Real-world long-term outcomes based on three therapeutic strategies in very old patients with three-vessel disease

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Abstract

Background: There are relatively limited data regarding real-world outcomes in very old patients with three-vessel disease (3VD) receiving different therapeutic strategies. This study aimed to perform analysis of long-term clinical outcomes of medical therapy (MT), coronary artery bypass grafting (CABG), and percutaneous coronary intervention (PCI) in this population.

Methods: We included 711 patients aged ≥ 75 years from a prospective cohort of patients with 3VD. Consecutive enrollment of these patients began from April 2004 to February 2011 at Fu Wai Hospital. Patients were categorized into three groups (MT, n = 296; CABG, n = 129; PCI, n = 286) on the basis of different treatment strategies.

Results: During a median follow-up of 7.25 years, 262 deaths and 354 major adverse cardiac and cerebrovascular events (MACCE) occurred. Multivariate Cox analysis showed that the risk of cardiac death was significantly lower for CABG compared with PCI (adjusted hazard ratio [HR] = 0.475, 95% confidence interval [CI] 0.232–0.974, P = 0.042). Additionally, MACCE appeared to show a trend towards a better outcome for CABG (adjusted HR = 0.759, 95% CI 0.536–1.074, P = 0.119). Furthermore, CABG was significantly superior in terms of unplanned revascularization (adjusted HR = 0.279, 95% CI 0.079–0.982, P = 0.047) and myocardial infarction (adjusted HR = 0.196, 95% CI 0.043–0.892, P = 0.035). No significant difference in all-cause death between CABG and PCI was observed. MT had a higher risk of cardiac death than PCI (adjusted HR = 1.636, 95% CI 1.092–2.449, P = 0.017). Subgroup analysis showed that there was a significant interaction between treatment strategy (PCI vs. CABG) and sex for MACCE (P = 0.026), with a lower risk in men for CABG compared with that of PCI, but not in women.

Conclusions: CABG can be performed with reasonable results in very old patients with 3VD. Sex should be taken into consideration in therapeutic decision-making in this population.

Keywords: Three-vessel disease, Very old patients, Medical therapy, Coronary artery bypass grafting, Percutaneous coronary intervention

Background

Coronary artery disease (CAD) is common in aging populations [1]. The number of older patients with CAD requiring coronary revascularization is dramatically increasing worldwide [2]. Three-vessel disease (3VD) is a serious type of CAD and accounts for nearly 30% of patients with CAD [3, 4]. Furthermore, 3VD has higher
risk of death than that of single-vessel disease [5], especially in older patients who tend to have severe comorbidities. Numerous randomized trials have previously compared the relative results of coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) in terms of multivessel disease [6–9]. However, these studies did not focus on the very old population with 3VD. Limited real-world data with long-term follow-up are available on outcomes of very old patients with 3VD receiving different treatment strategies. Therefore, the present study aimed to conduct a comprehensive analysis of real-world outcomes among patients with 3VD aged ≥ 75 years undergoing PCI, CABG or medical therapy (MT) alone. The preliminary results of this study were reported in the 30th Great Wall International Congress of Cardiology scientific abstract [10].

Methods
Study design and population
This study was derived from an observational cohort consisting of 8943 patients with 3VD. These patients were prospectively and consecutively enrolled at Fu Wai Hospital from April 2004 to February 2011 (Beijing, China). The definition of 3VD was angiographic narrowing of ≥ 50% in the left circumflex, left anterior descending, and right coronary arteries, with or without involvement of the left main artery. In this study, the inclusion criteria were as follows: (1) patients who were ≥ 75 years of age; (2) patients who were willing to be followed up; and (3) patients with complete survival data. The final analysis included 711 patients with 3VD who were eligible. Because we obtained data of this post hoc analysis from a subpopulation of the 3VD cohort, the sample size was determined by the number of patients who met the inclusion criteria instead of being calculated in advance. The choice of therapeutic strategy was based on contemporary clinical guidelines, the judgement of cardiologist teams, and the patient’s personal preference [11, 12]. Before the PCI procedure, patients were treated with aspirin and clopidogrel (300 mg or 600 mg, loading dose), and they received standard dual antiplatelet therapy for no less than 1 year after the procedure. The choice of equipment, drugs, and techniques during PCI was at the discretion of the operators. For patients who underwent CABG, standard bypass techniques were used with preferably grafting of the left internal mammary artery to the left anterior descending artery. Experienced surgeons performed the procedure either using on-pump or off-pump surgical techniques on the basis of their individual preference. The ethics committee of Fu Wai Hospital approved this study and it adhered to the Declaration of Helsinki. Informed consent was provided by all participants.

