Off-pump versus on-pump coronary artery bypass grafting: A systematic review and meta-analysis of propensity score analyses

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Objective: Despite numerous randomized and nonrandomized trials on off- and on-pump coronary artery bypass grafting, it remains open which method is superior. Patient selection and small sample sizes limit the evidence from randomized trials; lack of randomization limits the evidence from nonrandomized trials. Propensity score analyses are expected to improve on at least some of these problems. We aimed to systematically review all propensity score analyses comparing off- and on-pump coronary artery bypass grafting.

Methods: Propensity score analyses comparing off- and on-pump surgery were identified from 8 bibliographic databases, citation tracking, and a free web search. Two independent reviewers abstracted data on 11 binary short-term outcomes.

Results: A total of 35 of 58 initially retrieved propensity score analyses were included, accounting for a total of 123,137 patients. The estimated overall odds ratio was less than 1 for all outcomes, favoring off-pump surgery. This benefit was statistically significant for mortality (odds ratio, 0.69; 95% confidence interval, 0.60–0.75), stroke, renal failure, red blood cell transfusion ($P < .0001$), wound infection ($P < .001$), prolonged ventilation ($P < .01$), inotropic support ($P = .02$), and intraaortic balloon pump support ($P = .05$). The odds ratios for myocardial infarction, atrial fibrillation, and reoperation for bleeding were not significant.

Conclusions: Our systematic review and meta-analysis of propensity score analyses finds off-pump surgery superior to on-pump surgery in all of the assessed short-term outcomes. This advantage was statistically significant and clinically relevant for most outcomes, especially for mortality, the most valid criterion. These results agree with previous systematic reviews of randomized and nonrandomized trials. (J Thorac Cardiovasc Surg 2010;140:829-35)

Supplemental material is available online.

Coronary artery disease is still the most frequent cause of death in industrialized countries. In middle-aged cohorts, coronary artery disease has a prevalence of approximately 20%. More than 50,000 patients undergo coronary artery bypass grafting (CABG) in Germany annually. There is a trend to higher patient age and an increasing prevalence of comorbidities.[1] Today's surgical standard involves coronary revascularization with heart–lung machine support and cardioplegia-induced cardiac arrest, the so-called on-pump technique. Although this technique is routinely used, there are still morbidity and mortality risks, attributed to a systemic inflammatory response and to atheromatous macroembolization. Because of these adverse side effects, the standard technique has been challenged in recent years by the emerging off-pump technique, which avoids the use of cardiopulmonary bypass and cardioplegia. The question of which method is superior is one of the most hotly debated and polarizing issues in cardiac surgery.[2]

Because of the public health and economic impacts of this question, a large number of randomized clinical trials (RCTs) were conducted. Most of them are summarized in systematic reviews.[3,4] These systematic reviews show a trend toward an advantage of off-pump surgery in terms of the clinically relevant postoperative outcomes mortality, stroke, and myocardial infarction. The observed effects are not always found to be statistically significant, mostly because of limited sample sizes.

In addition to these RCTs, a number of nonrandomized trials have been conducted. The respective data were also collected in a systematic review.[5] It is commonly agreed that results from observational studies should not be used for making treatment recommendations. Nonrandomized studies, however, avoid 2 important deficiencies of RCTs. First, RCTs are frequently conducted in highly selected patient groups,[6] enrolling patients who are younger and

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Abbreviations and Acronyms
CABG = coronary artery bypass grafting
CI = confidence interval
OR = odds ratio
RBC = red blood cell
RCT = randomized clinical trial

healthier than the average patient.[7] Second, and this is of special concern in cardiac surgery, clinically relevant outcomes are only rarely observed. That is, RCTs intended to find differences between treatments require large sample sizes to detect differences between those rarely occurring outcomes. For example, a study designed to detect a postoperative mortality reduction from 3% to 2% with 80% power and 5% type I error would require more than 8000 patients. This number should be compared with the sample size of the largest RCTs published up to date,[8] which included 388 patients. The number of patients included in the largest systematic review of RCTs to date was 5537 (from 66 trials).[4] Therefore, not even the largest systematic reviews on this topic would have enough power to find the postulated difference in postoperative mortality.

Lack of randomization is of course the reason for distrusting observational studies as a basis for treatment recommendations. Randomization ensures that all relevant (known and unknown) prognostic and risk factors are balanced across treatment groups. In observational studies, we have to rely on statistical methods such as stratification, matching, or multivariate adjustment to adjust for baseline differences in treatment groups. A promising technique for this adjustment is the so-called propensity score method, which, if conducted with matching on the propensity score, achieves a kind of pseudorandomization. This ensures that at least the known and measured prognostic factors are balanced. The propensity score method, proposed as early as the 1980s,[9] has only recently been applied to clinical research, but sees increasing use, especially in cardiology and cardiac surgery.[10] Moreover, there are indications that the propensity score method is statistically superior to the standard methods for multivariate adjustment,[11,12] especially when the number of events is low as in CABG.[12]

In the following, we report on a systematic review and meta-analysis comparing off-pump and on-pump CABG explicitly including only propensity score analyses.

MATERIALS AND METHODS

Search Strategy

Searches were conducted independently by 2 persons (O.K., biostatistician; B.v.S., medical student) in the first week of February 2006. Our search strategy was 3-fold: First, we searched the literature databases MEDLINE, EMBASE, American College of Physicians Journal Club, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, EBM Reviews, and Web of Science for the keywords ''Propensity'' and ''Off-Pump.'' Second, we analyzed the citations of 6 methodical articles[9,13-17] on propensity score analysis via Web of Science (http://www.isiknowledge.com) because there is evidence that failure to use citation tracking may cause bias from overlooked studies.[18] Third, we searched the open web-based scientific databases Google scholar (http://scholar.google.com), Scirus (http://www.scirus.com), and Vivísimo clustering (http://vivisimo.com), also with the keywords ''Propensity'' and ''Off-Pump.'' Finally, we checked the references of all available articles. Meeting abstracts and unpublished reports were included. Authors of meeting abstracts were contacted by e-mail for additional information on the described studies. There were no restrictions on language or time of publication.

