Efficacy and effectiveness of on- versus off-pump coronary artery bypass grafting: A meta-analysis of mortality and survival

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ABSTRACT

Background: Despite many studies comparing on- versus off-pump coronary artery bypass graft (CABG), there is no consensus as to whether one of these techniques offers patients better outcomes.

Methods: We searched PubMed from inception to June 30, 2015, and identified additional studies from bibliographies of meta-analyses and reviews. We identified 42 randomized controlled trials (RCTs) and 31 rigorously adjusted observational studies (controlling for the Society of Thoracic Surgeons-recognized risk factors for mortality) reporting mortality for off-pump versus on-pump CABG at specified time points. Trial data were extracted independently by 2 researchers using a standardized form. Differences in probability of mortality (DPM) were estimated for the RCTs and observational studies separately and combined, for time points ranging from 30 days to 10 years.

Results: RCT-only data showed no significant differences at any time point, whereas observational-only data and the combined analysis showed short-term mortality favored off-pump CABG ($n = 1.2$ million patients; 36 RCTs, 26 observational studies; DPM [95% confidence interval (CI)], -44.8% [-45.4% , -43.8%]) but that at 5 years it was associated with significantly greater mortality ($n = 60,405$ patients; 3 RCTs, 5 observational studies; DPM [95% CI], 10.0% [5.0% , 15.0%]). At 10 years, only observational data were available, and off-pump CABG showed significantly greater mortality (DPM [95% CI], 14.0% [11.0% , 17.0%]).

Conclusions: Evidence from RCTs showed no differences between the techniques, whereas rigorously adjusted observational studies (with >1.1 million patients) and the combined analysis indicated that off-pump CABG offers lower short-term mortality but poorer long-term survival. These results suggest that, in real-world settings, greater operative safety with off-pump CABG comes at the expense of lasting survival gains. (J Thorac Cardiovasc Surg 2018;155:172-9)

Does off- or on-pump CABG offer patients better chances of survival?

Central Message

Evidence from randomized controlled trials showed no differences between on- versus off-pump coronary artery bypass graft surgery, but rigorously-adjusted real-world data indicated that off-pump coronary artery bypass graft surgery offers lower short-term mortality but poorer long-term survival.

Perspective

Many studies have compared outcomes of off- and on-pump coronary artery bypass graft surgery (CABG), reporting inconsistent results. Here, a comprehensive picture of the evidence comparing on- and off-pump CABG (both randomized controlled trials and rigorously adjusted observational studies) suggests that, in real-world settings, off-pump CABG may offer greater operative safety but at the expense of lasting survival gains.

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An estimated 800,000 people undergo coronary artery bypass graft (CABG) surgery worldwide each year.¹ Off-pump CABG, which was introduced in the 1980s to

expand access to CABG to patients in developing countries in which cardiopulmonary bypass was either not available or cost prohibitive,² now accounts for greater

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Abbreviations and Acronyms

CABG = coronary artery bypass graft
 RCT = randomized controlled trial
 STS = Society of Thoracic Surgeons

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than 60% of CABG procedures performed in Asia and 15% to 20% of those performed in Western nations.²⁻⁴ Widespread interest in this technique has been fueled by the possibility that avoiding cardiopulmonary bypass can reduce the adverse complications seen after conventional CABG. Possible disadvantages, however, include greater technical complexity and reduced graft patency and completeness of revascularization.⁵⁻⁷

Many studies—observational and randomized controlled trials (RCTs)—have compared outcomes after off- and on-pump CABG, with results ranging from equivalent outcomes to favoring off-pump or on-pump CABG. This has led to meta-analyses attempting to consolidate the evidence—more than 20 looking at various outcomes and subgroups of studies have been published since 2003. However, those examining mortality in the general population of patients undergoing CABG have focused on short- or long-term⁸⁻¹⁰ results only and/or, with few exceptions,^{8,9,11,12} exclusively on RCTs. The wealth of data from rigorous observational studies (covering >1.1 million patients to date) frequently is ignored. RCTs and observational studies each have their own strengths and weaknesses. Although RCTs remain the gold standard for establishing causation between a therapy and outcomes, they are best suited to evaluating straightforward, discrete interventions in controlled environments, and study findings frequently do not translate into benefits in real-world settings, leaving uncertainty about how therapies should be best applied within the larger environment of the health care delivery system.¹³