Study endpoints
We obtained information on the medical history and in-hospital data through the electronic record system of our hospital. Patients were followed up by certificated clinical research coordinators through telephone, follow-up letter, or outpatient visit. The last follow-up was finished on March 2016. All-cause death was the primary endpoint. Major adverse cardiac and cerebrovascular events (MACCE, which consisted of unplanned revascularization, stroke, myocardial infarction and all-cause death) and cardiac death were the secondary endpoints. Unless unequivocal non-cardiac causes could be established, all deaths were considered cardiac deaths.

Statistical analysis
Data are shown as means with standard deviations to describe continuous variables of baseline characteristics. Percentages and frequencies are shown for categorical variables. Differences in categorical variables of baseline characteristics were compared with the Pearson chi-square test and Fisher’s exact test. Differences in continuous variables of baseline characteristics were compared with ANOVA and the Kruskal–Wallis test. A survival curve was shown by using the Kaplan–Meier method and compared by using the log-rank test. Variables that were considered clinically relevant or showed a significant univariate relationship with outcomes were incorporated into multivariate Cox analysis. Variables for adjustment included clinical presentation, age, sex, body mass index, diabetes, hypertension, hyperlipidemia, chronic kidney disease, peripheral artery disease, previous stroke, SYNTAX score, previous myocardial infarction, smoker, left ventricular ejection fraction, and left main disease. Interaction was tested by using the Cox regression model to assess the effects of therapeutic strategies in subgroups. Statistical significance was defined as a two-sided α = 0.05. The statistical analyses mentioned above were performed by using IBM® SPSS® v25.0.0.0 software (IBM Inc., Armonk, NY, USA). Moreover, we performed competing risk regression analysis with sub-distribution hazard models for cardiac death and other cardiovascular endpoints, considering competing risks for non-cardiac death and all-cause death, respectively. Inverse probability of treatment weighting (IPTW) regression analysis based on propensity score was also performed in order to better balance the discrepancies among groups. Standardized mean differences were compared to evaluate the degree of baseline variable balance. A standardized mean difference less than 0.1 was regarded as a high degree of balance. The covariates included in propensity score model were as follows: age, sex, BMI, diabetes, hypertension, hyperlipidemia, previous MI, previous stroke,
chronic kidney disease, peripheral artery disease, smoker, clinical presentation, left main disease, LVEF and SYNTAX score. R software (version 4.0.2) was used to perform competing risk and IPTW regression analysis.

Results
This study included 711 patients for analysis, among whom 286 received PCI, 129 received CABG, and 296 received MT (Fig. 1). There were 204 female (28.7%) patients, and the median age was 77 years (interquartile range 75–79 years). Patients in the PCI group were more frequently women compared with those in the other two groups. Patients in the CABG or MT group had higher rates of chronic kidney disease, peripheral artery disease, hyperlipidemia, and significant left main disease, as well as a higher SYNTAX score compared with those in the PCI group (Table 1). The standardized mean difference values of all baseline variables except Clopidogrel after IPTW were less than 0.1 (Additional file 1: Table S1).

The median follow-up period was 7.25 years (interquartile range 5.75–8.75 years). During this period, 262 patients had all-cause death of whom there were 36 in the CABG group, 99 in the PCI group, and 127 in the MT group. The CABG group showed better results of unplanned revascularization (2.3% vs. 8.4%, \(P=0.020\)), myocardial infarction (1.6% vs. 6.3%, \(P=0.037\)), and cardiac death (7.8% vs. 15.7%, \(P=0.026\)) compared with the PCI group. However, the rates of stroke, MACCE, and all-cause death were not significantly different between these two groups. For patients in the PCI or CABG group, the rates of cardiac death and all-cause death were significantly lower (all \(P<0.05\)) compared with those in the MT group. Furthermore, the CABG group had a significantly higher rate of stroke (12.4% vs. 5.7%, \(P=0.018\)) and lower rate of MACCE (41.1% vs. 53.0%, \(P=0.023\)) compared with the MT group (Table 2). Kaplan–Meier curves for the overall study population showed similar results (Fig. 2).