Data Collection and Management

Full-text versions of all initially retrieved publications were read independently by 2 reviewers (O.K., B.v.S.). Data were abstracted into a self-developed case report form, which had been tested in a small pilot review encompassing 5 studies. The data collected by both reviewers were entered in a database, and disagreements were located by automatic comparisons. Agreement between reviewers was checked on a previously selected subgroup of abstracted items (inclusion of study, high-risk population, type of propensity analysis, reporting of confounders in the propensity score model). All disagreements on abstracted data were resolved by consensus and by discussion with a third reviewer (J.B.).

Inclusion Criteria

Studies were included in the meta-analysis if they reported a comparison of at least an off-pump with an on-pump group and made use of a propensity score analysis for comparing treatments. Randomized controlled trials, observational studies without a propensity score analysis, and systematic reviews with no new original data were excluded. For inclusion, studies also had to provide at least one of the binary clinical outcomes mortality, stroke, myocardial infarction, atrial fibrillation, renal failure, inotropic support, red blood cell (RBC) transfusion, wound infection, reoperation for bleeding, intraaortic balloon pump support, or prolonged ventilation. Only short-term or in-hospital outcomes were considered. Studies with mere experimental outcomes were excluded. We always kept the outcome definitions of the original researchers. Double publications were removed, but data from the same study populations were included if these populations did not completely overlap in the propensity score analyses.

Statistical Methods

For descriptive purposes, absolute and relative frequencies are reported for categoric variates. The odds ratio (OR) was used to describe treatment effects. From studies using regression adjustment or stratification in the propensity score analysis, the ORs with the corresponding confidence intervals (CIs) were extracted directly from the text. In studies with a matched propensity score analysis, we used the absolute numbers of events and calculated ORs with CIs using standard methods. Studies with zero events were corrected by the ''reciprocal of the opposite treatment arm'' method.[19] In one study a relative risk was used to describe the treatment effect. Because ORs and relative risks are approximately equal for rare outcomes, we equated this relative risk with an OR.

For combining ORs from different studies, the random effects inverse-variance method[20] was applied, that is, ORs from the individual studies were combined as weighted averages. The random effects method, compared with the fixed effects method, was chosen because it allows heterogeneous treatment effects between studies and is slightly more conservative. However, as a sensitivity analysis, the fixed effects estimates are also presented. All calculations were performed with log-transformed ORs, and results were retransformed for presentation. Although it is well known that the inverse-variance method has deficiencies, we emphasize that it is the

only method applicable with our approach where absolute numbers of events are only available in cases of matched propensity score analyses. To facilitate interpretation of results, we also computed summary numbers needed to treat (number needed to treat with off-pump surgery to avoid 1 additional event) for each clinical outcome. Numbers needed to treat were derived from the combined ORs using the ideas of Zhang and Yu.[21] The required baseline risk data were calculated from the studies that reported a matched propensity score analysis, because absolute frequencies are only available in these cases. To assess heterogeneity between studies, we performed the standard test for homogeneity (based on Cochran's Q)[20] and the recently proposed I^2 statistic.

Meta-regression on location of study (Northern America vs others), type of propensity score analysis (matching vs nonmatching), population risk (high risk vs standard risk), volume per year (defined as the number of patients divided by the length of the observation period, but only in single-center studies), and percentage of off-pump cases in the general study population (not necessarily equal to this percentage in the propensity score population) was conducted to judge the influence of these factors on heterogeneity. For this meta-regression, all outcomes were combined in a single data set, and the analysis was adjusted for correlated (within study) outcomes by using a random effects model.[20] All statistical estimates are given with their 95% CIs. The study database was programmed in Microsoft ACCESS (Microsoft Corp, Redmond, Wash), and all statistical analyses were conducted with SAS, 9.1.2. (SAS Institute Inc, Cary, NC).

RESULTS

The initial search yielded 58 publications, of which 39 (66%) were found in the described literature databases, 8 (14%) were found by citation tracking, and 11 (19%) were found in the open scientific databases.

Thirty-five of the initial 58 publications (60%) were included in the final analyses (Table E1), 24 (69%) from the described literature databases, 3 (9%) from citation tracking, and 8 (22%) from the open scientific databases (Figure 1). Five publications were excluded because they did not compare an off-pump with an on-pump group; 6 publications were excluded because they made no or wrong use of the propensity score method; and 4 publications were systematic reviews without new original data. In 6 publications, no information was given on the prespecified outcomes, and in 1 publication results from the propensity score analysis were given only narratively. One publication was removed because of double publication.

Table 1 provides an overview of the included studies: Sixteen studies (46%) were conducted in Europe, and the remaining were conducted in Northern America. Authors of 19 propensity score analyses (54%) reported on a high-risk population. The 35 studies account for a total of 123,137 observations; 49,718 procedures (40.4%) were conducted off-pump. The online supplement shows the estimated ORs for the single studies numerically (Table E2) and graphically (Figure E1).

