

Nicolau, J. C. et al. (2019) Does prior coronary angioplasty affect outcomes of surgical coronary revascularization? Insights from the STICH trial. *International Journal of Cardiology*, 291, pp. 36-41. (doi:<u>10.1016/j.ijcard.2019.03.029</u>)

There may be differences between this version and the published version. You are advised to consult the publisher's version if you wish to cite from it.

http://eprints.gla.ac.uk/182871/

Deposited on: 26 March 2019

Enlighten – Research publications by members of the University of Glasgow <u>http://eprints.gla.ac.uk</u>

Accepted Manuscript

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



Jose C. Nicolau, Susanna R. Stevens, Hussein R. Al-Khalidi, Fabio B. Jatene, Remo H.M. Furtado, Luis A.O. Dallan, Luiz A.F. Lisboa, Patrice Desvigne-Nickens, Haissam Haddad, E. Marc Jolicoeur, Mark C. Petrie, Torsten Doenst, Robert E. Michler, E. Magnus Ohman, Jyotsna Maddury, Imtiaz Ali, Marek A. Deja, Jean L. Rouleau, Eric J. Velazquez, James A. Hill

PII: DOI: Reference:	S0167-5273(19)30541-8 https://doi.org/10.1016/j.ijcard.2019.03.029 IJCA 27529
To appear in:	International Journal of Cardiology
Received date:	28 January 2019
Revised date:	25 February 2019
Accepted date:	14 March 2019

Please cite this article as: J.C. Nicolau, S.R. Stevens, H.R. Al-Khalidi, et al., Does prior coronary angioplasty affect outcomes of surgical coronary revascularization? Insights from the STICH trial, International Journal of Cardiology, https://doi.org/10.1016/j.ijcard.2019.03.029

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

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

Jose C. Nicolau, MD,^a Susanna R. Stevens, MS,^b Hussein R. Al-Khalidi, PhD,^b Fabio B. Jatene, MD,^a Remo H. M. Furtado, MD,^a Luis A. O. Dallan, MD,^a Luiz A. F. Lisboa, MD,^a Patrice Desvigne-Nickens, MD,^c Haissam Haddad, MD,^d E. Marc Jolicoeur, MD,^e Mark C. Petrie, MBChB,^f Torsten Doenst, MD, PhD,^g Robert E. Michler, MD,^h E. Magnus Ohman, MD,^b Jyotsna Maddury, MD,ⁱ Imtiaz Ali, MD,^j Marek A. Deja, MD, PhD,^k Jean L. Rouleau, MD,^e Eric J. Velazquez, MD,¹ James A. Hill, MD^m

^aInstituto do Coracao (InCor), Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil ^bDuke Clinical Research Institute and Department of Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, NC, USA ^cDivision of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA ^dDepartment of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada ^eMontreal Heart Institute, Université de Montréal, Quebec, Canada ¹BHF Cardiovascular Research Centre, University of Glasgow, Glasgow, United Kingdom ^gDepartment of Cardiothoracic Surgery, University of Jena, Jena, Germany ^hDepartment of Cardiothoracic Surgery, Montefiore Medical Center/Albert Einstein College of Medicine, New York, NY, USA ⁱDepartment of Cardiology, Nizams Institute of Medical Sciences, Hyderabad, India ¹Libin Cardiovascular Institute of Alberta, University of Calgary, Foothills Medical Centre, Calgary, Alberta, Canada ^kDepartment of Cardiac Surgery, Medical University of Silesia, Katowice, Poland ¹Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, USA ^mDepartment of Medicine, University of Florida, Gainesville, FL, USA

Total Word Count: 4,807 (from Title page through Tables)

Corresponding Author: Jose C. Nicolau Aureliano Coutinho 355; apt. 1401; São Paulo, Brazil, 01224-020 Telephone: +55-11-26615058; Fax: +55-11-30883809 E-mail: jose.nicolau@incor.usp.br

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

C^K

Key Words: coronary artery bypass surgery, heart failure, left ventricular dysfunction, percutaneous coronary intervention

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 \leq 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).

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 more than 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 \leq 35% to CABG plus MED or MED alone) whether prior PCI influences the benefit of CABG compared to MED.

METHODS

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 (18, 5). 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 (eg. 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.

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-byprior 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.

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.

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).

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 (Figure 1 and Supplemental Figure 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.

DISCUSSION

In this high-risk population comprised of patients with LVEF \leq 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 more than 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.

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, 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).

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 $\leq 35\%$ 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.

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.

Conclusion

In the STICH population of patients with ischemic heart disease and LVEF \leq 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.

Acknowledgements

The authors thank Carlos José Dornas Gonçalves, MD for his suggestions on the analyses and Vanessa Moore for her editorial assistance with this manuscript.

Sources of Funding

This work was supported by the National Institutes of Health, National Heart, Lung, and Blood Institute grants U01 HL069015, U01 HL069013, and R01 HL105853. This work is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute or National Institutes of Health.