Variables that were adjusted for in multivariate analysis included clinical presentation, age, sex, body mass index, diabetes, hypertension, hyperlipidemia, chronic kidney disease, peripheral artery disease, previous stroke, the SYNTAX score, previous myocardial infarction, smoker, left ventricular ejection fraction, and left main disease. Variables that were entered into multivariate Cox analysis were considered clinically relevant or showed a univariate relationship with outcomes. Multivariate analysis showed that the outcomes of unplanned revascularization, myocardial infarction, and cardiac death were significantly lower in the PCI and CABG groups compared with the MT group. However, the rates of stroke and MACCE were significantly lower in the CABG group compared with the MT group. Kaplan–Meier curves for the overall study population showed similar results (Fig. 2).

Fig. 1 A flow chart for subject selection. 3VD three-vessel disease, CABG coronary artery bypass grafting, MT medical therapy, PCI percutaneous coronary intervention
revascularization (adjusted hazard ratio [HR] = 0.279, 95% confidence interval [CI] 0.079–0.982, *P* = 0.047), myocardial infarction (adjusted HR = 0.196, 95% CI 0.043–0.892, *P* = 0.035), and cardiac death (adjusted HR = 0.475, 95% CI 0.232–0.974, *P* = 0.042) were significantly better with CABG than with PCI. Furthermore, MACCE appeared to show a trend towards a better outcome for CABG (adjusted HR = 0.759, 95% CI 0.536–1.074, *P* = 0.119). PCI was related to a similar risk of long-term stroke and all-cause death compared with CABG, and was related to a lower risk of cardiac death (adjusted HR = 0.611, 95% CI 0.408–0.915, *P* = 0.017) compared with MT (Table 3). Furthermore, similar results were obtained by competing risk and IPTW regression analysis (Additional file 2: Table S2, Additional file 3: Table S3).

### Table 1 Baseline characteristics of the study population

| Variable                           | PCI (n = 286) | CABG (n = 129) | MT (n = 296) | P value |
|------------------------------------|--------------|---------------|-------------|---------|
| Age (years)                        | 77.4 ± 2.5   | 76.8 ± 1.9    | 77.4 ± 2.5  | 0.029   |
| Female                             | 92 (32.2)    | 23 (17.8)     | 89 (30.1)   | 0.009   |
| Body mass index (kg/m²)            | 25.0 ± 3.0   | 25.1 ± 3.1    | 24.9 ± 3.0  | 0.352   |
| **Risk factors and comorbidities** |              |               |             |         |
| Hypertension                       | 203 (71.0)   | 93 (72.1)     | 212 (71.6)  | 0.970   |
| Diabetes mellitus                  | 103 (36.0)   | 42 (32.6)     | 107 (36.1)  | 0.750   |
| Previous myocardial infarction     | 85 (29.7)    | 50 (38.8)     | 101 (34.1)  | 0.176   |
| Hyperlipidemia                     | 123 (43.0)   | 60 (46.5)     | 162 (54.7)  | 0.016   |
| Stroke                             | 38 (13.3)    | 13 (10.1)     | 42 (14.2)   | 0.588   |
| Peripheral artery disease          | 13 (4.5)     | 23 (17.8)     | 28 (9.5)    | <0.001  |
| Chronic kidney disease             | 2 (0.7)      | 2 (1.6)       | 11 (3.7)    | 0.031   |
| Smoker                             | 113 (39.5)   | 56 (43.4)     | 123 (41.6)  | 0.738   |
| **Clinical presentation**          |              |               |             |         |
| Stable angina pectoris             | 81 (28.3)    | 51 (39.5)     | 80 (27.0)   | 0.027   |
| ACS                                | 205 (71.7)   | 78 (60.5)     | 216 (73.0)  | 0.027   |
| Left main disease                  | 57 (19.9)    | 66 (51.2)     | 104 (35.1)  | <0.001  |
| Left ventricular ejection fraction <40% | 3 (1.0) | 2 (1.6) | 5 (1.7) | 0.797 |
| Creatinine (μmol/L)                | 89.7 ± 20.6  | 89.3 ± 17.8   | 92.5 ± 26.0 | 0.251   |
| Creatinine clearance (ml/min)      | 58.6 ± 14.6  | 60.4 ± 12.9   | 57.8 ± 16.3 | 0.256   |
| **SYNTAX score**                   |              |               |             |         |
| ≤ 22                               | 135 (47.2)   | 20 (15.5)     | 76 (25.7)   | <0.001  |
| 23–32                              | 103 (36.0)   | 42 (32.6)     | 108 (36.5)  | 0.752   |
| ≥ 33                               | 47 (16.4)    | 67 (51.9)     | 111 (37.5)  | <0.001  |
| **Medication upon discharge**      |              |               |             |         |
| Aspirin                            | 275 (96.2)   | 119 (92.2)    | 272 (91.9)  | 0.082   |
| Clopidogrel                        | 256 (89.5)   | 11 (8.5)      | 119 (40.2)  | <0.001  |
| Beta-blockers                      | 242 (84.6)   | 103 (79.8)    | 253 (85.5)  | 0.329   |
| Statins                            | 284 (99.3)   | 128 (99.2)    | 295 (99.7)  | 0.781   |
| Angiotensin converting enzyme inhibitors | 277 (96.9) | 126 (97.7) | 285 (96.3) | 0.743   |
| Nitrates                           | 256 (89.5)   | 117 (90.7)    | 276 (93.2)  | 0.271   |
| Calcium channel blockers           | 278 (97.2)   | 126 (97.7)    | 287 (97.0)  | 0.917   |