Table 2 reports the results of the meta-analyses for the specific outcomes. For all 11 outcomes we find an estimated OR less than 1 in favor of off-pump surgery. This effect is highly significant ($P < .0001$) for the outcomes mortality, stroke, renal failure, and RBC transfusion; significant for wound infection ($P < .001$), prolonged ventilation ($P < .01$), intraaortic balloon pump support ($P = .01$) and inotropic support ($P = .02$); and borderline significant for reoperation for bleeding ($P = .06$). Insignificant ORs near 1 were observed for myocardial infarction and atrial fibrillation. Estimates from the fixed effects model differed only slightly from the random effect estimates. Heterogeneity of studies for the different outcomes varied widely. A very large heterogeneity was found for the outcomes inotropic support and RBC transfusion, and large heterogeneity for reoperation and atrial fibrillation. All other outcomes showed at most moderate or no heterogeneity.

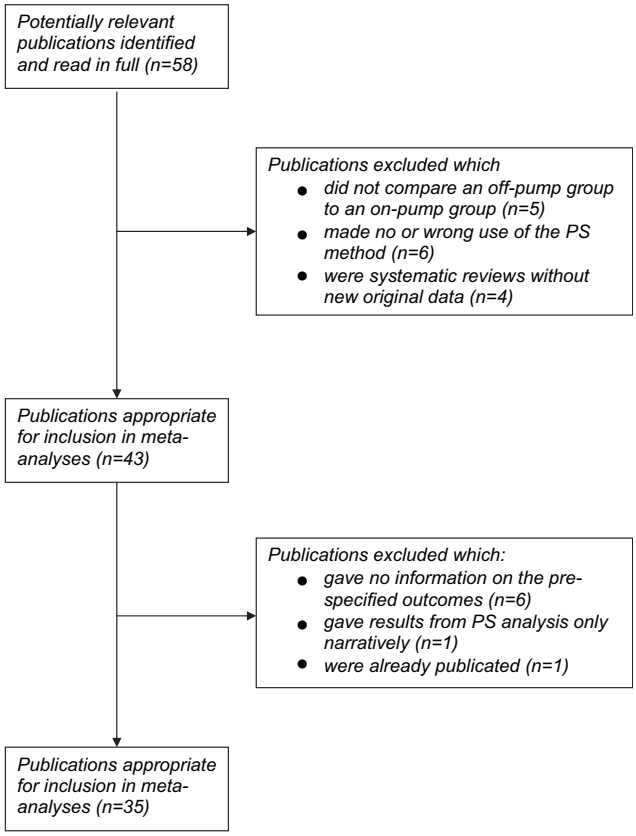

FIGURE 1. Flow diagram of initially retrieved and eventually included studies. *PS,* Propensity score.

In meta-regression, heterogeneity of treatment effects could not be explained by the study location (Northern America vs Europe, $P = .33$), type of propensity score analysis (matching vs nonmatching, $P = .99$), population risk (high risk vs standard, $P = .65$), volume per year ($P = .55$), or percentage of off-pump cases in the general study population ($P = .25$).

DISCUSSION

Our systematic review and meta-analysis of propensity score analyses finds off-pump surgery superior to on-pump surgery with respect to all of the assessed short-term

TABLE 1. Included studies

					PS analysis population			General population
Study	Observation period	Study location	Study centers (no.)	Are patients from a high-risk group (as reported from the authors)? If yes, which risk?	Average patient age, y	Gender (% male)	Proportion of off-pump cases (%)	Proportion of off-pump cases (%)
Ascione 2002	04/96–04/01	England	1	Overweight (BMI $\geq$ 25)	63.0	79.5	23.7 (674/2844)	23.7 (674/2844)
Ascione 2003	04/96–08/02	England	1	Severe LV dysfunction (EF < 30%)	65.3	90.4	29.6 (74/250)	29.6 (74/250)
Boening 2003	01/98–12/01	Germany	1	No	65.5	–	42.6 (72/169)	20.5 (133/650)
Calafiore 2003a	11/94–12/01	Italy	1	No	64.4	83.2	50.0 (961/1922)	–
Calafiore 2003b	11/94–12/01	Italy	1	EuroSCORE $\geq$ 6	70.1	71.7	50.0 (510/1020)	–
Calafiore 2005	11/94–12/01	Italy	1	No	62.6	86.1	50.0 (597/1194)	–
Chukwuemeka 2005	00/95–00/03	Canada	1	Preoperative renal dysfunction	70.3	64.4	25.0 (146/584)	5.5 (158/2869)
Frankel 2005	01/98–06/02	USA	1	No	–	–	50.0 (2141/4282)	41.2(3646/8843)
Grunkemeier 2002	00/98–00/00	USA	9	No	66.5	73.1	31.8 (990/3110)	15.0 (1194*/7955)
Ivanov 2006	00/96–00/02	Canada	1	No	–	–	50.0 (503/1006)	4.5 (514/11368)
Karthik 2003	04/97–03/02	England	2	Nonelective CABG	65.0	72.4	50.4 (417/828)	48.1 (1813/3771)
Karthik 2004	04/97–03/02	England	2	Peripheral vascular disease	65.6	79.4	50.0 (211/422)	48.1 (1813/3771)
Lamy 2005	03/01–12/02	Canada	14	No	64.6	–	50.0 (1233/2466)	49.5 (1657/3350)
Lee 2006	07/99–01/04	Canada	1	No	–	–	50.0 (165/330)	48.1 (290/603)
Lu 2005	04/97–04/03	Great Britain	1	LMS disease	65.7	80.5	21.6 (259/1197)	21.6 (259/1197)
Mack 2004a	00/99–00/01	USA	4	Multivessel disease	–	–	50.0 (5774/11548)	41.9 (7283/17401)
Mack 2004b	01/98–03/02	USA	82	Women	68.8	0.0	50.0 (3688/7376)	19.4 (4250/21902)
Magee 2002	01/98–07/00	USA	2	Multivessel disease	–	–	33.3 (1606*/4818)	23.5 (1983/8449)
Magee 2003	01/99–12/00	USA	–	>2 grafts	68.0	68.6	50.0 (16937/33874)	8.8 (17969/204602)
Meco 2004	–	Italy	–	Age > 75 y	–	–	65.5 (78/119)	–
Oo 2003	04/97–09/02	England	1	EuroSCORE $\geq$ 6	71.4	72.6	50.4 (196/389)	–
Pandey 2005	04/97–09/02	England	1	No	61.9	80.8	50.0 (360/720)	17.4 (987/5679)
Patel 2002a	04/97–05/01	England	2	No	62.0	78.1	48.0 (1117/2327)	48.0 (1117/2327)
Patel 2002b	04/97–03/01	England	4	No	62.8	79.1	7.7 (843/10941)	7.7 (843/10941)
Sabik 2002	01/97–06/00	USA	1	No	66.0	69.5	50.0 (406/812)	13.0 (481/3712)
Saunders 2004	00/96–00/02	USA	1	Functional mitral regurgitation	–	–	50.0 (127/254)	20.6 (222/1078)
Seif 2005	00/93–00/04	USA	1	No	–	–	25.0 (1913/7641)	–
Sharony 2004	06/93–10/02	USA	1	Atheromatous aortic disease	73.0	68.8	50.0 (245/490)	28.5 (281/985)
Srinivasan 2004	04/97–09/02	England	1	Diabetes	65.2	77.0	19.6 (186/951)	19.6 (186/951)
Stamou 2002	06/94–12/00	USA	1	No	–	–	50.0 (1670/3340)	22.3 (2320/10389)
Stamou 2004	10/98–06/01	USA	1	No	–	–	50.0 (1833*/3666*)	44.6 (2477/5554)
Stamou 2005	01/00–12/00	USA	1	Parsonnet score $\geq$ 20 points	71.0	48.3	61.4 (315/513)	61.4 (315/513)
Stamou 2006	01/00–10/03	USA	2	Nonelective CABG	–	–	50.0 (2013/4026)	36.3 (2273/6260)
Weerasinghe 2005	01/01–11/03	England	3	Multivessel disease	64.5	73.7	40.0 (817/2041)	40.0 (817/2041)
Williams 2005	01/98–09/03	USA	1	No	63.5	69.8	11.3 (641/5667)	11.3 (641/5667)

