome													
Death	139	1797	7.7	55	514	11	33	611	5.4	51	672	7.6	0.001
Death (patients with cardiac arrest and/or cardiogenic shock at presentation)	20	59	34	10	25	40	3	10	30	7	24	29	0.71
Death (patients with new STE/LBBB on index ECG)	69	627	11	38	293	13	7	139	5.0	24	195	12	0.01
Cardiac arrest/VF	148	1780	8.3	65	509	13	31	604	5.1	52	667	7.8	<0.001
Sustained VT	80	1788	4.5	34	510	6.7	16	609	2.6	30	669	4.5	0.001
New episode of HF or pulmonary edema	389	1794	22	115	513	22	153	612	25	121	669	18	0.33
New cardiogenic shock	162	1796	9.0	70	513	14	45	611	7.4	47	672	7.0	<0.001
Recurrent angina	503	1796	28	120	514	23	177	611	29	206	671	31	0.04
Re-infarction	46	1267	3.6	16	408	3.9	13	394	3.3	17	465	3.7	0.71
Renal failure	138	1781	7.8	39	509	7.7	59	608	9.7	40	664	6.0	0.24
Atrial fibrillation/flutter	261	1793	15	55	511	11	155	612	25	51	670	7.6	<0.001
Stroke	19	1789	1.1	2	511	0.4	13	609	2.1	4	669	0.6	0.02
Death/re(MI)/stroke	133	1265	11	51	406	13	37	395	9.4	45	464	14	0.26
Non-CABG major bleeding, plus haemorrhagic stroke	53	1772	3.0	30	505	5.9	7	603	1.2†	16	664	2.4	n/a
Non-CABG major bleeding w/o haemorrhagic stroke	74	1774	4.2	31	506	6.1	27	608	4.5	16	665	2.4	0.23
Six-month outcomes (follow-up rate if survived to discharge)	1206	1658	73	312	459	68	437	578	76	457	621	74	0.01
Death	70	1206	5.8	17	312	5.4	7	437	1.6	46	457	10	0.005
Death (patients with new STE/LBBB on index ECG)	33	404	8.2	14	178	7.9	3	97	3.1	16	129	12	0.19
Myocardial infarction	29	1136	2.6	14	293	4.8	3	417	0.7	12	426	2.8	<0.001
Stroke	15	1143	1.3	3	295	1.0	5	421	1.2	7	427	1.6	0.99
Re-hospitalization for CV reason	199	1166	17	68	299	23	45	426	11	86	441	20	<0.001
Cardiac catheterization	121	1128	11	66	295	22	20	414	4.8	35	419	8.4	<0.001
PCI	65	1104	5.9	32	287	11	15	404	3.7	18	413	4.4	<0.001
CABG	243	1116	22	34	292	12	30	405	7.4	179	419	43	0.06

*PCI vs. CABG.
CABG, coronary artery bypass graft; CV, cardiovascular; ECG, electrocardiogram; LBBB, left bundle branch block; PCI, percutaneous coronary intervention; STE, ST elevation; VF, ventricular fibrillation; VT, ventricular tachycardia.

which were lower for CABG than for PCI in the recent SYNTAX registry of patients who were not candidates for randomization in the SYNTAX study.[14]

In the present study, in-hospital death and cardiac arrest were less frequent in the CABG group, as was death, myocardial infarction, and revascularization from hospital discharge to 6 months. After adjustment, CABG revascularization was strongly and significantly associated with survival from discharge to 6 months in comparison with the group who did not undergo revascularization. Percutaneous coronary intervention was also significantly and positively associated with survival over the same period, although with a lower magnitude.

Whether or not the difference in survival between the two modes of revascularization is due to the treatment strategies themselves or to differences in the patient populations undergoing such treatment is not possible to determine in this observational study. Although we attempted to adjust for all confounding variables measured, other important clinical or angiographic parameters that influence clinical outcome may have been overlooked or not even collected and we could not adjust for the selection of patients into the treatment groups. Moreover, considering PCI and CABG as time-varying covariates is a statistical approach that carries its own limitations. Half of the patients in the PCI group underwent revascularization on the day of admission, accumulating all the risks of the ACS event and of the revascularization procedure in the first 24 h, while the median time to revascularization was 4.5 days in the CABG group, selecting out patients who died from the event or developed a contraindication to surgery during the waiting period. Finally, CABG patients had a significant excess of stroke in comparison with the other two groups, a complication of CABG also identified in the SYNTAX study. Whether the procedure of revascularization itself or other factors such as single vs. double antiplatelet therapy is involved in this excess risk of stroke cannot be determined from our study. Altogether, the triple ischaemic endpoint (death, re-infarction, or stroke) did not differ significantly between groups during the hospital phase.