As a result, evidence from traditional RCTs generally needs to be supplemented by evidence from effectiveness studies to usefully inform clinical practice.¹³ Here, we provide a comprehensive picture regarding the outcomes associated with off- versus on-pump CABG by assessing both the efficacy (RCTs) and the effectiveness (observational studies)¹⁴ of these techniques in terms of mortality and survival. Recognizing that RCT and observational

data provide valuable insight into particular aspects of questions about efficacy and effectiveness when examined separately, we report results for the subgroups of RCTs and observational studies in isolation. In addition, by using the risk-adjusted results from methodologically rigorous observational studies, we combined the results of all the included studies to provide an overall estimate that summarizes both the experimental and real-world evidence comparing off- versus on-pump CABG.

METHODS

Search Strategy

We conducted a systematic search in PubMed (which accesses MEDLINE, PreMEDLINE, HealthSTAR, the Cochrane Database of Systematic Reviews, publisher-supplied citations, and other related databases) using the search string “Coronary Artery Bypass”[Mesh] AND (“Coronary Artery Bypass, Off-Pump”[Mesh] OR off-pump) AND on-pump AND mortality, and applying the Article type (Clinical Trial, Comparative Study, Meta-Analysis, Review, Systematic Reviews), Species (Humans), and Language (English) filters. Bibliographies of meta-analyses and review articles were reviewed for relevant articles, and the search was last run on June 30, 2015.

Study Inclusion and Exclusion Criteria

Our study focused on the efficacy and effectiveness of on- versus off-pump CABG techniques in the general elective CABG patient population (rather than in specific subgroups, such as CABG patients with a particular comorbidity), with the goal of producing results that would be highly generalizable to the real world and that provide a more comprehensive picture regarding the outcomes associated with these techniques. We therefore included all studies (RCTs and observational study in which the risk-adjustment accounted, at minimum, for the relevant risk factors for mortality recognized by the Society of Thoracic Surgeons [STS]¹⁵) comparing short-term (operative, in-hospital, or 30-days) or long-term (≥ 1 year) all-cause mortality for patients undergoing on-pump versus off-pump isolated CABG. We excluded articles if they (1) reported results only of a literature review or meta-analysis; (2) were restricted to patients with a specific demographic characteristic (eg, age < 50 years), cardiac condition (eg, ejection fraction $\leq 35\%$), comorbidity (eg, diabetes), or undergoing a specific type of CABG procedure (eg, redo procedures) or CABG with a simultaneous or synchronous additional procedure; (3) reported results of an observational study in which the mortality/survival comparison for on-pump versus off-pump CABG was not risk adjusted to account, at minimum, for the relevant risk factors for mortality recognized by the STS; or (4) used the same study cohort as another included study and reported mortality at the same time points.

Data Abstraction and Management

Abstracts and full text of the articles retrieved through the systematic search were reviewed independently by at least 2 investigators, with D.S. and G.F. acting as the final arbiters. For included studies, 2 investigators independently collected information on the participants (cohort size and number of subjects in each study group), the type of study (RCT or observational study) and the number of all-cause deaths (in the case of observational studies, the adjusted estimate of the number of all-cause deaths) at each time point reported. There were no missing data, and, while levels of disagreement varied between investigator pairings, they were generally low (<2%) and easily reconciled through discussion. Reconciled data were entered into RevMan 5.2.¹⁶

Assessment of Risk of Bias

The included studies were assessed for risk of bias using the tool described in the Cochrane handbook¹⁶ for systematic reviews of interventions, adapted, for the observational studies, for application to nonrandomized study designs. Each article was evaluated independently by 2 investigators, with D.S. and G.F. acting as the final arbiters, who judged them to have low, high, or unclear risk of bias in each of the domains shown in Figure 2. Funnel plots were generated to assess publication bias.