BMI, Body mass index; *LV*, left ventricular; *EF*, ejection fraction; *CABG*, coronary artery bypass grafting; *LMS*, left main stem stenosis. *Numbers estimated from the text.

TABLE 2. Results of meta-analyses

Response	No. of studies (patients)	OR (95% CI) *P* value, REM	*P* value homogeneity	I^2 (%)	NNT (95% CI)	OR (95% CI) *P* value, FEM
Mortality	28 (100,066)	0.69 (0.60–0.75) $P < .0001$	.18	14	189 (155–251)	0.70 (0.65–0.76) $P < .0001$
Stroke	22 (55,290)	0.42 (0.33–0.54) $P < .0001$	.16	16	104 (90–132)	0.49 (0.41–0.58) $P < .0001$
Myocardial infarction	14 (35,951)	0.97 (0.73–1.30) $P = .86$	.06	32	2685 (254 to –229)	0.91 (0.74–1.11) $P = .35$
Atrial fibrillation	11 (29,343)	0.92 (0.80–1.05) $P = .20$	.01	51	79 (33 to –143)	0.85 (0.80–0.91) $P < .0001$
Renal failure	17 (38,866)	0.60 (0.51–0.70) $P < .0001$	.21	11	82 (67–110)	0.59 (0.53–0.66) $P < .0001$
Inotropic support	7 (6,153)	0.59 (0.38–0.90) $P = .02$	$P < .0001$	82	8 (5–41)	0.65 (0.56–0.75) $P < .0001$
RBC transfusion	8 (16,685)	0.36 (0.25–0.54) $P < .0001$	$P < .0001$	91	9 (7–13)	0.49 (0.44–0.54) $P < .0001$
Wound infection	13 (33,030)	0.59 (0.45–0.77) $P < .001$	.97	0	314 (235–553)	0.59 (0.45–0.77) $P < .0001$
Reoperation for bleeding	14 (39,480)	0.76 (0.57–1.02) $P = .06$	<.01	50	195 (107 to –2753)	0.69 (0.59–0.81) $P < .0001$
IABP support	7 (9703)	0.60 (0.41–0.89) $P = .01$	.18	10	245 (164–904)	0.57 (0.43–0.76) $P < .001$
Prolonged ventilation	6 (8675)	0.71 (0.56–0.89) $P < .01$	.32	0	116 (77–312)	0.74 (0.61–0.90) $P = .002$

OR, Odds ratio; *CI,* confidence interval; *REM,* random effects model; *NNT,* number needed to treat; *FEM,* fixed effects model; *RBC,* red blood cell; *IABP,* intraaortic balloon pump.

outcomes. This advantage was statistically significant and clinically relevant for most outcomes, especially for the most valid outcome of mortality. This study is the first to systematically collect evidence only from propensity score analyses, a statistical technique for analyzing nonrandomized trials that finds increasing use in cardiac surgery and that is especially suited for situations with rare outcomes.

