Does prior coronary angioplasty affect outcomes of surgical coronary revascularization? Insights from the STICH trial

Jose C. Nicolau [a,*], Susanna R. Stevens [b], Hussein R. Al-Khalidi [b], Fabio B. Jatene [a], Remo H.M. Furtado [a], Luis A.O. Dallan [a], Luiz A.F. Lisboa [a], Patrice Desvigne-Nickens [c], Haissam Haddad [d], E. Marc Jolicoeur [e], Mark C. Petrie [f], Torsten Doenst [g], Robert E. Michler [h], E. Magnus Ohman [b], Jyotsna Maddury [i], Imtiaz Ali [j], Marek A. Deja [k], Jean L. Rouleau [e], Eric J. Velazquez [l], James A. Hill [m]

[a] Instituto do Coracao (InCor), Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil
[b] Duke Clinical Research Institute and Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, NC, USA
[c] Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA
[d] Department of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada
[e] Montreal Heart Institute, Université de Montréal, Quebec, Canada
[f] BHF Cardiovascular Research Centre, University of Glasgow, Glasgow, United Kingdom
[g] Department of Cardiothoracic Surgery, University of Jena, Jena, Germany
[h] Department of Cardiothoracic Surgery, Montefiore Medical Center/Albert Einstein College of Medicine, New York, NY, USA
[i] Department of Cardiology, Nizams Institute of Medical Sciences, Hyderabad, India
[j] Libin Cardiovascular Institute of Alberta, University of Calgary, Foothills Medical Centre, Calgary, Alberta, Canada
[k] Department of Cardiac Surgery, Medical University of Silesia, Katowice, Poland
[l] Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, USA
[m] Department of Medicine, University of Florida, Gainesville, FL, USA

ARTICLE INFO

ABSTRACT

Background: The STICH trial showed superiority of coronary artery bypass plus medical treatment (CABG) over medical treatment alone (MED) in patients with left ventricular ejection fraction (LVEF) ≤35%. In previous publications, percutaneous coronary intervention (PCI) prior to CABG was associated with worse prognosis.
Objectives: The main purpose of this study was to analyse if prior PCI influenced outcomes in STICH.
Methods and results: Patients in the STICH trial (n = 1212), followed for a median time of 9.8 years, were included in the present analyses. In the total population, 156 had a prior PCI (74 and 82, respectively, in the MED and CABG groups). In those with vs. without prior PCI, the adjusted hazard-ratios (aHRs) were 0.92 (95% CI = 0.74–1.15) for all-cause mortality, 0.85 (95% CI = 0.64–1.11) for CV mortality, and 1.43 (95% CI = 1.15–1.77) for CV hospitalization. In the group randomized to CABG without prior PCI, the aHRs were 0.82 (95% CI = 0.70–0.95) for all-cause mortality, 0.75 (95% CI = 0.62–0.90) for CV mortality and 0.67 (95% CI = 0.56–0.80) for CV hospitalization. In the group randomized to CABG with prior PCI, the aHRs were 0.76 (95% CI = 0.50–1.15) for all-cause mortality, 0.81 (95% CI = 0.49–1.36) for CV mortality and 0.61 (95% CI = 0.41–0.90) for CV hospitalization. There was no evidence of interaction between randomized treatment and prior PCI for any endpoint (all adjusted p > 0.05).
Conclusion: In the STICH trial, prior PCI did not affect the outcomes of patients whether they were treated medically or surgically, and the superiority of CABG over MED remained unchanged regardless of prior PCI.
Clinical trial registration: Clinicaltrials.gov; Identifier: NCT00023595

© 2019 Elsevier B.V. All rights reserved.

1. Introduction

Coronary artery bypass graft (CABG) surgery has been established as the standard of care for patients with multi-vessel coronary artery disease (CAD) and left ventricular (LV) dysfunction [1,2]. Although this was first suggested by subgroup analyses from older randomized trials, in subgroup analyses with small numbers of patients [3,4], more recently the STICH trial definitely demonstrated a significant long-term mortality reduction favoring CABG versus medical treatment alone (MED) specifically in patients with LVEF ≤35% [5,6].

Whether the same benefit could be conferred by percutaneous coronary intervention (PCI) is a matter of debate [7–10], with a meta-analysis demonstrating superiority of PCI and CABG over MED, with survival advantage favoring CABG in comparison with PCI [11].

* Corresponding author at: Aureliano Coutinho 355, apt. 1401, São Paulo 01224-020, Brazil.
E-mail address: jose.nicolau@incor.usp.br (J.C. Nicolau).