Statistical Analysis and Data Synthesis

Summary of measures. Odds ratios (short-term mortality: operative/in-hospital/30-day), relative risk (long-term mortality: 1, 3, 5, and 10 years), differences in probability of mortality, and 95% confidence intervals based on Mantel-Haenszel χ^2 were estimated to compare mortality after off-pump versus on-pump CABG. Crude deaths were used to estimate the measure of associations described above in RCTs—expected deaths based on the adjusted point estimate were used for each observational study. Expected deaths were used for observational studies so that patient case-mix was appropriately accounted for in the analysis.

Given the large number of studies considered, and, more importantly, the large cohort sizes of some of these studies, the summary estimates were calculated with a fixed effect meta-analysis approach.¹⁷ A sensitivity analysis that used a random effects model also was conducted.

Subgroup analysis. Estimates and forest plots were presented overall and for the subgroups of RCTs and risk-adjusted observational studies. By limiting the included observational studies to those adjusted for, at minimum, the relevant STS risk factors, and by using the adjusted odds and risk ratios they reported to estimate the number of deaths in the on- versus off-pump groups for this meta-analysis, the analysis for the observational studies was adjusted for a comprehensive array of clinical and nonclinical risk factors to account for patient case-mix.

Heterogeneity. Tests of heterogeneity were conducted. Each analysis that yielded a significant ($\alpha = 0.05$) heterogeneity test result was repeated twice, first excluding the studies with the largest, then those with the smallest, cohort sizes until the heterogeneity test result was nonsignificant—estimates were then compared with those obtained in presence of heterogeneity.

Sensitivity analyses. For all study time-points, irrespective of the heterogeneity test results, sensitivity analyses were conducted. We excluded the largest and then the smallest studies, and compared the estimates computed with the ones obtained without excluding large or small studies. We then assessed possible bias from our study exclusion criteria by repeating our analyses including those studies we excluded based on their study populations being limited to patients with a specific demographic (sex, or age ≥ 75 years) or clinical characteristic (eg, patients with diabetes, or patients on dialysis), and compared the study estimates. We also repeated the analyses including those studies excluded for having inadequate risk adjustment.

All the analyses were conducted with The Cochrane Collaboration Review Manager 5.2 software. Because only previously published data were collected for and used in this study, institutional review board approval was not sought.

RESULTS

Included Studies

Figure 1 shows the inclusion/exclusion flowchart for studies considered for this meta-analysis; characteristics of the 73 included studies are summarized in Table E1, and the excluded studies are listed in the Online Data Supplement.

Risk of Bias

Overall, the risk of bias in the included studies was low (Figure 2). Likewise, the funnel plots (not shown) did not

show any asymmetry indicating concerns about publication bias.

Synthesis of Results

Short term mortality was investigated in ~ 1.2 million patients and long-term mortality (≥ 1 year) in $\sim 91,000$ patients. Table 1 shows odds ratios, relative risks, and 95% confidence intervals at each time point.

Figures 3 and 4 show details and Forest plots for the fixed-effect short-term mortality and 5- and 10-year survival analyses respectively. Results are reported for RCTs and adjusted observational studies, both separately and combined.

Heterogeneity and Sensitivity Analyses

The sensitivity analyses confirmed our results and heterogeneity did not affect study findings. This included the sensitivity analyses conducted to determine whether the exclusion of studies limited to patients with a specific demographic or clinical characteristic biased our results.