Our results have to be compared with the existing knowledge on the topic, especially with previous meta-analyses of randomized[3-5] and nonrandomized trials[5] (Figure 2). It should be noted that there is only a small overlap (n = 7) of our studies and the observational studies included in Wijeysundera and colleagues'[5] review. As such, our results can be considered roughly independent of Wijeysundera and colleagues' results. Compared with the results of randomized trials, our results are not contradictory; our estimates are well within the CIs of estimates from randomized trials. Of course, CIs from RCTs are larger, reflecting smaller

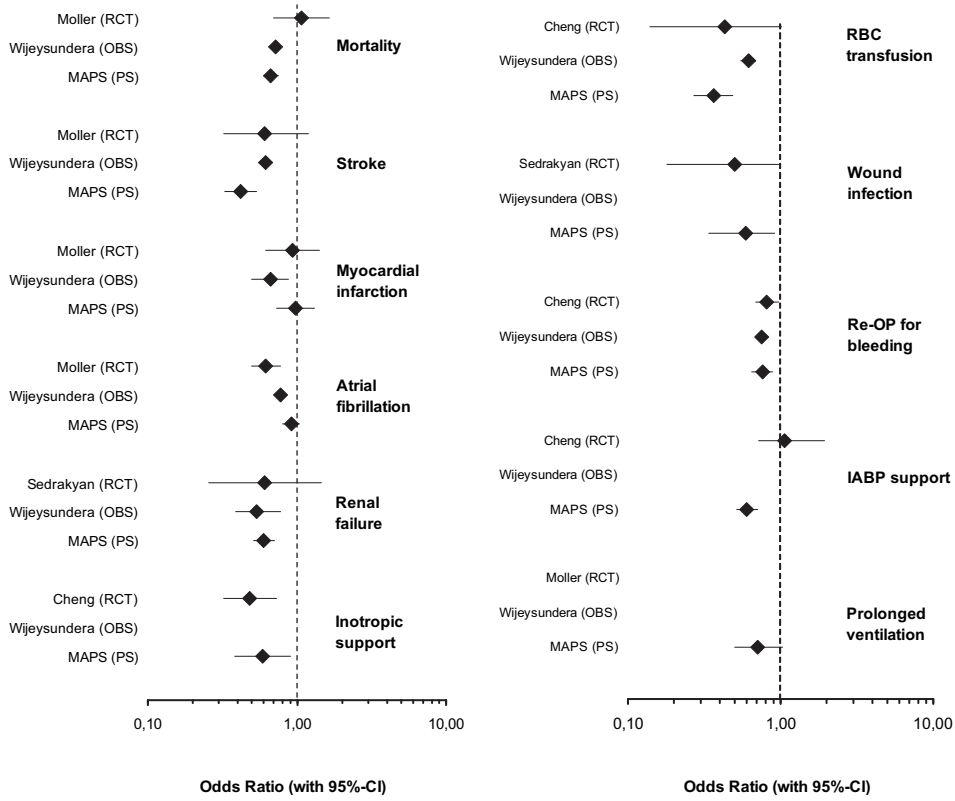

FIGURE 2. Results from previous meta-analyses of RCTs, observational studies, and our propensity-score analyses for all our prespecified outcomes. For the meta-analyses of RCTs, we give the results from the most recent meta-analyses. Results are shown as ORs with 95% CIs. In cases for which the previous meta-analyses reported relative risks, we recalculated the OR by using the formula of Zhang and Yu.[21] *RCT,* Randomized clinical trial; *OBS,* observational study; *PS,* propensity score; *RBC,* red blood cell; *OP,* operation; *IABP,* intraaortic balloon pump; *CI,* confidence interval.

sample sizes. We also expect randomized trials to be performed in selected populations, and certain differences between RCTs and our propensity score analyses are not surprising. Compared with previous nonrandomized trials, there is agreement in most of the outcomes. But we also find a nonoverlapping CI for stroke and only succinct overlapping intervals for atrial fibrillation and RBC transfusion. It should be noted, however, that the large sample sizes in both Wijeysundera and colleagues' review and our study guarantee small CIs, and not all significant differences can be considered clinically relevant.

Our systematic review, which is the first to explicitly include only propensity score analyses, also contributes to the body of methodical knowledge. Only approximately 70% of the studies were found in the standard literature databases. This underlines the importance of a free web search and, especially important for propensity score analyses, citation tracking of classic articles describing the propensity score method. We were not surprised by the results of our meta-regression on the influence of type of propensity score analysis. Although current guidelines favor the use of matching,[22] we found no differences between studies using matching and those using other techniques for adjusting for the propensity score. This was already stressed in the initial propensity score article by Rosenbaum and Rubin.[9] However, and somewhat contrary to common perception, there were no differences in effects from high-risk and low-risk populations.

Any systematic review and meta-analysis is vulnerable to publication bias, that is, the selective reporting of trials depending on study results. Funnel plots were proposed to graphically assess publication bias. We drew funnel plots for all our outcomes. All plots indicated no publication bias (Figure E2). Moreover, because the comparison between off- and on-pump in CABG is such a hotly debated issue,[2] we expect most (or hopefully all) of the studies to be submitted and published, as predicted by Sedrakyan and colleagues.[3]

Study Limitations

Our study has some limitations. We reported only short-term outcomes; data on graft patency or revascularization rates are missing. This is problematic because new evidence suggests that the on-pump technique may result in better graft patency.[23] Graft patency data were omitted because they are rarely reported, and patients frequently are lost to follow-up.