In previous reports, prior PCI has been associated with worse short-term outcomes after CABG [12–14] and to increased long-term postoperative mortality [15]. However, this claim has been disputed by recent reports. Ueki et al. analyzing >48,000 individuals undergoing CABG (12,437 with prior PCI), found the same operative mortality (1.2%) in the groups with or without prior PCI. Mariscalco et al. found an odds-ratio of 0.90 (with vs. without prior PCI) for in-hospital mortality (p = 0.81), raising the question whether there could be any influence of selection bias due to inclusion of prior PCI in an urgent setting in the previous studies [16,17]. However, none of those reports specifically addressed the high-risk population with severe LV dysfunction. Therefore, we sought to investigate in the STICH trial (which randomized patients with LVEF ≤35% to CABG plus MED or MED alone) whether prior PCI influences the benefit of CABG compared to MED.

2. Methods

2.1. Population

The STICH trial was a prospective, multicenter, randomized trial sponsored by the National Heart, Lung and Blood Institute that enrolled 1212 individuals from 22 countries and 99 sites. STICH trial hypothesis 1 enrollment criteria, as well as the main results, have been published previously [5,18]. Briefly, patients with multi-vessel CAD and LVEF ≤35% who were deemed suitable for surgical revascularization were randomized to optimal medical treatment with or without CABG and followed-up for a median of 9.8 years after a protocol amendment to the initial planned 5-year follow-up [6]. The main exclusion criteria were presence of a left main coronary stenosis of 50% or more of the artery diameter, Canadian Cardiovascular Society class III or IV angina on MED, plan for PCI and history of acute myocardial infarction within 30 days. STICH hypothesis 1 investigated whether CABG would be superior to MED in terms of the main primary endpoint of all-cause mortality, as well as the secondary endpoints of cardiovascular mortality, the composite of all-cause death or hospitalization due to cardiovascular (CV) causes, and CV hospitalization.

For the purposes of the present study, the database from the trial was retrospectively analyzed regarding whether patients had undergone PCI prior to enrollment. Data was not available regarding details of the PCI procedure including vessels involved, timing of the procedures in relation to study entry, use and type of stents or clinical circumstances (e.g. acute coronary syndromes or elective, etc.).

The authors reviewed the data, participated in the analyses and wrote the manuscript, and assume responsibility for the completeness and accuracy of the data and the analyses and for the fidelity of the study to the trial protocol.

2.2. Statistical analyses

Baseline patient characteristics are summarized for those with and without prior PCI. Unless otherwise noted, continuous variables are depicted as medians (25th, 75th percentiles) and prior PCI groups compared with Wilcoxon rank-sum tests. Categorical variables are summarized as counts (percentages) and groups were compared with Pearson's chi-square or Fisher's exact tests as appropriate.

For the comparison of outcomes (all-cause mortality, CV mortality, CV hospitalization, and the composite of all-cause death or CV hospitalization) for patients with and without prior PCI, Cox proportional hazards models were fit. Results are presented as number of events, Kaplan-Meier rate at 10 years, hazard ratio with 95% confidence interval (CI), and p-value. Unadjusted models were adjusted for variables that were associated with any outcome at 0.05 level of significance. Adjusted models were developed from Cox models using backward elimination method. The following baseline variables were selected at the 0.05 level of significance: age, sex, region, creatinine clearance, randomized treatment, prior CABG, number and location of diseased vessels, heart rate, NYHA class III or IV, atrial fibrillation, moderate or severe mitral regurgitation, end systolic volume index, diabetes, stroke, current smoking, chronic renal insufficiency, depression, and ACE/ARB use. There were a few missing values in this study and a multiple imputation technique was used.

Cox proportional hazards models including treatment, prior PCI, and the treatment-by-prior PCI history interaction were used to test for a differential treatment effect (CABG versus MED) in patients with or without prior PCI. Adjusted and unadjusted models were fit for treatment as randomized and as received. Kaplan-Meier plots have been produced for prior PCI vs. no prior PCI groups that were stratified by treatment. Unadjusted hazard ratios and 95% confidence intervals for treatment with CABG are provided for those with and without prior PCI along with the interaction p-value.

As a sensitivity analysis, the unadjusted models for the association between prior PCI and outcomes were adjusted for propensity score. The propensity scores were calculated using a logistic regression model including clinically important variables and variables associated with having prior PCI in current data. Variables included sex, age, race, previous CABG, previous internal cardiac defibrillator, diabetes, NYHA class, weight, creatinine, systolic blood pressure, angina, moderate or severe mitral regurgitation, smoking, hypercholesterolemia, prior myocardial infarction, ejection fraction, ACE/ARB, statins, potassium sparing diuretic, number of diseased vessels and disease of proximal left anterior

descending. We checked for confounding and the departure from the linearity assumption among covariates before adjusting the model to get the propensity scores.

All statistical analyses were two-sided and a p-value <0.05 was considered as statistically significant. SAS version 9.4 (SAS Institute, Inc., Cary, NC) was used for all statistical analyses.

3. Results

Of the 1212 patients enrolled (602 randomized to MED and 610 to CABG), 156 (12.9%) had a prior PCI (74 in the MED group and 82 in the CABG group). Patients with prior PCI more frequently had a history of hyperlipidemia, myocardial infarction, and moderate or severe mitral regurgitation. They had greater severity of angina, more frequently implanted with a cardioverter defibrillator, and were less likely to have disease in the left anterior descending artery. Clinical characteristics are shown by PCI history in Table 1 with groups further grouped by randomized treatment in Supplemental Table 1.