DISCUSSION

In this meta-analysis, we assessed both the efficacy and the effectiveness of the 2 operative techniques in 73 studies comparing mortality in ~ 1.2 million patients undergoing on-pump versus off-pump isolated CABG procedures. Overall and in the subgroup of risk-adjusted observational studies, we observed a significant 43% reduction in risk of short-term mortality associated with off-pump CABG; however, no similar advantage was observed in the subgroup of RCTs. Looking at the long-term results, we found that, overall, any early advantage for off-pump was lost by 1 year and became a significant disadvantage by 5 years. The same held true for the subgroup of risk-adjusted observational studies, with the disadvantage being sustained at 10 years, a period over which patients undergoing off-pump CABG had a statistically significant 15% greater risk of mortality. In the subgroup of RCTs reporting survival at 5 years, there was no significant difference (the 2 larger RCTs showed a nonsignificant benefit with on-pump, whereas the 1 smaller RCT showed a significant benefit with off-pump); no RCT data were available at 10 years. Taken together, the results from the combined analysis, summarizing both experimental and real-world setting data, and from the adjusted observational studies alone suggest that any perioperative advantage the off-pump technique offers likely comes at the price of poorer long-term outcomes.

One possible explanation for this “price” is that less-complete revascularization is achieved with off-pump CABG. Poorer quality of anastomoses and inadequacy of revascularization have been raised as concerns.³ Although there is some evidence that these problems are less prevalent in more recent studies,⁷ other results show them to be

FIGURE 1. Study inclusion and exclusion flowchart. *Sensitivity analyses that included the studies excluded because they were limited to subgroups based on particular demographic or clinical characteristics (eg, patients age ≥ 75 years, or patients with diabetes) or because they used risk adjustment strategies that did not account for the relevant risks factors for mortality recognized by the Society of Thoracic Surgeons were conducted to ensure these exclusions did not bias our results. The sensitivity analyses extended to these excluded studies confirmed the study results. CABG, Coronary artery bypass graft.

ongoing⁶ and the associated loss of survival substantial (37%).¹⁸ Unfortunately, few of the studies in our meta-analysis provided information on graft patency and completeness of revascularization, so we could not include these factors.

Another possible explanation for the long-term poorer outcomes with off-pump CABG is selection bias inherent

in the observational studies—including immeasurable subjective bias that may be inherent in surgeons' decision-making that cannot be accounted for through risk-adjustment. However, the fact that the subgroup analyses of the risk-adjusted observational studies suggest both significantly lower operative/in-hospital/30-day mortality and significantly lower 5 and 10-year survival

FIGURE 2. Risk of bias graph. *Applicable only to randomized controlled trials (42 of the 73 included articles). **For randomized controlled trials, we looked for allocation bias and whether or not an intention-to-treat analysis was used; for observational studies, we determined the risk of selection bias based on whether the same inclusion/exclusion criteria applied to the on- and off-pump groups, and a combination of whether the reported characteristics of the 2 groups showed imbalance and the adequacy of the risk adjustment method applied. †Whether different methods were used to determine mortality/survival between the 2 groups. ‡Studies were considered to have a high risk of attrition bias if >20% of patients were lost to follow-up. §Studies were considered to have a high risk of reporting bias if there was evidence that prespecified outcomes were not reported. ¶Other sources of bias included any limitations on the study population that did not trigger our exclusion criteria (eg, limited to age >65 years, or to “low risk” patients), and whether patients converted from off-pump to on-pump during surgery were analyzed as part of the off-pump group (low risk) or on-pump group (high risk) or excluded (unclear risk).

associated with off-pump CABG makes the selection bias hypothesis unlikely.

Our short-term results are consistent with 3 previous meta-analyses: One that was limited to RCTs but observed a similar reduction in short-term mortality (18% lower odds of death) with off-pump CABG, and 2 which considered observational studies, and found much greater reductions in operative mortality (>30%).^{11,12,19} However, 3 other recent meta-analyses (all limited to RCTs), including the 2012 Cochrane Systematic Review, showed no significant difference in short-term mortality.^{10,20,21} Our long-term results are consistent with the largest and most recent meta-analyses that examined mortality at time points greater than 30 days post-CABG: 2 were limited to RCTs and report a substantially greater increase in the risk of death associated with off-pump CABG (~35%)^{21,22} than the 10% and 14% increases we observed at 5 and 10 years; the remaining 2 included both RCTs and observational studies—one found no significant difference

at 1 to 5 years, but a 6% increased risk of death at >5 years,⁸ the other reported a statistically significant 7% increase in long-term all-cause mortality with off-pump CABG.⁹

Few results of RCTs were available for several of the time points past 5 years postsurgery. However, the 8 studies reporting 5-year results and the 5 studies reporting 10-year results provided ~60,000 patients for each of these time points, bolstering the strength of the conclusions we can draw while waiting for the long-term results of the 2 large RCTs^{23,24} that offer the best opportunity for detecting differences in survival.