It is tempting to speculate why most of the CABG procedures are still performed on-pump. Off-pump surgery is technically more demanding than the on-pump technique performed under cardioplegic arrest. Only a small number of centers train their staff in the former technique. Therefore, off-pump surgery is part of just a limited number of a surgeon's armamentarium. This contrasts with the experience in other centers, for example, Emory University in Atlanta, where more than 80% of surgical revascularizations are performed off-pump.[24] In countries such as Japan or India, the percentage is greater than 50%.[25] Authors from these countries have demonstrated that an off-pump program can be established without risk and with good patient outcomes. As we show in our article, the evidence remains ambiguous at this time. This is also reflected in the American Heart Association's scientific statement article.[2] Lack of a compelling indication is certainly a significant reason for not abandoning the standard technique in favor of one that is highly challenging.

CONCLUSIONS

Current evidence from nonrandomized trials of any design suggests that off-pump CABG is superior, at least with respect to short-term outcomes. This finding is in line with the collected evidence from the present randomized trials. In the future, large ongoing randomized trials, among them the CORONARY trial from Canada (4700 patients planned, expected end of recruiting phase: May 2014, ClinicalTrials.gov Identifier: NCT00463294) and the ROOBY trial[26] (2200 patients planned, expected end of recruiting phase: November 2008) will contribute to the definite answer. Long-term follow-up of patients from current trials will provide additional evidence.

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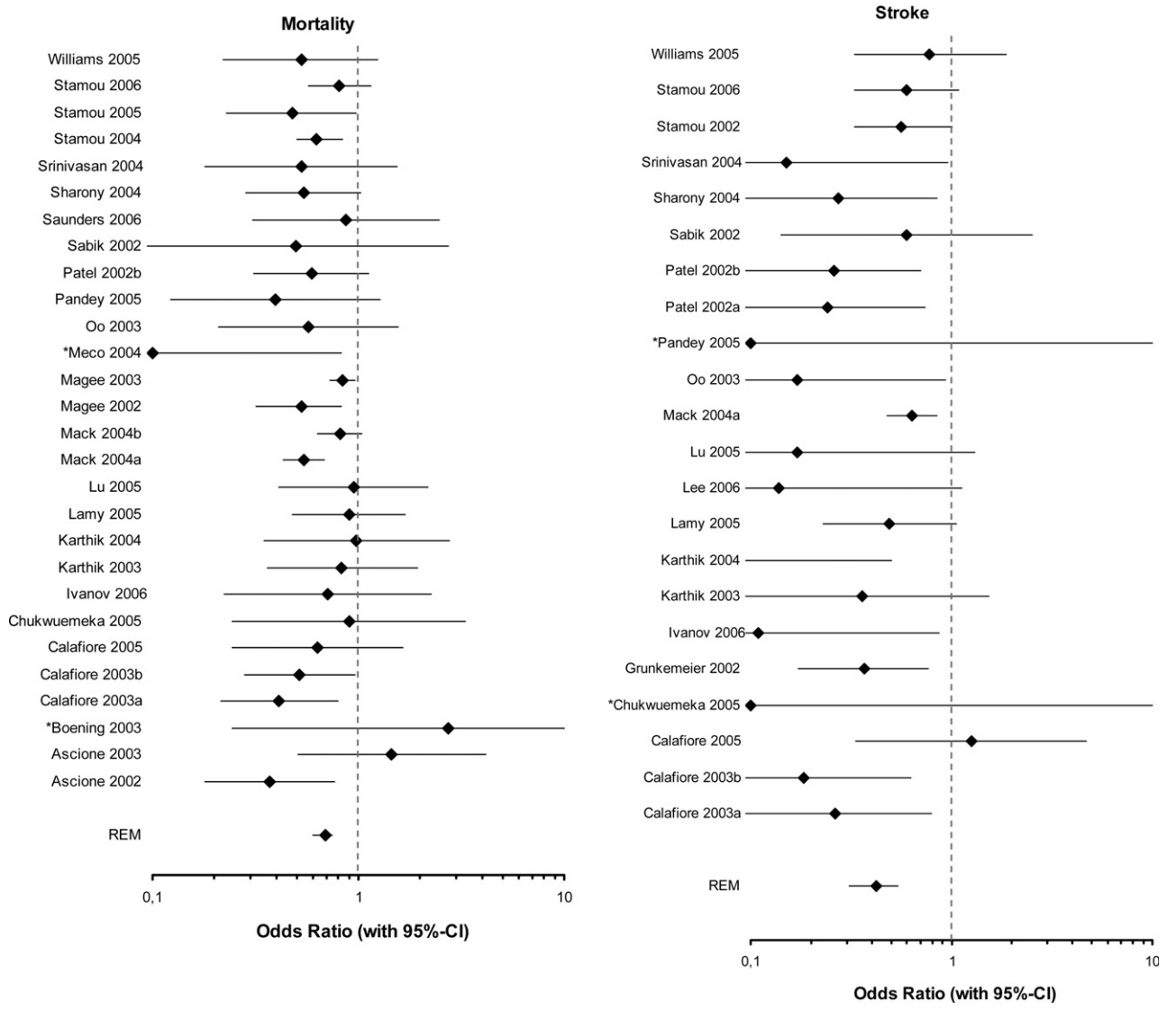


FIGURE E1. Forest plots for all outcomes. To enhance readability, x-axes are only drawn from 0.1 to 10. CIs having values outside this range are marked by an asterisk (*). *CI,* Confidence interval; *RBC,* red blood cell; *IABP,* intraaortic balloon pump.