3.1. Relationship between prior PCI and outcomes

As can be seen in Table 2, Kaplan-Meier rates at 10 years were respectively 60.2% and 64.3% for patients with or without previous PCI for all-cause mortality (adjusted HR = 0.92, 95% CI, 0.74–1.15), and 44.5% compared with 51.0% for CV mortality, respectively (adjusted HR = 0.85, 95% CI, 0.64–1.11). Conversely, all-cause mortality or CV hospitalization (adjusted HR = 1.19, 95% CI 0.99–1.44) and CV hospitalization alone (adjusted HR 1.43, 95% CI, 1.15–1.77) were greater in patients with prior PCI. There were no significant differences regarding the main causes of hospitalization between patients with or without prior PCI: heart failure (27% vs. 29%, respectively), unstable angina (15% vs. 11%), arrhythmias (11% vs. 10%) or infection (9% vs. 8%). In the sensitivity analysis adjusted for the propensity to have prior PCI, similar results for mortality were observed for all-cause and CV mortalities, but the hazard ratio of CV hospitalization in patients with prior PCI was no longer significant (adjusted HR = 1.20 (95% CI, 0.95–1.50) (Supplement Table 2).

3.2. Influence of prior PCI on outcomes in the STICH trial

By intention to treat, the reduced risk of all-cause mortality, CV mortality, CV hospitalization, and the all-cause mortality or CV hospitalization composite that was observed with CABG and MED in comparison with MED alone overall in the trial, was not dependent on whether patients had PCI prior to randomization. Interaction p-values were not significant for any endpoint with or without adjustment (Fig. 1 and Supplemental Fig. 1). By treatment received, as can be seen in Table 3, the results were similar to the previous ones, with no significant interaction for any of the analyzed endpoints.

4. Discussion

In this high-risk population comprised of patients with LVEF ≤35%, our results showed that prior PCI was not associated with an increased risk of all-cause and CV mortality. Moreover, in the STICH trial CABG remained superior to MED whether patients were treated with or without PCI prior to enrollment.

The prevalence of prior PCI has been increasing steadily in patients undergoing CABG [19,20]. The prevalence in the present experience (12.9%) is similar to the median of 12.7% reported by Mehta et al. in a meta-analysis that included >34,000 patients (about 10% with heart failure) [19], and similar to the incidence found by Nauffal et al. in patients with triple-vessel disease and diabetes (12.8%) [21], and lower than the incidences described by Niclauss (24%) [20] and O'Neill (19%) [22]. These differences may be related to the time period reported in the respective studies or some other factor.

Table 1
Baseline patient characteristics by prior PCI.