Our results have important implications regarding the use of off-pump versus on-pump CABG. They strengthen the conclusions of recent studies^{9,21,22} that off-pump CABG offers patients poorer long-term survival. Being drawn from a set of high-quality studies, not limited either in the time-frame for which outcomes were considered nor to the unique context of RCTs, our results provide the most

TABLE 1. Odds ratios, relative risks, and differences in probability of mortality (with 95% CIs) after off- vs on-pump CABG, by time

Mortality Time point	Number of studies				Off-pump vs on-pump CABG			
					Fixed effect model		Random effects model	
					Relative risk (95% CI)	Difference in probability of mortality (95% CI)	Relative risk (95% CI)	Difference in probability of mortality (95% CI)
Short term	62	36	26	1,216,924	0.81 (0.78, 0.83)*	−44.8 (−45.4, −43.8)	0.72 (0.66, 0.79)*	−41.9 (−44.1, −39.8)
1 y	14	9	5	61,064	0.96 (0.89, 1.04)	4.2 (4.0, 12.4)	0.96 (0.89, 1.04)	4.2 (4.0, 12.4)
3 y	5	2	3	50,186	1.05 (0.99, 1.12)	5.0 (−1.0, 12.0)	1.07 (0.95, 1.20)	7.0 (−5.3, 20.0)
5 y	8	3	5	60,495	1.10 (1.05, 1.15)	10.0 (5.0, 15.0)	1.11 (1.03, 1.20)	11.0 (3.0, 20.0)
10 y	5	0	5	59,125	1.14 (1.11, 1.17)	14.0 (11.0, 17.0)	1.12 (1.00, 1.25)	12.0 (0.0, 25.0)

CABG, Coronary artery bypass graft; RCT, randomized controlled trial; CI, confidence interval. *Odds ratio (95% CI).

Operative/in-hospital/30-day mortality

FIGURE 3. Forest plot summarizing meta-analysis results for short term mortality (operative/in-hospital/30-day). Estimates for studies reporting zero events in both study arms were computed by setting 1 event per arm. *M-H*, Mantel-Haenszel; *CI*, confidence interval; *RCT*, randomized controlled trial.

FIGURE 4. Forest plots summarizing meta-analysis results for 5- and 10-year survival. *M-H*, Mantel-Haenszel; *CI*, confidence interval; *RCT*, randomized controlled trial.

comprehensive picture of the evidence that cardiothoracic surgeons should be considering when advising patients on the choice between on- and off-pump CABG.

Lastly, our results are particularly valuable because they provide the full picture regarding the efficacy (experimental data) and effectiveness (real-world data) of off- and on-pump CABG in terms of mortality and survival by presenting and summarizing, combined and separately, RCT and observational study data. Although the RCT-only data provide insight into how the techniques compare in the regimented and idealized conditions of clinical trials (including experienced clinical teams and surgeons who have specialized in a particular technique, as well as resources for protocol-dictated patient follow-up), data from the rigorously adjusted observational studies allow for the assessment of how the techniques compare in the real-world. These data are critical because the evidence derived from RCTs can be difficult to translate into the real-world setting, where the clinical experience and resources available, as well

as the characteristics of the patient population, may differ greatly from the protocol-driven RCT framework. The differences observed in our results between the RCT-only and the observational studies-only analyses demonstrates the well-recognized complexity of translating RCT results to the broader, real-world setting and patient population.

The majority of CABG procedures in Western nations are still performed on-pump, but there has been substantial interest in the off-pump technique, with some institutions reporting its use in 90% of cases.²⁵ Our results show that, before this trend gains any further ground, we must look critically at the evidence for clinical benefit with off-pump versus on-pump CABG to avoid decisions that may ultimately deprive patients of the long-term benefits they seek through CABG.