Relationship with Industry and Other Entities: Dr. Nicolau reports research grants (modest) from Amgen, Bayer, Bristol-Myers Squibb, DalCor, Janssen, Sanofi, AstraZeneca, Boehringer Ingelheim, Novartis, and Pfizer; and consulting/advisory board fees (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.

REFERENCES

- 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. Patel MR, Calhoon JH, Dehmer GJ, Grantham JA, Maddox TM, Maron DJ, Smith PK. 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 2017;69:2212-41.

- 3. Veterans ACABSCSG. Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. N Engl J Med 1984;311:1333-9.
- Passamani E, Davis KB, Gillespie MJ, Killip T. A randomized trial of coronary artery bypass surgery. Survival of patients with a low ejection fraction. N Engl J Med 1985;312:1665-71.
- 5. Velazquez EJ, Lee KL, Deja MA, Jain A, Sopko G, Marchenko A, Ali IS, Pohost G, Gradinac S, Abraham WT, Yii M, Prabhakaran D, Szwed H, Ferrazzi P, Petrie MC, O'Connor CM, Panchavinnin P, She L, Bonow RO, Rankin GR, Jones RH, Rouleau JL; STICH Investigators. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med 2011;364:1607-16.
- Velazquez EJ, Lee KL, Jones RH, Al-Khalidi HR, Hill JA, Panza JA, Michler RE, Bonow RO, Doenst T, Petrie MC, Oh JK, She L, Moore VL, Desvigne-Nickens P, Sopko G, Rouleau JL; STICHES Investigators.Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy. N Engl J Med 2016;374:1511-20.
- Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003;361:13-20.
- Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, Ståhle E, Feldman TE, van den Brand M, Bass EJ, Van Dyck N, Leadley K, Dawkins KD, Mohr FW; SYNTAX Investigators. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961-72.

- Bangalore S, Guo Y, Samadashvili Z, Blecker S, Hannan EL. Revascularization in Patients With Multivessel Coronary Artery Disease and Severe Left Ventricular Systolic Dysfunction: Everolimus-Eluting Stents Versus Coronary Artery Bypass Graft Surgery. Circulation 2016;133:2132-40.
- Kang SH, Lee CW, Baek S, Lee PH, Ahn JM, Park DW, Kang SJ, Lee SW, Kim YH, Park SW, Park SJ. Comparison of Outcomes of Coronary Artery Bypass Grafting Versus Drug-Eluting Stent Implantation in Patients With Severe Left Ventricular Dysfunction. Am J Cardiol 2017;120:69-74.
- 11. Wolff G, Dimitroulis D, Andreotti F, Kołodziejczak M, Jung C, Scicchitano P, Devito F, Zito A, Occhipinti M, Castiglioni B, Calveri G, Maisano F, Ciccone MM, De Servi S, Navarese EP. 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 2017;10:e003255.
- Hassan A, Buth KJ, Baskett RJ, Ali IS, Maitland A, Sullivan JA, Ghali WA, Hirsch GM. The association between prior percutaneous coronary intervention and short-term outcomes after coronary artery bypass grafting. Am Heart J 2005;150:1026-31.
- Thielmann M, Leyh R, Massoudy P, Neuhäuser M, Aleksic I, Kamler M, Herold U, Piotrowski J, Jakob H. Prognostic significance of multiple previous percutaneous coronary interventions in patients undergoing elective coronary artery bypass surgery. Circulation 2006;114:I441-7.
- Lisboa LA, Mejia OA, Dallan LA, Moreira LF, Puig LB, Jatene FB, Stolf NA. Previous percutaneous coronary intervention as risk factor for coronary artery bypass grafting. Arq Bras Cardiol 2012;99:586-95.

- Mannacio V, Di Tommaso L, De Amicis V, Lucchetti V, Pepino P, Musumeci F, Vosa C. Previous percutaneous coronary interventions increase mortality and morbidity after coronary surgery. Ann Thorac Surg 2012;93:1956-62.
- Ueki C, Miyata H, Motomura N, Sakaguchi G, Akimoto T, Takamoto S. Previous Percutaneous Coronary Intervention Does Not Increase Adverse Events After Coronary Artery Bypass Surgery. Ann Thorac Surg 2017;104:56-61.
- 17. Mariscalco G, Rosato S, Serraino GF, Maselli D, Dalén M, Airaksinen JKE, Reichart D, Zanobini M, Onorati F, De Feo M, Gherli R, Santarpino G, Rubino AS, Gatti G, Nicolini F, Santini F, Perrotti A, Bruno VD, Ruggieri VG, Biancari F. 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 2018;11:e005650.
- 18. Velazquez EJ, Lee KL, O'Connor CM, Oh JK, Bonow RO, Pohost GM, Feldman AM, Mark DB, Panza JA, Sopko G, Rouleau JL, Jones RH; STICH Investigators. The rationale and design of the Surgical Treatment for Ischemic Heart Failure (STICH) trial. J Thorac Cardiovasc Surg 2007;134:1540-7.
- Mehta GS, LaPar DJ, Bhamidipati CM, Kern JA, Kron IL, Upchurch GR Jr, Ailawadi G. Previous percutaneous coronary intervention increases morbidity after coronary artery bypass grafting. Surgery 2012;152:5-11.
- Niclauss L, Colombier S, Prêtre R. Percutaneous coronary interventions prior to coronary artery bypass surgery. J Card Surg 2015;30:313-8.