**ACS** acute coronary syndrome
Subgroup analysis showed a significant interaction between treatment strategy (PCI vs. CABG) and sex for MACCE ($P = 0.026$). In male patients, CABG showed significantly better results regarding MACCE than PCI (HR = 0.560, 95% CI 0.378–0.831). However, in female patients, these two strategies had a similar benefit of survival from MACCE (HR = 2.064, 95% CI 0.991–4.301) (Table 4).

**Discussion**

In the present study, our main findings were as follows. (1) CABG was related to lower risk of long-term unplanned revascularization, myocardial infarction, and cardiac death compared with PCI. (2) There was no difference in the rate of all-cause death between CABG and PCI. (3) The interaction effect between sex and treatment strategy (PCI vs. CABG) was significant for MACCE.

In recent years, with the techniques of PCI and CABG dramatically advancing, the relative benefits of CABG versus PCI in patients with multivessel disease have been debated regarding the long-term prognosis [6–9, 13–16]. Generally, CABG tends to have a better benefit regarding all-cause death or MACCE/MACE. Among patients with multivessel disease, a large proportion of these patients are older adults resulting from their increased longevity [17, 18]. However, there have been no randomized trials for comparing the effect of PCI and CABG in very old patients with multivessel disease, such as 3VD. Moreover, results from previous observational studies and pooled-analysis were heterogeneous [19–22]. Therefore, questions persist concerning the optimal treatment strategy of very old patients with 3VD.

We found that CABG significantly reduced long-term cardiac death, as well as unplanned revascularization and myocardial infarction, compared with
PCI. Similarly, the SYNTAX trial [23] showed that, for patients with complex CAD, CAbG was related to a significant reduction in cardiac mortality versus PCI. This was mainly because CAbG reduced myocardial infarction-related mortality, particularly in patients with 3VD. The CREDO Kyoto sub-analysis study on age and sex showed that the interaction effects between age and therapeutic strategies (PCI vs. CAbG) was significant for cardiac death. There was also an excess risk of mortality in patients aged ≥ 74 years with 3VD, while there was a neutral risk in younger patients [24]. In real clinical practice, older patients prefer less invasive PCI rather than CAbG compared with younger patients. The present study suggested that CAbG could also be an advisable option for very old patients aged ≥ 75 years, especially in those who have complex coronary anatomy unfavorable for PCI. This finding might help further decision-making on the choices of coronary revascularization strategies in patients with 3VD.