Conflicts of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: coronary artery bypass graft, mortality, meta-analysis, off-pump surgery

TABLE E1. Characteristics of the 73 included studies

	Study type	Cohort size	Period during which surgeries were performed	Time points at which mortality results were reported/included in the meta-analysis
RCTs				
Vural and colleagues (1995) ^{E1}	RCT	25 off-pump, 25 on-pump	Not reported	Short term
Ascione and colleagues (1999) ^{E2}	RCT	40 off-pump, 40 on-pump	Not reported	Short term
Czerny and colleagues (2001) ^{E3}	RCT	40 off-pump, 40 on-pump	Not reported	Short term
van Dijk and colleagues (2001) ^{E4}	RCT	142 off-pump, 139 on-pump	3/1998 to 8/2000	Short term
Angelini and colleagues (2002) ^{E5}	Pooled analysis of 2 RCTs	200 off-pump, 201 on-pump	3/1997 to 8/1998; 9/1998 to 11/1999	Short term, 2 y
Tang and colleagues (2002) ^{E6}	RCT	20 off-pump, 20 on-pump	Not reported	Short term
Carrier and colleagues (2003) ^{E7}	RCT	28 off-pump, 37 on-pump	10/2001 to 9/2002	Short term
Lee and colleagues (2003) ^{E8}	RCT	30 off-pump, 30 on-pump	4/1999 to 9/2001	Short term
Muneretto and colleagues (2003) ^{E9}	RCT	88 off-pump, 88 on-pump	1/2000 to 1/2002	Short term, 1 y
Nathoe and colleagues (2003) ^{E10}	RCT	142 off-pump, 139 on-pump	3/1998 to 8/2000	1 y
Chen et al (2004) ^{E11}	RCT	150 off-pump, 150 on-pump	6/2001 to 4/2003	Short term
Gerola and colleagues (2004) ^{E12}	RCT	80 off-pump, 80 on-pump	Not reported	Short term
Légaré and colleagues (2004) ^{E13}	RCT	150 off-pump, 150 on-pump	8/1999 to 3/2003	Short term
Nathoe and colleagues (2004) ^{E14}	RCT	132 off-pump, 117 on-pump	3/1998 to 8/2000	Short term, 1 y
Straka and colleagues (2004) ^{E15}	RCT	204 off-pump, 184 on-pump	5/2000 to 6/2002	Short term
Velissaris and colleagues (2004) ^{E16}	RCT	26 off-pump, 26 on-pump	Not reported	Short term
Wan and colleagues (2004) ^{E17}	RCT	18 off-pump, 19 on-pump	Not reported	Short term
Staton and colleagues (2005) ^{E18}	RCT	100 off-pump, 97 on-pump	Not reported	Short term
Lingaas and colleagues (2006) ^{E19}	RCT	60 off-pump, 60 on-pump	Not reported	Short term
Paparella and colleagues (2006) ^{E20}	RCT	15 off-pump, 16 on-pump	Not reported	Short term
Tatoulis and colleagues (2006) ^{E21}	RCT	50 off-pump, 50 on-pump	Not reported	Short term
Hernandez and colleagues (2007) ^{E22}	RCT	99 off-pump, 102 on-pump	1/2001 to 1/2004	Short term
Karolak and colleagues (2007) ^{E23}	RCT	150 off-pump, 150 on-pump	8/1999 to 3/2003	4 y
Motallebzadeh and colleagues (2007) ^{E24}	RCT	108 off-pump, 104 on-pump	8/2002 to 3/2004	Short term
van Dijk et al (2007) ^{E25}	RCT	142 off-pump, 139 on-pump	1998 to 2000	5 y
Bednar and colleagues (2008) ^{E26}	RCT	40 off-pump, 40 on-pump	5/2005 to 12/2006	Short term
Medved and colleagues (2008) ^{E27}	RCT	30 off-pump, 30 on-pump	1/15/2006 to 6/30/2007	Short term
Nogueira and colleagues (2008) ^{E28}	RCT	105 off-pump, 97 on-pump	1/2002 to 12/2006	Short term
Angelini and colleagues (2009) ^{E29}	RCT	200 off-pump, 201 on-pump	3/1997 to 8/1998; 9/1998 to 11/1999	6 y
Shroyer and colleagues (2009) ^{E30}	RCT	1104 off-pump, 1099 on-pump	2/2002 to 5/2008	Short term, 1 y
Hueb and colleagues (2010) ^{E31}	RCT	155 off-pump, 153 on-pump	3/2001 to 3/2006	Short term, 5 y
Mantovani and colleagues (2010) ^{E32}	RCT	12 off-pump, 13 on-pump	Not reported	Short term
Møller and colleagues (2010) ^{E33}	RCT	176 off-pump, 163 on-pump	4/2002 to 3/2006	Short term
Serrano and colleagues (2010) ^{E34}	RCT	40 off-pump, 41 on-pump	3/2001 to 3/2006	Short term, 1 y
Sousa Uva and colleagues (2010) ^{E35}	RCT	75 off-pump, 75 on-pump	4/2005 to 7/2007	Short term, 1 y
Michaux and colleagues (2011) ^{E36}	RCT	25 off-pump, 25 on-pump	Not reported	Short term, 1 y, 2 y
Møller and colleagues (2011) ^{E37}	RCT	176 off-pump, 163 on-pump	4/2002 to 3/2006	3 y
Puskas and colleagues (2011) ^{E38}	RCT	98 off-pump, 99 on-pump	3/2000 to 8/2001	Short term, 1 y, 2 y, 3 y, 4 y, 5 y, 6 y, 7 y, 8 y
Houliand and colleagues (2012) ^{E39}	RCT	450 off-pump, 450 on-pump	Not reported	Short term