- 21. Nauffal V, Schwann TA, Yammine MB, El-Hage-Sleiman AK, El Zein MH, Kabour A, Engoren MC, Habib RH. Impact of prior intracoronary stenting on late outcomes of coronary artery bypass surgery in diabetics with triple-vessel disease. J Thorac Cardiovasc Surg 2015;149:1302-9.
- 22. O'Neal WT, Efird JT, Anderson CA, Kindell LC, O'Neal JB, Bruce Ferguson T, Randolph Chitwood W, Kypson AP. The impact of prior percutaneous coronary intervention on longterm survival after coronary artery bypass grafting. Heart Lung Circ 2013; 22: 940-5.
- 23. Songur MÇ, Özyalçin S, Özen A, Şimşek E, Kervan Ü, Taşoğlu İ, Kaplan S, Köse K, Ulus AT. Does really previous stenting affect graft patency following CABG? A 5-year follow-up: The effect of PCI on graft survival. Heart Vessels 2016;31:457-64.
- Freemantle N, Milojevic M, Lim S, Fremes S, Pagano D. 32nd EACTS Annual Meeting clinical trials update: ART, IMPAG, MITRA-FR and COAPT. Eur J Cardiothorac Surg 2018; doi:10.1093/ejcts/ezy396
- 25. Bonaros N, Vill D, Wiedemann D, Fischler K, Friedrich G, Pachinger O, Grimm M, Schachner T. Major risk stratification models do not predict perioperative outcome after coronary artery bypass grafting in patients with previous percutaneous intervention. Eur J Cardiothorac Surg 2011;39:e164-9.
- 26. Luthra S, Leiva Juárez MM, Senanayake E, Luckraz H, Billing JS, Cotton J, Norell MS. Percutaneous intervention before coronary artery bypass surgery does not unfavorably impact survival: A single-center propensity-matched analysis. Ann Thorac Surg 2016;102:1911-8.
- Chocron S, Baillot R, Rouleau JL, Warnica WJ, Block P, Johnstone D, Myers MG, Calciu CD, Nozza A, Martineau P, van Gilst WH; 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 2008;29:673-9. Kother

Figure Legends

Figure 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

Supplemental Figure 1. Coronary artery bypass versus medical treatment only. Kaplan-Meier rates of all-cause mortality (A), cardiovascular mortality (B), all-cause mortality of cardiovascular hospitalization (C) and cardiovascular hospitalization (D).

Dashed lines represent those randomized to medical therapy and solid lines those randomized to CABG plus medical therapy.

		, ,		
	All patients	No prior PCI	Prior PCI	
	(N=1212)	(N=1056)	(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 <i>,</i> 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

Table 1. Baseline patient characteristics by prior PCI

	All patients	No prior PCI	Prior PCI	
	(N=1212)	(N=1056)	(N=156)	p-value
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%)	
1	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

	All patients	No prior PCI	Prior PCI	
	(N=1212)	(N=1056)	(N=156)	p-value
Surgical characteristics in those randomized to and	N=555	N=485	N=70	
received surgery				
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%)	
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.

or CCCC

Table 2. Association between prior PCI and outcomes*

	Total e	events					
	(KM rate a	t 10 years)	Unadjuste	d	Adjusted	*	
Outcome	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	
*Intention to treat analyses							

*Intention to treat analyses

**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

		C	No Prior PCI			Prior PCI				
Outcome	MED	CABG	Unadjusted HR (95% Cl)	Adjusted [*] HR (95% Cl)	MED	CABG	Unadjusted HR (95% CI)	Adjusted [*] HR (95% CI)	Unadjusted interaction p-value	Adjusted [*] interaction p-value
All-cause mortality	350 (70.1%)	314 (58.7%)	0.76 (0.65, 0.88)	0.75 (0.64 <i>,</i> 0.88)	52 (67.1%)	41 (53.3%)	0.65 (0.43, 0.98)	0.63 (0.41 <i>,</i> 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 <i>,</i> 0.95)	0.58 (0.34, 0.97)	0.502	0.581

			No Prior PCI			Prior PCI				
Outcome	MED	CABG	Unadjusted HR (95% CI)	Adjusted [*] HR (95% Cl)	MED	CABG	Unadjusted HR (95% CI)	Adjusted [*] HR (95% CI)	Unadjusted interaction p-value	Adjusted [*] interaction p-value
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

*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.

.ironic renal insu



Figure 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

Page 23

Highlights

- Prior reports suggested an association of prior PCI with worse outcomes after CABG
- Patients with severe LV dysfunction were under-represented in those studies
- STICH trial demonstrated survival benefit with CABG in severe LV

dysfunction

- This benefit was consistent regardless of the presence of prior PCI
- Prior PCI should not contra-indicate CABG in patients with LV dysfunction