	All patients (N = 1212)	No prior PCI (N = 1056)	Prior PCI (N = 156)	p-Value
Age (years)	60 (54, 67)	60 (54, 67)	59 (54, 67)	0.518
Female sex	148 (12.2%)	123 (11.6%)	25 (16.0%)	0.119
Race				<0.001
White	827 (68.2%)	698 (66.1%)	129 (82.7%)	
Black	31 (2.6%)	26 (2.5%)	5 (3.2%)	
Asian	209 (17.2%)	193 (18.3%)	16 (10.3%)	
Other	145 (12.0%)	139 (13.2%)	6 (3.8%)	
Body mass index (kg/m^2)	26.8 (24.0, 29.8)	26.7 (23.9, 29.7)	27.8 (24.4, 30.2)	0.059
Systolic blood pressure (mmHg)	120 (110, 130)	120 (110, 130)	120 (108, 130)	0.019
Diastolic blood pressure (mmHg)	78 (70, 80)	80 (70, 80)	75 (68, 80)	0.072
Heart rate (bpm)	74 (66, 82)	74 (66, 81)	72 (66, 84)	0.828
Hemoglobin (g/dL)	13.9 (12.7, 14.9)	13.9 (12.7, 14.9)	13.9 (12.7, 14.7)	0.213
Cockcroft-Gault creatinine clearance (mg/dL)	76.5 (60.5, 95.9)	76.1 (60.4, 94.8)	80.1 (61.7, 104.8)	0.119
LVEF	28 (22, 34)	28 (23, 34)	26 (21, 33)	0.197
ESVI (mL/m^2)	78.0 (60.9, 99.1)	77.8 (60.6, 99.1)	80.4 (61.6, 99.0)	0.495
Diabetes	478 (39.4%)	415 (39.3%)	63 (40.4%)	0.796
Hyperlipidemia	730 (60.3%)	623 (59.1%)	107 (68.6%)	0.024
Hypertension	728 (60.1%)	628 (59.5%)	100 (64.1%)	0.270
Peripheral vascular disease	184 (15.2%)	166 (15.7%)	18 (11.5%)	0.174
Myocardial infarction	934 (77.1%)	799 (75.7%)	135 (86.5%)	0.003
Stroke	92 (7.6%)	80 (7.6%)	12 (7.7%)	0.959
Moderate or severe mitral regurgitation	220 (18.2%)	179 (17.0%)	41 (26.3%)	0.005
Prior ICD	29 (2.4%)	20 (1.9%)	9 (5.8%)	0.008
Prior CABG	36 (3.0%)	29 (2.7%)	7 (4.5%)	0.212
Atrial fibrillation or flutter	153 (12.6%)	131 (12.4%)	22 (14.1%)	0.551
Current smoking	252 (20.8%)	219 (20.8%)	33 (21.2%)	0.910
CCS angina class				0.006
0	442 (36.5%)	383 (36.3%)	59 (37.8%)	
I	187 (15.4%)	167 (15.8%)	20 (12.8%)	
II	525 (43.3%)	464 (43.9%)	61 (39.1%)	
III	48 (4.0%)	36 (3.4%)	12 (7.7%)	
IV	10 (0.8%)	6 (0.6%)	4 (2.6%)	
NYHA class				0.356
I	139 (11.5%)	121 (11.5%)	18 (11.5%)	
II	626 (51.7%)	547 (51.8%)	79 (50.6%)	
III	412 (34.0%)	361 (34.2%)	51 (32.7%)	
IV	35 (2.9%)	27 (2.6%)	8 (5.1%)	
Baseline medications				
ACE inhibitor or ARB	1085 (89.5%)	938 (88.8%)	147 (94.2%)	0.040
Beta blocker	1036 (85.5%)	898 (85.0%)	138 (88.5%)	0.257
Aspirin	1002 (82.7%)	874 (82.8%)	128 (82.1%)	0.826
Clopidogrel	208 (17.2%)	176 (16.7%)	32 (20.5%)	0.234
Antiarrhythmic (including amiodarone)	128 (10.6%)	112 (10.6%)	16 (10.3%)	0.894
Digoxin	245 (20.2%)	215 (20.4%)	30 (19.2%)	0.743
Insulin	197 (16.3%)	168 (15.9%)	29 (18.6%)	0.397
Oral diabetic agent	286 (23.6%)	252 (23.9%)	34 (21.8%)	0.570
Nitrate	646 (53.3%)	562 (53.2%)	84 (54.2%)	0.820
Statin	983 (81.1%)	847 (80.2%)	136 (87.2%)	0.038
Warfarin	127 (10.5%)	111 (10.5%)	16 (10.3%)	0.923
Diuretic-loop thiazide	791 (65.3%)	700 (66.3%)	91 (58.7%)	0.064
Diuretic-potassium sparing	556 (45.9%)	473 (44.8%)	83 (53.2%)	0.049
Coronary anatomy				
Number of diseased vessels (75%)				0.046
0	25 (2.1%)	19 (1.8%)	6 (3.9%)	
1	282 (23.3%)	243 (23.0%)	39 (25.2%)	
2	462 (38.2%)	395 (37.4%)	67 (43.2%)	
3	442 (36.5%)	399 (37.8%)	43 (27.7%)	
Left main stenosis ≥50%	32 (2.6%)	28 (2.7%)	4 (2.6%)	1.000
Proximal LAD stenosis ≥75%	826 (68.2%)	734 (69.5%)	92 (59.4%)	0.011
Surgical characteristics in those randomized to and received surgery	N = 555	N = 485	N = 70	
Number of conduits				0.399
1	69 (12.4%)	63 (13.0%)	6 (8.6%)	
2	175 (31.5%)	148 (30.5%)	27 (38.6%)	
3	236 (42.5%)	206 (42.5%)	30 (42.9%)	
>3	75 (13.5%)	68 (14.0%)	7 (10.0%)	
Number of arterial conduits				0.819
0	50 (9.0%)	44 (9.1%)	6 (8.6%)	
1	446 (80.4%)	388 (80.0%)	58 (82.9%)	
>1	59 (10.6%)	53 (10.9%)	6 (8.6%)	
Number of distal anastomoses				0.312
0	7 (1.3%)	5 (1.0%)	2 (2.9%)	
1	63 (11.4%)	57 (11.8%)	6 (8.7%)	
2	128 (23.1%)	109 (22.5%)	19 (27.5%)	

Table 1 (continued)

	All patients (N = 1212)	No prior PCI (N = 1056)	Prior PCI (N = 156)	p-Value
3	221 (39.9%)	192 (39.6%)	29 (42.0%)	
4	98 (17.7%)	91 (18.8%)	7 (10.1%)	
>4	37 (6.7%)	31 (6.4%)	6 (8.7%)	

LVEF = left ventricular ejection fraction; ESVI = end systolic volume index; ICD = internal cardiac defibrillator; CABG = coronary artery bypass graft; CCS=Canadian Cardiovascular Society; NYHA = New York Heart Association; ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; LAD = left anterior descending artery.

