Survival probability loss from percutaneous coronary intervention compared with coronary artery bypass grafting across age groups

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Background: Whether the survival benefit from coronary artery bypass grafting (CABG), compared with percutaneous coronary intervention (PCI), for multivessel disease extends to the older segment of the population remains unclear. We aimed to investigate whether the effect on survival of PCI compared with CABG is related to the age of the patient.

Methods: Propensity score–matching analysis was conducted on 6723 patients (PCI = 1097, CABG = 5626) with multivessel coronary artery disease. In the PCI group, drug-eluting stents were used in 917 (83.5%) patients; bare metal stents were used in only 180 patients (16.5%). Nonparametric, bootstrap, point-wise confidence limits were obtained for PCI:CABG odds and hazard ratios for early (within 12 months) and late hazard phase (beyond 12 months) for a variety of age groups.

Results: After a mean follow-up time of 5.5 ± 3.2 years, a total of 301 deaths were recorded in the matched sample (208 in the PCI group and 93 in the CABG group). Overall survival was 95% ± 0.6% versus 95% ± 0.6% at 1 year, 84% ± 1.0% versus 92.4% ± 0.8% at 5 years, and 75% ± 1.6% versus 90% ± 1.0% at 8 years, for the PCI and CABG groups, respectively (log rank $P < .001$). PCI did not confer any significant benefit compared with CABG during the early hazard phase (within 12 months), but the survival-probability loss from PCI compared with CABG during the late hazard phase was present across all age groups. The hazard ratio declined from 3.8 to 3.4 and was statistically significant (lower limit >1 across all ages, ranging from 1.5 to 2.4).

Conclusions: Compared with PCI, CABG leads to a significant reduction in late-phase mortality across all age groups. (J Thorac Cardiovasc Surg 2015;149:479-84)

See related commentary on pages 485-6.

Supplemental material is available online.

The optimal treatment approach for patients with multivessel coronary artery disease (CAD) remains controversial.[1] Recent, large observational studies[2-4] show that patients with multivessel CAD have a long-term survival advantage with coronary artery bypass grafting (CABG) compared with percutaneous coronary intervention (PCI). Several contemporary trials have reported similar mortality rates with these 2 treatment techniques[5-7]; however, all of these trials were underpowered to detect a difference in all-cause mortality. A recent meta-analysis[8] that did not have the power limitation of those trials found that in patients with multivessel CAD, CABG leads to an unequivocal reduction in long-term mortality, compared with PCI, regardless of whether patients are diabetic. However, elderly patients were, in general, not included in the meta-analysis, or represented a small proportion of the trial population; therefore, whether these results apply to the older segment of the patient population needs to be determined.

Despite a lack of evidence that it is more effective, PCI is currently preferred for older patients, owing to the perceptions that CABG has higher operative mortality and that the potential survival advantage gained with CABG may be overshadowed in the elderly because of their limited life expectancy.[9] The elderly represent one of the most rapidly expanding segments of the population in Western countries.[10] Thus, determining the optimal strategy for revascularization in this complex context is an issue of

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Abbreviations and Acronyms

BMS	= bare metal stents
CABG	= coronary artery bypass grafting
CAD	= coronary artery disease
CI	= confidence interval
DES	= drug-eluting stents
HR	= hazard ratio
LAD	= left anterior descending
LMD	= left main disease
PCI	= percutaneous coronary intervention

public health concern. Therefore, we aimed to investigate whether the effect of PCI compared with CABG on survival is related to the patient's age.

METHODS

Study Population

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local ethical committee approved the study, and the requirement for individual patient consent was waived. We retrospectively analyzed data collected prospectively from the institutional surgical and interventional database (PATS; Dendrite Clinical Systems, Ltd, Oxford, UK) from April 2001 to May 2013. The PATS database captures detailed information on a wide range of preoperative, intraoperative, and hospital postoperative variables (including complications and mortality) for all patients undergoing surgical or percutaneous myocardial revascularization in our institution. The database is maintained by a team of full-time clinical information analysts, who are responsible for continuous prospective data collection as part of a continuous audit process. Data collection is validated regularly.