All-cause death in our study was comparable between the CAbG and PCI groups. A previous study reported that CAbG was better for an older age compared with PCI in patients with 3VD [24]. However, another study showed that long-term outcomes after CAbG tended to be worse in older patients than in younger patients [25]. Older patients have increased risk factors and higher comorbidities than younger patients, as well as a limited life expectancy. These factors may impair the long-term advantages of CAbG over PCI in reducing the risk of all-cause death. This is because a substantial number of older patients are likely to die from non-cardiac causes during a relatively long follow-up period. Indeed, we found that cardiac causes only accounted for approximately 40% of deaths in the CAbG and PCI groups. The majority of deaths in the CAbG and PCI group were non-cardiac, which supports our view to a certain extent. Additionally, the rate of stroke in the CAbG group was higher than that in the PCI group, but this was not significant. Older patients are considered to have more perioperative strokes after CAbG than after PCI [26]. However, the risk of stroke after CAbG has significantly decreased because of increasingly refined perioperative management and operative techniques in recent years.

**Fig. 2** Cumulative survival curves for the primary and secondary endpoints in three treatment groups. Cumulative incidence curves for all-cause death (a), cardiac death (b), myocardial infarction (c), revascularization (d), stroke (e), and major adverse cardiac and cerebrovascular events (f). MACCE: major adverse cardiac and cerebrovascular events.
In our study, the risk of all-cause death was not significantly different between MT and PCI. However, PCI significantly reduced the risk of cardiac death compared with MT, which suggested that PCI might have a benefit for the heart.

Notably, we found a significant interaction between treatment strategy (PCI vs. CABG) and sex for MACCE. In male patients, CABG was significantly associated with a decreased risk of MACCE compared with PCI, while no such association was observed in female patients. A prospective multicenter registry showed that male patients with multivessel disease presenting with acute non-ST-segment elevation myocardial infarction had improved survival and reduced MACE with CABG compared with PCI at 5 years [28]. However, in female patients, a long-term benefit from CABG was not observed in this previous study. The difference between sexes could be related to factors such as coronary artery size, the amount of grafts received, use of arterial grafts, and diverse surgical methods [29–31]. Therefore, sex should be taken into consideration in selecting revascularization strategies for patients aged ≥ 75 years with 3VD.

Several limitations of this study need to be addressed. First, although multivariate analysis was performed to evaluate many confounders, residual confounding from other unmeasured factors might have been present. Second, generalization of results might be limited because data were obtained from a single-center cohort and the sample size was relatively small. More studies with a larger sample size are warranted to further

### Table 3 Multivariate cox regression analysis of different treatment strategies on clinical outcomes

|                  | PCI          |           | Hazard ratio (95% confidence interval) | p   |           | Hazard ratio (95% confidence interval) | p   |
|------------------|--------------|-----------|----------------------------------------|-----|-----------|----------------------------------------|-----|
|                  | CABG         | MT        |                                        |     |           |                                        |     |
| All cause death  | Ref          |           | 0.802 (0.528–1.218)                    | 0.300 |           | 1.289 (0.962–1.728)                    | 0.090 |
| Cardiac death    | Ref          |           | 0.475 (0.232–0.974)                    | 0.042 |           | 1.636 (1.092–2.449)                    | 0.017 |
| Revascularization| Ref          |           | 0.279 (0.079–0.982)                    | 0.047 |           | 0.867 (0.453–1.660)                    | 0.666 |
| Myocardial infarction | Ref           |           | 0.196 (0.043–0.892)                    | 0.035 |           | 1.060 (0.508–2.210)                    | 0.877 |
| Stroke           | Ref          |           | 1.356 (0.668–2.755)                    | 0.400 |           | 0.769 (0.403–1.468)                    | 0.426 |
| MACCE            | Ref          |           | 0.759 (0.536–1.074)                    | 0.119 |           | 1.123 (0.874–1.443)                    | 0.363 |