Evidence-based practice guidelines recommend rapid access to angiography and revascularization in both high-risk non-ST

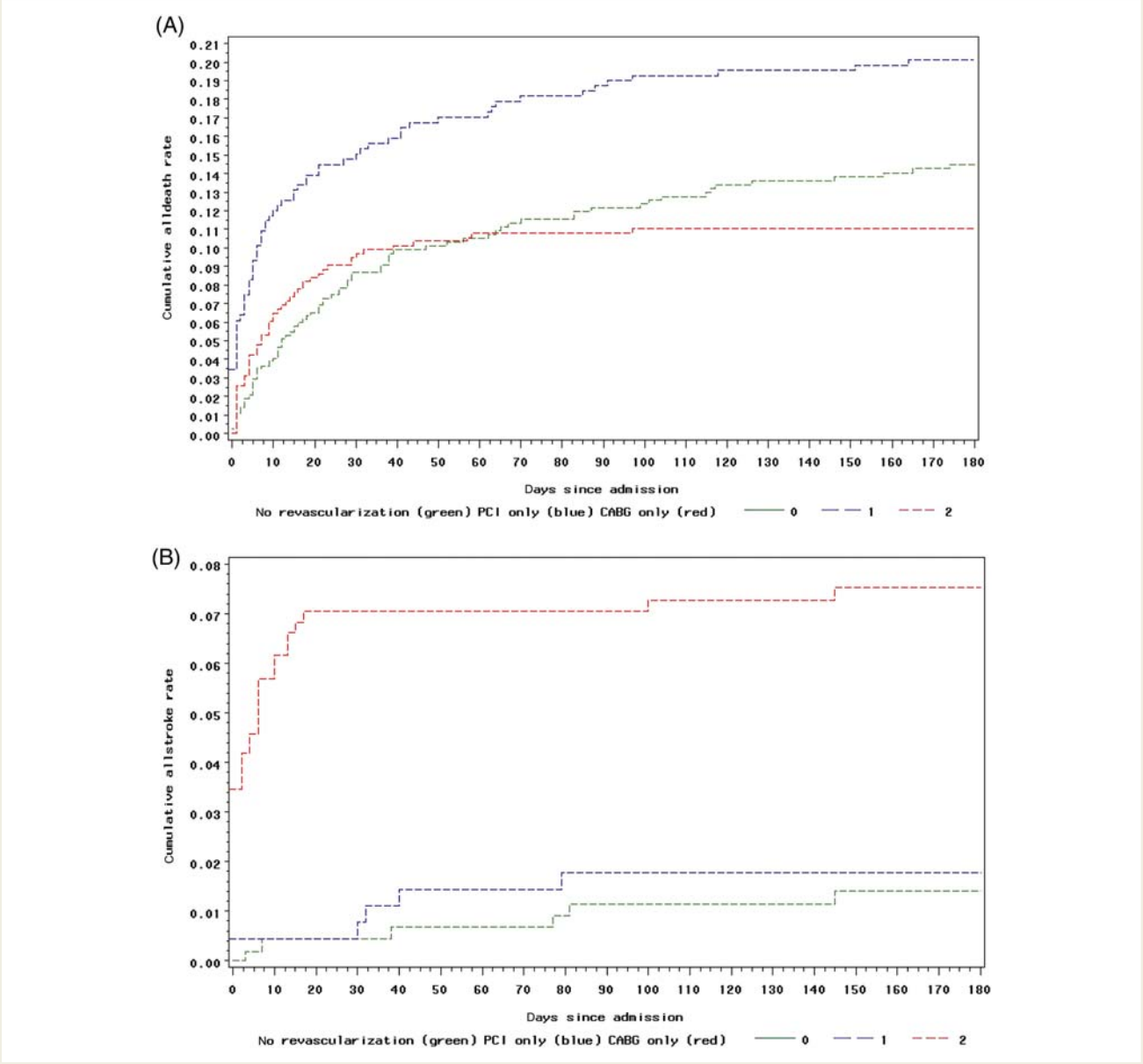

Figure 3 (*A*) Cumulative death rate by revascularization group as a time-varying covariate. The number of patients analysed in each group were as follows: $n = 513$ for percutaneous coronary intervention, $n = 607$ for coronary artery bypass graft, and $n = 670$ for neither. (*B*) Cumulative rate of stroke by revascularization group as a time-varying covariate. The number of patients analysed in each group were as follows: $n = 492$ for PCI, $n = 581$ for CABG, and $n = 633$ for neither.