Patients included in the final analysis met the following criteria: (1) they had multivessel CAD, defined as the presence of ≥2 diseased vessels, including the left anterior descending (LAD) and/or the unprotected left main coronary artery, and (2) treatments included PCI or CABG (with at least 1 internal thoracic artery routinely used to graft the LAD). Exclusion criteria were that patients had (1) acute ST elevation myocardial infarction treated by primary PCI or salvage CABG, (2) rescue PCI, and/or (3) previous CABG (Figure E1). Overall, 6723 patients who underwent myocardial revascularization for multivessel CAD were included in the final analysis (PCI = 1097, CABG = 5626). In the PCI group, drug-eluting stents (DES) were used in 917 (83.5%) patients; bare metal stents (BMS) were used in only 180 patients (16.5%).

Pretreatment Variables and Study Endpoint

The effect of PCI compared with CABG was adjusted for the following pretreatment variables: age, female gender, prior New York Heart Association functional class III-IV, prior myocardial infarction, prior PCI, diabetes mellitus, previous stroke, current smoking, chronic obstructive pulmonary disease, diseased vessels, left main disease (LMD), left ventricular ejection fraction <50%, serum creatinine concentration of >200 μmol/L, body mass index, and nonelective admission for index procedure.

The primary endpoint was all-cause death during follow-up (common closing date). All-cause death is the most robust and unbiased index because no adjudication is required; thus, inaccurate or biased documentation or clinical assessments are avoided.[11] Information about death was obtained from the institutional database and the General Register Office for all patients.

Statistical Analysis

For baseline characteristics, variables are summarized as a mean for continuous variables, and as a proportion for categoric variables. Multiple imputation, using a bootstrapping-based expectation-maximization algorithm, was used to address missing data (Amelia II: A Program for Missing Data: http://www.jstatsoft.org/v45/i07/). The fraction of missing data ranged from 0% (number of vessels diseased) to 10.1% (body mass index). To control for measured potential confounders in the data set, a propensity score was generated for each patient from a multivariable logistic regression model based on pretreatment covariates as independent variables with treatment type (PCI vs CABG) as a binary dependent variable[12] (R package version 1.42: http://CRAN.R-project.org/package=nonrandom). The resulting propensity score represented the probability that a patient underwent PCI rather than CABG (C-statistic: 0.78). Pairs of patients receiving PCI and CABG were derived using greedy 1:1 matching with a calliper of width 0.20 standard deviations of the logit of the propensity score.[13] The quality of the match was assessed by comparing selected pretreatment variables in propensity score–matched patients using the standardized mean difference, by which an absolute standardized difference of >10% is suggested to represent meaningful covariate imbalance.

Time-segmented semiparametric Cox proportional hazards regression analysis[14] was conducted in the matched sample to assess the impact of revascularization strategies on mortality across age groups. The hazard function was used as a guide to determine approximate time points for the end of the early hazard phase and the beginning of the late phase (R package version 1.2.5: http://CRAN.R-project.org/package=muhaz). Second-order interaction between the treatment indicator and the patient's age (treatment*age) was forced in the 2 Cox models on early and late hazard phases.

Age linearity was assessed using a likelihood ratio test, including age as either a linear term or with a restricted spline fit (Table E1). The likelihood ratio test showed that the linear term for age alone was adequate for the early phase, but the restricted cubic spline form yielded a better fit for the late phase. A Schoenfeld residuals test ruled out violation of the proportional hazard assumption (Table E2 and Figure E2). The effect of treatment across age groups on early and late mortality hazard phases was obtained using nonparametric bootstrap covariance analysis for regression coefficients (n = 1000 repetitions) (R package version 4.2-0: http://CRAN.R-project.org/package=rms). Subgroup analysis was performed according to the use of DES in the PCI group, the presence of LMD, and the number of diseased vessels. R version 3.1.0 (http://www.R-project.org) was used for statistical analysis. A *P* value <.05 was considered significant for all tests.

Propensity Score Matching

Table 1 summarizes the distribution of pretreatment variables in the PCI group and in the unmatched and matched CABG group, with relative standardized mean difference and *P* value. Before matching, patients treated with PCI were significantly different from those treated by CABG; overall, 7 of 14 pretreatment covariates showed a standardized mean difference >10%. In particular, CABG patients were more likely to have diabetes mellitus and more likely to present with triple-vessel disease and LMD. PS matching created a total of 1097 matching sets. After matching, all covariates were well balanced among the 2 groups.

RESULTS

Overall Survival

After a mean follow-up time of 5.5 ± 3.2 years, a total of 301 deaths were recorded in the matched sample (208 in the PCI group; 93 in the CABG group). Death occurred