**Favor CABG**

|                  | PCI          |           | Hazard ratio (95% confidence interval) | p   |
|------------------|--------------|-----------|----------------------------------------|-----|
| All cause death  | Ref          |           | 0.622 (0.421–0.920)                    | 0.017 |
| Cardiac death    | Ref          |           | 0.290 (0.148–0.569)                    | < 0.001 |
| Revascularization| Ref          |           | 0.322 (0.092–1.119)                    | 0.074 |
| Myocardial infarction | Ref           |           | 0.185 (0.042–0.838)                    | 0.026 |
| Stroke           | Ref          |           | 1.764 (0.868–3.586)                    | 0.117 |
| MACCE            | Ref          |           | 0.676 (0.487–0.938)                    | 0.019 |

**Favor PCI**

**Favor MT**

*MACCE major adverse cardiac and cerebrovascular events*
confirm our study findings. Third, more specific details about revascularization procedures and drug information as well as functional tests for ischemia would be useful. However, such data were not collected.

**Conclusion**

CABG can be performed with reasonable results in very old patients with 3VD. Sex should be taken into consideration in therapeutic decision-making in this population.

**Abbreviations**

3VD: three-vessel disease; CABG: coronary artery bypass grafting; CAD: coronary artery disease; LVEF: left ventricular ejection fraction; MACCE: major adverse cardiac and cerebrovascular events; MACE: major adverse cardiovascular events; MI: myocardial infarction; MT: medical therapy; PCI: percutaneous coronary intervention.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12872-021-02067-6.

**Additional file 1:** Table S1. Baseline characteristics of the study population before and after inverse probability of treatment weighting.

**Additional file 2:** Table S2. Competing risks regression for cardiac death and other cardiovascular endpoints.

**Additional file 3:** Table S3. Inverse probability of treatment weighting (IPTW) regression analysis based on propensity score.

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**Authors’ contributions**

BX, RH, RG, ZG, LS and JY contributed to the study design. LJ, LX, and YZ contributed to the data acquisition. DY drafted the manuscript. DY, SJ, CZ, RL, JX contributed to the analysis, or interpretation of data of the work. JY critically revised the manuscript. All authors have read and approved the manuscript.

| Table 4 Subgroup analysis on all-cause death and MACCE between PCI and CABG |
|-------------------------------------------------|-------------------------------------------------|----------------|
| Subgroup                                      | PCI (95% confidence interval) | MACCE (95% confidence interval) |
| Overall                                       | 1.028 (0.761–1.393)           | 1.059 (0.752–1.525)           |
| Sex                                           | 1.43                          | 1.35                          |
| Female                                        | 1.665 (1.069–2.594)           | 2.064 (1.099–3.901)           |
| Clinical presentation                         | 0.487                         | 0.350                         |
| Stable AP                                     | 1.029 (0.689–1.620)           | 0.324 (0.627–1.214)           |
| ACS                                           | 0.512 (0.327–0.797)           | 0.508 (0.374–0.718)           |
| Diabetes                                      | 0.811                         | 0.987                         |
| Yes                                           | 1.015 (0.406–2.635)           | 0.700 (0.393–1.252)           |
| No                                            | 0.765 (0.448–1.306)           | 0.752 (0.480–1.234)           |
| SYNTAX score                                  | 0.426                         | 0.398                         |
| 0–22                                          | 0.451 (0.276–0.739)           | 0.1463 (0.069–0.732)          |
| 23–32                                         | 0.611 (0.272–1.372)           | 0.587 (0.303–1.137)           |
| ≥33                                           | 0.577 (0.305–1.091)           | 0.557 (0.313–0.921)           |
| Left main disease                             | 0.410                         | 0.389                         |
| Yes                                           | 0.527 (0.266–1.044)           | 0.634 (0.338–1.125)           |
| No                                            | 1.068 (0.629–1.814)           | 0.850 (0.529–1.355)           |
| Favor CABG vs Favor PCI                       |                                |                               |
| MACCE major adverse cardiac and cerebrovascular events, Stable AP stable angina pectoris, ACS acute coronary syndrome