Table 2
Association between prior PCI and outcomes.[a]

Outcome	Total events (KM rate at 10 years)		Unadjusted		Adjusted[b]	
	No prior PCI (n = 1056)	Prior PCI (n = 156)	HR (95% CI) for prior PCI	p-Value	HR (95% CI) for prior PCI	p-Value
All-cause mortality	649 (64.3%)	91 (60.2%)	0.88 (0.71, 1.10)	0.261	0.92 (0.74, 1.15)	0.475
Cardiovascular mortality	478 (51.0%)	60 (44.5%)	0.79 (0.60, 1.03)	0.080	0.85 (0.64, 1.11)	0.235
All-cause mortality or CV hospitalization	850 (83.5%)	135 (89.1%)	1.20 (1.00, 1.44)	0.050	1.19 (0.99, 1.44)	0.065
CV hospitalization	514 (64.1%)	104 (80.0%)	1.51 (1.22, 1.87)	<0.001	1.43 (1.15, 1.77)	0.001

[a] Intention to treat analyses.

[b] Models are adjusted for baseline age, sex, region, creatinine clearance, randomized treatment, prior CABG, diseased vessels, heart rate, NYHA class, AF, MR, ESVI, diabetes, stroke, current smoking, chronic renal insufficiency, depression, and ACE/ARB u.

4.1. Relationship between prior PCI and outcomes in patients submitted to CABG

Contrary to our results, although not unanimously, previous publications, mainly in patients with preserved LV function, have suggested that the presence of prior PCI is associated with worse short- and long-term prognosis of patients who underwent CABG [12–15], which could be influenced by a decrease in the number of grafts utilized in patients with prior PCI [12]. In the present study, the number of grafts was similar in patients with or without prior PCI in accordance to Thielmann et al. findings [13]. Songur et al. analyzing patency rates in patients with or without prior PCI, found significantly higher graft patency rates for the group without prior PCI in left anterior descending, circumflex, and right coronary arteries at a mean time of 60 months [23], which could be related to competitive flow, as suggested by the results of the recently presented IMPAG trial [24]. Conversely, the EuroSCORE and the STS risk model have been found to be inaccurate in predicting outcomes after CABG in patients with prior PCI, with an area under the curve (EuroSCORE) for 30-day mortality of 0.875 for patients without prior PCI, and only 0.552 for patients with prior PCI [25].

In our patients assigned to CABG, we found a non-significant decrease in all-cause and CV mortality rates for those with prior PCI (HR = 0.85 and 0.84, respectively) as compared with those without prior PCI, a finding similar to that of Luthra et al., who described higher survival rates for patients having CABG with prior PCI and LVEF<30%, but not for those with LVEF >30% [26]. Finally, for CV hospitalization,
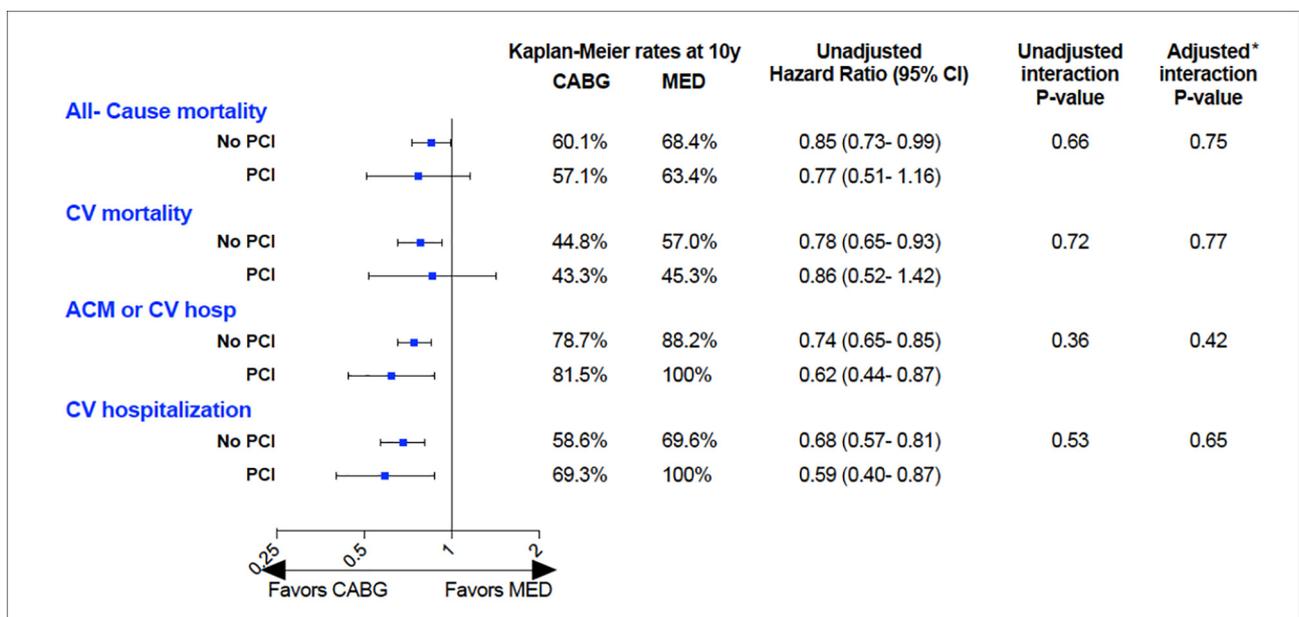