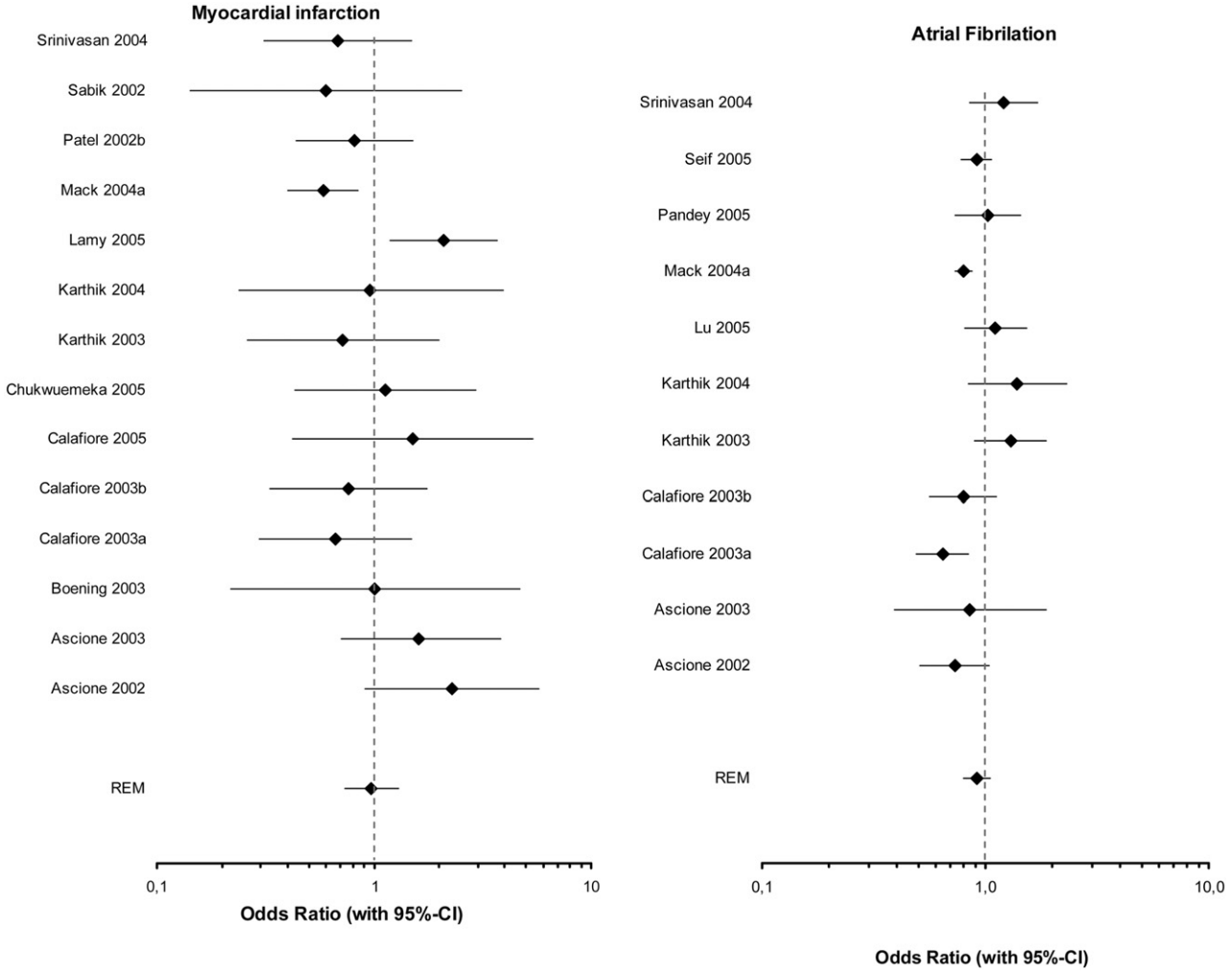


FIGURE E1. Continued

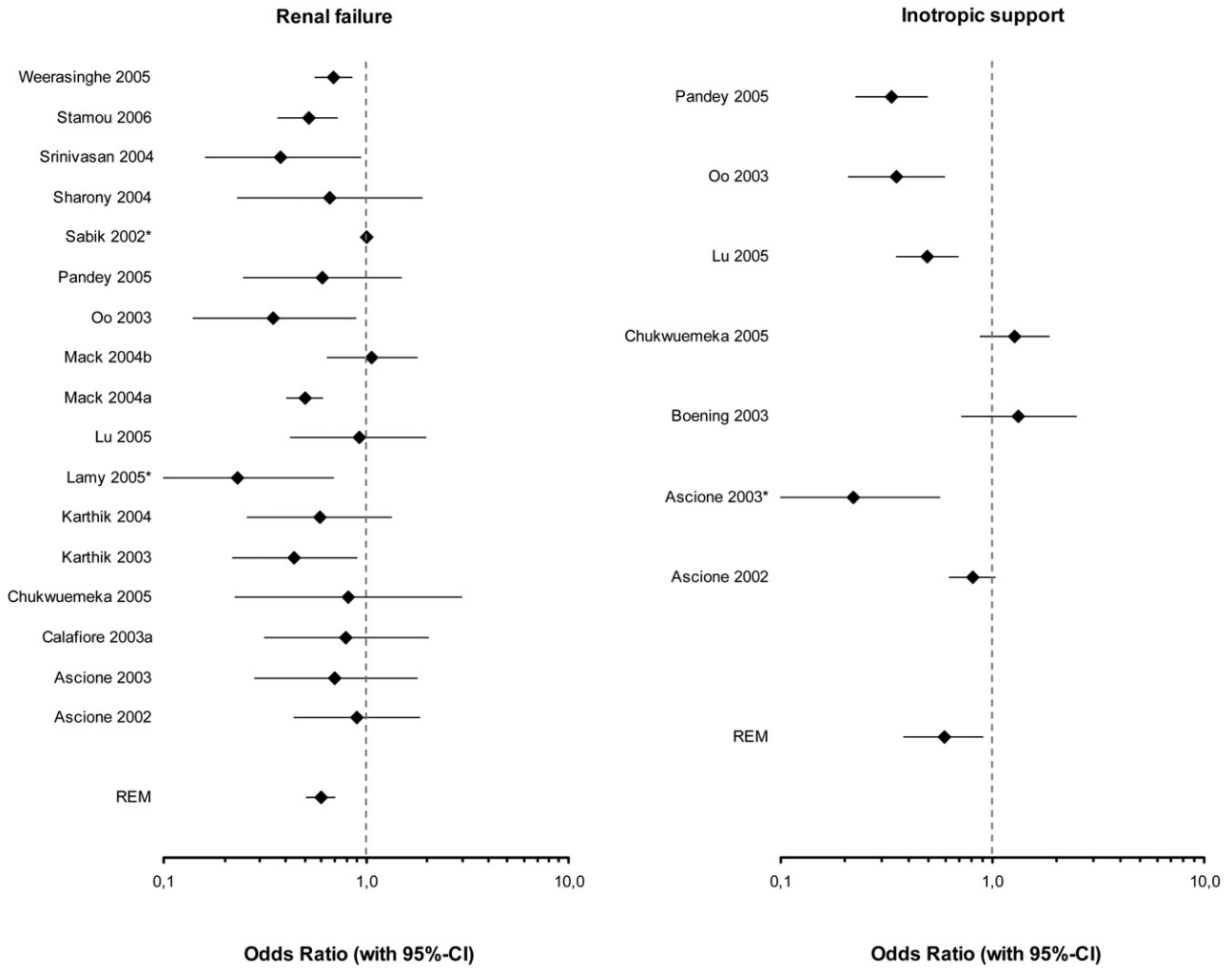