† P value for interaction in each subgroup analysis.
References
1. Dobesh PP, Beavers CJ, Herring HR, Spinler SA, Stacy ZA, Trujillo TC. Key articles and guidelines in the management of acute coronary syndrome and in percutaneous coronary intervention: 2012 update. Pharmacotherapy. 2013;32(12):e348–86.
2. Cockburn J, Hildick-Smith D, Trivedi U, de Belder A. Coronary revascularization in the elderly. Heart. 2017;103(4):316–24.
3. Bradley SM, Sperutz JA, Kennedy KD, Nallamoorthy BK, Chan PS, Patel MR, Bryson CL, Malenka DJ, Rumsfeld JS. Patient selection for diagnostic coronary angiography and hospital-level percutaneous coronary intervention appropriateness: insights from the National Cardiovascular Data Registry. JAMA Intern Med. 2014;174(10):1620–9.
4. Patel MR, Peterson ED, Dai D, Brennan JM, Redberg RF, Anderson HV, Bryson CL, Malenka DJ, Rumsfeld JS. Low diagnostic yield of elective coronary angiography. N Engl J Med. 2010;362(10):886–95.
5. Min JK, Dunning A, Lin FY, Achenbach S, Al-Mallah M, Budoff MJ, Cadermartini F, Callister TQ, Chang HJ, Cheng V, et al. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings results from the International Multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23,854 patients without known coronary artery disease. J Am Coll Cardiol. 2011;58(8):849–60.
6. Daemen J, Boersma E, Flather M, Booth J, Stables R, Rodriguez A, Rodriguez-Garcillo G, Hrub WA, Lemos PA, Serruys PW. Life-long safety and efficacy of percutaneous coronary intervention with stenting and coronary artery bypass surgery for multivessel coronary artery disease: a meta-analysis with 5-year patient-level data from the ARTS, ERACI-II, MASS-II, and SoS trials. Circulation. 2008;118(11):1146–54.
7. Hlatky MA, Boothroyd DB, Bravata DM, Boersma E, Mack MJ, Moncrief MC, Holmes DR, Feldman TE, Stähle E, et al. Coronary artery bypass grafting vs. percutaneous coronary intervention for patients with three-vessel disease: final five-year follow-up of the SYNTAX trial. Eur Heart J. 2014;35(40):2821–30.
8. Head SJ, Davierwala PM, Serruys PW, Redwood SR, Colombo A, Mack MJ, Moncrief MC, Holmes DR, Feldman TE, Stähle E, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360(10):961–72.
9. Head SJ, Davierwala PM, Serruys PW, Redwood SR, Colombo A, Mack MJ, Moncrief MC, Holmes DR, Feldman TE, Stähle E, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360(10):961–72.
10. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hogenblen SM, et al. ACC/AHA/SCAI guideline for percutaneous coronary intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2011;58(24):e44–122.
11. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne BG, Cigarroa JE, Diteia VJ, Hiratzka LF, Hutter AM, et al. ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2011;58(24):213–210.
12. Serruys PW, Unger F, Sousa JE, Jatene A, Monics BH, Schonberger JP, Buller H, Bonier V, van den Brand MJ, van Herwerden LA, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med. 2001;344(15):1117–24.
13. Booth J, Clayton T, Pepper J, Nugara F, Flather M, Sigwart U, Stables RH. Randomized, controlled trial of coronary artery bypass surgery versus percutaneous coronary intervention in patients with multivessel coronary artery disease: six-year follow-up from the Stent or Surgery (SoS) Circulation. 2008;118(4):381–8.
14. Fernandez-Pereira C, Mieres J, Rodriguez AE. Long-term mortality after coronary revascularization in nondiabetic patients with multivessel disease. J Am Coll Cardiol. 2017;69(1):116–7.
15. Bankalore S, Guo Y, Samadashvili Z, Bleiker S, Xu J, Hannan EL. Evertori-mus-eluting stents or bypass surgery for multivessel coronary disease. N Engl J Med. 2015;372(13):1213–22.
16. Landes U, Bental T, Levi A, Assali A, Yaknin-Assa H, Lev EI, Rechavia E, Greenberg G, Orvin K, Kornowski R. Temporal trends in percutaneous coronary interventions thru the drug eluting stent era: insights from 18,641 procedures performed over 12-year period. Catheter Cardiovasc Interv. 2018;92(4):E262-e270.
17. Waldo SW, Secemsky EA, O’Brien C, Kennedy KD, Pomerantsev E, Sundt TM, McNulty EJ, Sicilia BM, Ye H. Surgical ineffectiveness and mortality among patients with unprotected left main or multivessel coronary artery disease undergoing percutaneous coronary intervention. Circulation. 2014;130(23):2295–301.
18. Chang M, Lee CW, Ahn JM, Cavalcante R, Sotomi Y, Onuma Y, Park DW, Kang SJ, Lee SW, Kim YH, et al. Outcomes of coronary artery bypass graft surgery versus drug-eluting stents in older adults. J Am Geriatr Soc. 2017;65(3):625–30.
19. Nicolini F, Contini GA, Fortuna D, Pacini D, Gabbrieli D, Vagnoli L, Campo G, Manari A, Zussa C, Guastabotta P, et al. Coronary artery surgery versus percutaneous coronary intervention in octogenarians: long-term results. Ann Thorac Surg. 2015;99(2):567–74.
20. Graham MM, Ghali WA, Faris PD, Galbraith PD, Norris CM, Knudtson ML. Survival after coronary revascularization in the elderly. Circulation. 2002;105(20):2378–84.
21. Weintraub WS, Grau-Sepulveda MW, Weiss JM, O’Brien SM, Pettersson ED, Kolim F, Zhang Z, Klein LW, Shaw RE, McKay C, et al. Comparative effectiveness of revascularization strategies. N Engl J Med. 2012;366(16):1467–76.
22. Miljevic M, Head SJ, Pasarca CA, Serruys PW, Mohr FW, Moncrief MC, Mack MJ, Stähle E, Feldman TE, Dawkins KD, et al. Causes of death following
PCI versus CABG in complex CAD: 5-year follow-up of SYNTAX. J Am Coll Cardiol. 2016;67(1):42–55.