Fig. 1. Randomized treatment effects by history of PCI. * Models are adjusted for baseline age, sex, region, creatinine clearance, prior CABG, diseased vessels, heart rate, NYHA class, AF, MR, ESVI, diabetes, stroke, current smoking, chronic renal insufficiency, depression, and ACE/ARB use. CV = cardiovascular; ACM = all-cause mortality.

Table 3
Treatment as received effects by history of PCI.

Outcome	No Prior PCI				Prior PCI				Unadjusted interaction p-value	Adjusted[a] interaction p-value
	MED	CABG	Unadjusted HR (95% CI)	Adjusted[a] HR (95% CI)	MED	CABG	Unadjusted HR (95% CI)	Adjusted[a] HR (95% CI)		
All-cause mortality	350 (70.1%)	314 (58.7%)	0.76 (0.65, 0.88)	0.75 (0.64, 0.88)	52 (67.1%)	41 (53.3%)	0.65 (0.43, 0.98)	0.63 (0.41, 0.95)	0.500	0.414
Cardiovascular mortality	270 (59.2%)	214 (43.1%)	0.68 (0.57, 0.82)	0.67 (0.56, 0.81)	36 (52.5%)	24 (36.2%)	0.57 (0.34, 0.95)	0.58 (0.34, 0.97)	0.502	0.581
All-cause mortality or CV hospitalization	439 (87.6%)	417 (79.6%)	0.80 (0.70, 0.92)	0.81 (0.70, 0.93)	73 (100%)	62 (80.5%)	0.64 (0.45, 0.89)	0.67 (0.47, 0.94)	0.211	0.305
CV hospitalization	263 (67.6%)	254 (61.1%)	0.83 (0.70, 0.99)	0.86 (0.72, 1.02)	56 (100%)	48 (69.8%)	0.66 (0.45, 0.97)	0.72 (0.48, 1.06)	0.283	0.413

AF, MR, ESVI, diabetes, stroke, current smoking, chronic renal insufficiency, depression, and ACE/ARB use.
[a] Models are adjusted for baseline age, sex, region, creatinine clearance, prior CABG, diseased vessels, heart rate, NYHA class.

we observed a higher rate (statistically significant in the model adjusted by baseline variables but not significant in the model adjusted for propensity for prior PCI) during the follow-up in patients with prior PCI. Additionally, unstable angina requiring hospitalization was similar between the groups, contrary to the findings of Chocron et al. who found a higher incidence in patients with prior PCI, but in a population with LVEF >39% [27].

4.2. CABG vs. MED: the influence of prior PCI

Before the present analysis, no publications specifically assessed the role of prior PCI in patients with LVEF <35% submitted to CABG or MED. In a meta-analysis with 21 studies and >16,000 patients with LVEF <40%, Wolff et al. found a significant superiority of CABG over MED (HR = 0.66, p < 0.001) [11]. However, the important hypothesis that prior PCI could influence CABG results was not addressed in that publication. In this context, our results are reassuring, showing that CABG is superior to MED in patients with or without previous PCI, with consistent results for both as randomized and as treated analyses.

4.3. Study limitations

There are several limitations to the current study. First, although similar to other reports, the analysis is *post hoc* with a relatively small number of patients. Second, we collected no detailed information specific to the intervention performed. The modern practice of PCI is complex and how data from the current study relates to that practice is unknown and may have influenced the results [13,21]. However, this is the only report we are aware of limited to a population with LV dysfunction maintained on optimal medical therapy that analyzes the impact of prior PCI in patients undergoing CABG or maintained on MED alone. Finally, while our analysis is the largest so far to specifically assess the association of prior PCI and outcomes in patients with LV dysfunction treated with CABG, we cannot exclude that a lack of statistical power might have been an issue.

5. Conclusion

In the STICH population of patients with ischemic heart disease and LVEF ≤35%, patients with prior PCI did not have a worse prognosis compared to those who did not. Moreover, the previously demonstrated benefit of CABG plus optimal medical therapy over MED alone was maintained regardless of whether patients had prior PCI. This report supports the idea that prior PCI should not be a factor in whether to offer CABG to patients with LV dysfunction.