(Continued)

TABLE E1. Continued

	Study type	Cohort size	Period during which surgeries were performed	Time points at which mortality results were reported/included in the meta-analysis
Lamy and colleagues (2012) ^{E40}	RCT	2375 off-pump, 2377 on-pump	11/2006 to 10/2011	Short term
Lemma and colleagues (2012) ^{E41}	RCT	208 off-pump, 203 on-pump	12/2006 to 4/2010	Short term
Lamy and colleagues (2013) ^{E42}	RCT	2375 off-pump, 2377 on-pump	11/2006 to 10/2011	1 y
Risk-adjusted observational studies/adjustment technique				
Hernandez and colleagues (2001) ^{E43}	Multivariable regression, 12 risk factors	1741 off-pump, 6126 on-pump	1998 to 2000	Short term
Plomondon and colleagues (2001) ^{E44}	Propensity adjustment, 11 risk factors	680 off-pump, 1733 on-pump	10/1997 to 3/1999	Short term
Chamberlain and colleagues (2002) ^{E45}	Multivariable regression, 13 risk factors	332 off-pump, 1238 on-pump	4/1996 to 12/2000	Short term
Mack and colleagues (2002) ^{E46}	Multivariable regression, 23 risk factors	1929 off-pump, 10631 on-pump	1/1995 to 12/2000	Short term
Sabik and colleagues (2002) ^{E47}	Propensity matching, 10 risk factors	406 off-pump, 406 on-pump	1/1997 to 6/2000	Short term
Aldea and colleagues (2003) ^{E48}	Multivariable regression, 9 risk factors	1233 off-pump, 7169 on-pump	1/1999 to 12/2000	Short term
Boening and colleagues (2003) ^{E49}	Propensity matching, 11 risk factors	72 off-pump, 97 on-pump	1/1998 to 12/2001	Short term, 2 y
Sabik and colleagues (2004) ^{E50}	Propensity matching, 10 risk factors	406 off-pump, 406 on-pump	1/1997 to 7/2000	1 y, 2 y, 4 y
Stamou and colleagues (2004) ^{E51}	Propensity matching, 14 risk factors	1833 off-pump, 1833 on-pump	10/1998 to 6/2001	Short term
Calafiore and colleagues (2005) ^{E52}	Propensity matching, 36 risk factors	597 off-pump, 597 on-pump	11/1994 to 12/2001	Short term, 1 y 3 y 6 y
Lamy and colleagues (2005) ^{E53}	Propensity matching, 14 risk factors	1233 off-pump, 1233 on-pump	3/2001 to 12/2002	Short term, 1 y
Roscitano and colleagues (2005) ^{E54}	Matching, 20 risk factors	87 off-pump, 87 on-pump	5/2000 to 5/2002	Short term
Stamou and colleagues (2005) ^{E55}	Propensity adjustment, 12 risk factors	315 off-pump, 198 on-pump	1/1/2000 to 12/31/2000	Short term
Williams and colleagues (2005) ^{E56}	Propensity adjustment, 13 risk factors	641 off-pump, 5026 on-pump	1/1998 to 9/2003	Short term
Di Mauro and colleagues (2007) ^{E57}	Propensity matching, 17 risk factors	1069 off-pump, 1381 on-pump	11/1994 to 12/2001	Short term, 10 y
Hannan and colleagues (2007) ^{E58}	Multivariable regression, 12 risk factors	13889 off-pump, 35941 on-pump	2001 to 2004	Short term
Ivanov and colleagues (2008) ^{E59}	Propensity matching, 18 risk factors	503 off-pump, 503 on-pump	1996 to 2002	Short term
Lattouf and colleagues (2008) ^{E60}	Propensity adjustment, 40 risk factors	5667 off-pump, 7145 on-pump	1997 to 2006	1 y 3 y 5 y 10 y
Li and colleagues (2008) ^{E61}	Propensity matching, 40 risk factors	447 off-pump, 744 on-pump	1/1999 to 12/2003	Short term
Puskas and colleagues (2008) ^{E62}	Propensity adjustment, 40 risk factors	5667 off-pump, 7145 on-pump	1997 to 2006	Short term
Konety and colleagues (2009) ^{E63}	Propensity adjustment, 31 risk factors	26011 off-pump, 99344 on-pump	2000 to 2004	Short term