24. Yamaji K, Shiomi H, Morimoto T, Nakatsuma K, Toyota T, Ono K, Furukawa Y, Nakagawa Y, Kadota K, Ando K, et al. Effects of age and sex on clinical outcomes after percutaneous coronary intervention relative to coronary artery bypass grafting in patients with triple-vessel coronary artery disease. Circulation. 2016;133(19):1878–91.

25. Dalén M, Ivert T, Holzmann MJ, Sartipy U. Coronary artery bypass grafting in patients 50 years or younger: a Swedish nationwide cohort study. Circulation. 2015;131(20):1748–54.

26. Peterson ED, Alexander KP, Malenka DJ, Hannan EL, O’Connor GT, McCullister BD, Weintraub WS, Grover FL. Multicenter experience in revascularization of very elderly patients. Am Heart J. 2004;148(3):486–92.

27. Yanagawa B, Algarni KD, Yau TM, Rao V, Brister SJ. Improving results for coronary artery bypass graft surgery in the elderly. Eur J Cardiothorac Surg. 2012;42(3):507–12.

28. Kurlansky P, Herbert M, Prince S, Mack M. Coronary bypass versus percutaneous intervention: sex matters. The impact of gender on long-term outcomes of coronary revascularization. Eur J Cardiothorac Surg. 2017;51(3):554–61.

29. Hessian R, Jabagi H, Ngu JMC, Rubens FD. Coronary surgery in women and the challenges we face. Can J Cardiol. 2018;34(4):413–21.

30. Sotomi Y, Onuma Y, Cavalcante R, Ahn JM, Lee CW, van Klaveren D, de Winter RJ, Wykrzykowska JJ, Farooq V, Morice MC et al. Geographical Difference of the Interaction of Sex With Treatment Strategy in Patients With Multivessel Disease and Left Main Disease: A Meta-Analysis From SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery), PRECOMBAT (Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease), and BEST (Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients With Multivessel Coronary Artery Disease) Randomized Controlled Trials. Circ Cardiovasc Interv 2017; 10(5).

31. Tabata M, Grab JD, Khalpey Z, Edwards FH, O’Brien SM, Cohn LH, Bolman RM. Prevalence and variability of internal mammary artery graft use in contemporary multivessel coronary artery bypass graft surgery: analysis of the Society of Thoracic Surgeons National Cardiac Database. Circulation. 2009;120(11):935–40.

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