(modest) from Sanofi, Amgen, Vifor, and Servier, outside the submitted work. Dr. Furtado reports honoraria from AstraZeneca (modest) and grants (modest) from AstraZeneca, DalCor, Boehringer, Pfizer, Jansen and Sanofi, outside the submitted work. Dr. Velazquez reports research grants (significant) with Novartis, Amgen, National Heart, Lung, and Blood Institute, Pfizer and Alnylam and consultant/advisory board agreements (modest) with Novartis, Amgen, and Philips. Dr. Jolicoeur reports research grants (significant) from AstraZeneca, Boston Scientifics, and Philips, and consultant/advisory board agreements (modest) with Servier. All other co-authors have nothing to disclose.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.03.029.

References

[1] Authors/Task Force members, Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur. Heart J. 2014;35:2541–619.
[2] M.R. Patel, J.H. Calhoon, G.J. Dehmer, J.A. Grantham, T.M. Maddox, D.J. Maron, P.K. Smith, ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons, J. Am. Coll. Cardiol. 69 (2017) 2212–2241.
[3] Veterans ACABSCSG, Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina, N. Engl. J. Med. 311 (1984) 1333–1339.
[4] E. Passamani, K.B. Davis, M.J. Gillespie, T. Killip, A randomized trial of coronary artery bypass surgery. Survival of patients with a low ejection fraction, N. Engl. J. Med. 312 (1985) 1665–1671.
[5] E.J. Velazquez, K.L. Lee, M.A. Deja, A. Jain, G. Sopko, A. Marchenko, I.S. Ali, G. Pohost, S. Gradinac, W.T. Abraham, M. Yii, D. Prabhakaran, H. Szwed, P. Ferrazzi, M.C. Petrie, C.M. O'Connor, P. Panchavinnin, L. She, R.O. Bonow, G.R. Rankin, R.H. Jones, Rouleau JL; STICH Investigators, Coronary-artery bypass surgery in patients with left ventricular dysfunction, N. Engl. J. Med. 364 (2011) 1607–1616.
[6] E.J. Velazquez, K.L. Lee, R.H. Jones, H.R. Al-Khalidi, J.A. Hill, J.A. Panza, R.E. Michler, R.O. Bonow, T. Doenst, M.C. Petrie, J.K. Oh, L. She, V.L. Moore, P. Desvigne-Nickens, G. Sopko, J.L. Rouleau, STICHES Investigators, Coronary-artery bypass surgery in patients with ischemic cardiomyopathy, N. Engl. J. Med. 374 (2016) 1511–1520.
[7] E.C. Keeley, J.A. Boura, C.L. Grines, Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials, Lancet 361 (2003) 13–20.
[8] P.W. Serruys, M.C. Morice, A.P. Kappetein, A. Colombo, D.R. Holmes, M.J. Mack, E. Ståhle, T.E. Feldman, M. van den Brand, E.J. Bass, N. Van Dyck, K. Leadley, K.D. Dawkins, F.W. Mohr, SYNTAX Investigators, Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease, N. Engl. J. Med. 360 (2009) 961–972.
[9] S. Bangalore, Y. Guo, Z. Samadashvili, S. Blecker, E.L. Hannan, Revascularization in patients with multivessel coronary artery disease and severe left ventricular systolic