elevation and ST elevation ACS.[22–25] Patients with ULMCD are among the highest risk patients presenting with an ACS but current consensus guidelines do not address the optimal timing and mode of revascularization for these individuals. The adjusted 6-month survival benefit observed with revascularization in our study suggests that these recommendations may well apply to ACS with ULMCD. Percutaneous coronary intervention of ULMCD is frequently performed in ACS patients and recent reports suggest a larger clinical benefit with drug-eluting stents than with bare-metal stents.[26] Interestingly also, of the patients who did not undergo any type of revascularization during the index hospitalization, 43% underwent CABG revascularization during the 6-month period following discharge. This suggests that the initial very high risk of these patients should not preclude re-evaluation for potential revascularization at some point before hospital discharge.

Conclusions

Unprotected left main coronary disease in patients presenting with an ACS is a rare but serious situation, with high in-hospital mortality, especially in those presenting with STEMI and/or haemodynamic or arrhythmic instability. Percutaneous coronary intervention has become the most common strategy of revascularization in ACS patients with ULMCD and is generally preferred in

patients with multiple comorbidities and/or in very unstable patients. In contrast, CABG surgery, when possible, is often delayed by a few days and is associated with good 6-month survival. Therefore the two modes of revascularization appear complementary in this high-risk group.

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CARDIOVASCULAR FLASHLIGHT

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Secondary diaphragmatic rupture as a cause of worsening dyspnoea after blunt thorax trauma and consecutive pulmonary embolism

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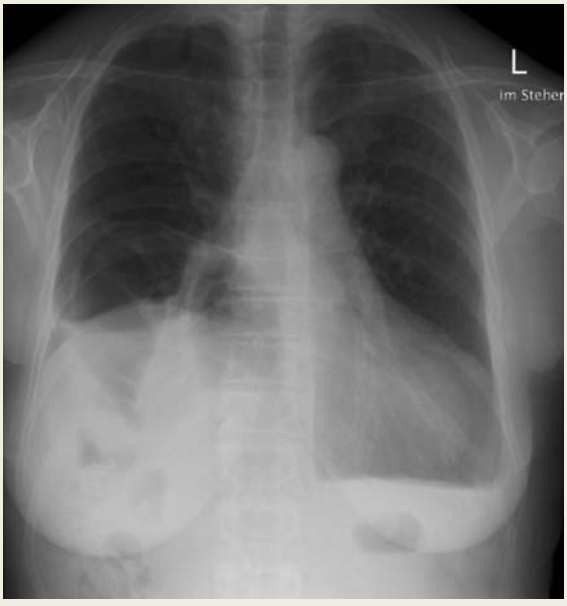
A 67-year-old woman had been wearing a seat-belt during a car accident. She was transferred to the trauma centre. During whole-body computed tomography (CT), bone fractures and relevant injuries of internal organs were ruled out.



Three days after the accident, the patient suffered from acute respiratory distress. A CT angiography revealed pulmonary embolism. The patient was transferred to the Medical Department. Transthoracic echocardiography revealed low-grade pulmonary hypertension and right ventricular enlargement and hypokinesia. Treatment consisted of oxygen supplementation, weight-adapted low molecular weight heparin (tinzaparine), and antiobiotics because of suspected pneumonia. The patient's condition improved subsequently. Eleven days after the accident, the patient again suffered from acute dyspnoea; arterial oxygen saturation without oxygen supplementation was 80%. Repeat echocardiography revealed normal left and right ventricular function and normal pulmonary artery pressure. Because of dullness to percussion and diminished breath sounds of the caudal right hemithorax, a chest radiograph was performed.

The findings were suspicious of diaphragmatic rupture (*Panel A*). The suspected herniation of the colon was confirmed by CT. The patient underwent laparotomy, at which time the diaphragm was repaired. Except for a subcapsular liver haematoma which was managed conservatively, the post-operative course was uneventful. The patient subsequently improved and was discharged 30 days after the accident with ongoing anticoagulation.

In the present case, clinical suspicion favoured repeat pulmonary embolism. Diaphragmatic rupture was suspected by chest radiograph and confirmed by CT. Secondary post-traumatic rupture is a rare complication of thoracic or abdominal trauma.