(Continued)

TABLE E1. Continued

	Study type	Cohort size	Period during which surgeries were performed	Time points at which mortality results were reported/included in the meta-analysis
Maganti and colleagues (2009) ^{E64}	Propensity matching, 18 risk factors	619 off-pump, 619 on-pump	1996 to 2004	Short term
Brizzio and colleagues (2010) ^{E65}	Propensity matching, 12 risk factors	1379 off-pump, 1379 on-pump	1/1998 to 12/2007	Short term
Emmert and colleagues (2011) ^{E66}	Propensity adjustment, 50 risk factors	2203 off-pump, 2111 on-pump	1999 to 2009	Short term
Filardo and colleagues (2011) ^{E67}	Propensity adjustment, 22 risk factors	732 off-pump, 7349 on-pump	1/1997 to 12/2008	5 y, 10 y
Marui and colleagues (Sept. 2012) ^{E68}	Propensity adjustment, 33 risk factors	1091 off-pump, 1377 on-pump	1/2000 to 12/2002	Short term, 5 y
Bakaeen and colleagues (2013) ^{E69}	Propensity matching, 19 risk factors	8911 off-pump, 26733 on-pump	10/1997 to 4/2011	1 y 3 y, 5 y, 10 y
Polonsky and colleagues (2013) ^{E70}	Multivariable regression, 31 risk factors	186138 off-pump, 689943 on-pump	1/2005 to 12/2010	Short term
Bakaeen et al (2014) ^{E71}	Propensity matching, 19 risk factors	11629 off-pump, 53468 on-pump	10/1997 to 4/2011	Short term
Raja et al (2014) ^{E72}	Propensity matching, 26 risk factors	307 off-pump, 397 on-pump	1/2002 to 12/2002	5 y, 10 y
Moss et al (2015) ^{E73}	Multivariable regression, 33 risk factors	9550 off-pump, 2529 on-pump	1/2002 to 7/2013	Short term

RCT, Randomized controlled trial.

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