[10] dysfunction: everolimus-eluting stents versus coronary artery bypass graft surgery, Circulation 133 (2016) 2132–2140.
[10] S.H. Kang, C.W. Lee, S. Baek, P.H. Lee, J.M. Ahn, D.W. Park, S.J. Kang, S.W. Lee, Y.H. Kim, S.W. Park, S.J. Park, Comparison of outcomes of coronary artery bypass grafting versus drug-eluting stent implantation in patients with severe left ventricular dysfunction, Am. J. Cardiol. 120 (2017) 69–74.
[11] G. Wolff, D. Dimitroulis, F. Andreotti, M. Kołodziejczak, C. Jung, P. Scicchitano, F. Devito, A. Zito, M. Occhipinti, B. Castiglioni, G. Calveri, F. Maisano, M.M. Ciccone, S. De Servi, E.P. Navarese, Survival benefits of invasive versus conservative strategies in heart failure in patients with reduced ejection fraction and coronary artery disease: a meta-analysis, Circ. Heart Fail. 10 (2017), e003255. .
[12] A. Hassan, K.J. Buth, R.J. Baskett, I.S. Ali, A. Maitland, J.A. Sullivan, W.A. Ghali, G.M. Hirsch, The association between prior percutaneous coronary intervention and short-term outcomes after coronary artery bypass grafting, Am. Heart J. 150 (2005) 1026–1031.
[13] M. Thielmann, R. Leyh, P. Massoudy, M. Neuhäuser, I. Aleksic, M. Kamler, U. Herold, J. Piotrowski, H. Jakob, Prognostic significance of multiple previous percutaneous coronary interventions in patients undergoing elective coronary artery bypass surgery, Circulation 114 (2006) I441–I447.
[14] L.A. Lisboa, O.A. Mejia, L.A. Dallan, L.F. Moreira, L.B. Puig, F.B. Jatene, N.A. Stolf, Previous percutaneous coronary intervention as risk factor for coronary artery bypass grafting, Arq. Bras. Cardiol. 99 (2012) 586–595.
[15] V. Mannacio, L Di Tommaso, V. De Amicis, V. Lucchetti, P. Pepino, F. Musumeci, C. Vosa, Previous percutaneous coronary interventions increase mortality and morbidity after coronary surgery, Ann. Thorac. Surg. 93 (2012) 1956–1962.
[16] C. Ueki, H. Miyata, N. Motomura, G. Sakaguchi, T. Akimoto, S. Takamoto, Previous percutaneous coronary intervention does not increase adverse events after coronary artery bypass surgery, Ann. Thorac. Surg. 104 (2017) 56–61.
[17] G. Mariscalco, S. Rosato, G.F. Serraino, D. Maselli, M. Dalén, J.K.E. Airaksinen, D. Reichart, M. Zanobini, F. Onorati, M. De Feo, R. Gherli, G. Santarpino, A.S. Rubino, G. Gatti, F. Nicolini, F. Santini, A. Perrotti, V.D. Bruno, V.G. Ruggieri, F. Biancari, Prior percutaneous coronary intervention and mortality in patients undergoing surgical myocardial revascularization: results from the E-CABG (European Multicenter Study on Coronary Artery Bypass Grafting) with a systematic review and meta-analysis, Circ. Cardiovasc. Interv. 11 (2018), e005650. .
[18] E.J. Velazquez, K.L. Lee, C.M. O'Connor, J.K. Oh, R.O. Bonow, G.M. Pohost, A.M. Feldman, D.B. Mark, J.A. Panza, G. Sopko, J.L. Rouleau, R.H. Jones, S.T.I.C.H. Investigators, The rationale and design of the Surgical Treatment for Ischemic Heart Failure (STICH) trial, J. Thorac. Cardiovasc. Surg. 134 (2007) 1540–1547.
[19] G.S. Mehta, D.J. LaPar, C.M. Bhamidipati, J.A. Kern, I.L. Kron, G.R. Upchurch Jr., G. Ailawadi, Previous percutaneous coronary intervention increases morbidity after coronary artery bypass grafting, Surgery 152 (2012) 5–11.
[20] L. Niclauss, S. Colombier, R. Prêtre, Percutaneous coronary interventions prior to coronary artery bypass surgery, J. Card. Surg. 30 (2015) 313–318.
[21] V. Nauffal, T.A. Schwann, M.B. Yammine, A.K. El-Hage-Sleiman, M.H. El Zein, A. Kabour, M.C. Engoren, R.H. Habib, Impact of prior intracoronary stenting on late outcomes of coronary artery bypass surgery in diabetics with triple-vessel disease, J. Thorac. Cardiovasc. Surg. 149 (2015) 1302–1309.
[22] W.T. O'Neal, J.T. Efird, C.A. Anderson, L.C. Kindell, J.B. O'Neal, T. Bruce Ferguson, W. Randolph Chitwood, A.P. Kypson, The impact of prior percutaneous coronary intervention on long-term survival after coronary artery bypass grafting, Heart Lung Circ. 22 (2013) 940–945.
[23] M.Ç. Songur, S. Özyalçin, A. Özen, E. Şimşek, Ü. Kervan, İ. Taşoğlu, S. Kaplan, K. Köse, A.T. Ulus, Does really previous stenting affect graft patency following CABG? A 5-year follow-up: the effect of PCI on graft survival, Heart Vessel. 31 (2016) 457–464.
[24] N. Freemantle, M. Milojevic, S. Lim, S. Fremes, D. Pagano, 32nd EACTS Annual Meeting clinical trials update: ART, IMPAG, MITRA-FR and COAPT, Eur. J. Cardiothorac. Surg. 55 (2) (2018) 186–190.
[25] N. Bonaros, D. Vill, D. Wiedemann, K. Fischler, G. Friedrich, O. Pachinger, M. Grimm, T. Schachner, Major risk stratification models do not predict perioperative outcome after coronary artery bypass grafting in patients with previous percutaneous intervention, Eur. J. Cardiothorac. Surg. 39 (2011) e164–e169.
[26] S. Luthra, M.M. Leiva Juárez, E. Senanayake, H. Luckraz, J.S. Billing, J. Cotton, M.S. Norell, Percutaneous intervention before coronary artery bypass surgery does not unfavorably impact survival: a single-center propensity-matched analysis, Ann. Thorac. Surg. 102 (2016) 1911–1918.
[27] S. Chocron, R. Baillot, J.L. Rouleau, W.J. Warnica, P. Block, D. Johnstone, M.G. Myers, C.D. Calciu, A. Nozza, P. Martineau, W.H. van Gilst, IMAGINE Investigators, Impact of previous percutaneous transluminal coronary angioplasty and/or stenting revascularization on outcomes after surgical revascularization: insights from the imagine study, Eur. Heart J. 29 (2008) 673–679.