FIGURE E1. Continued

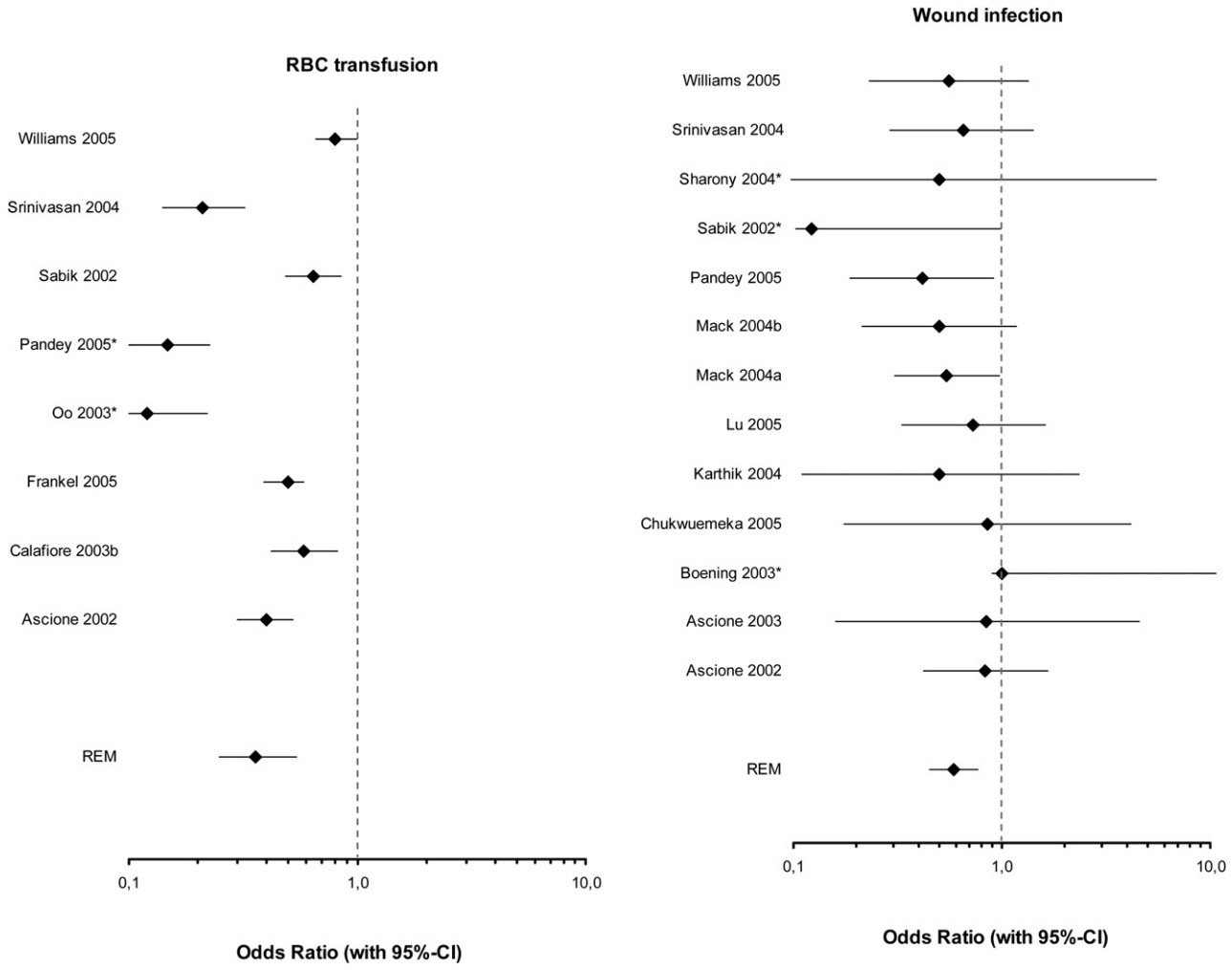
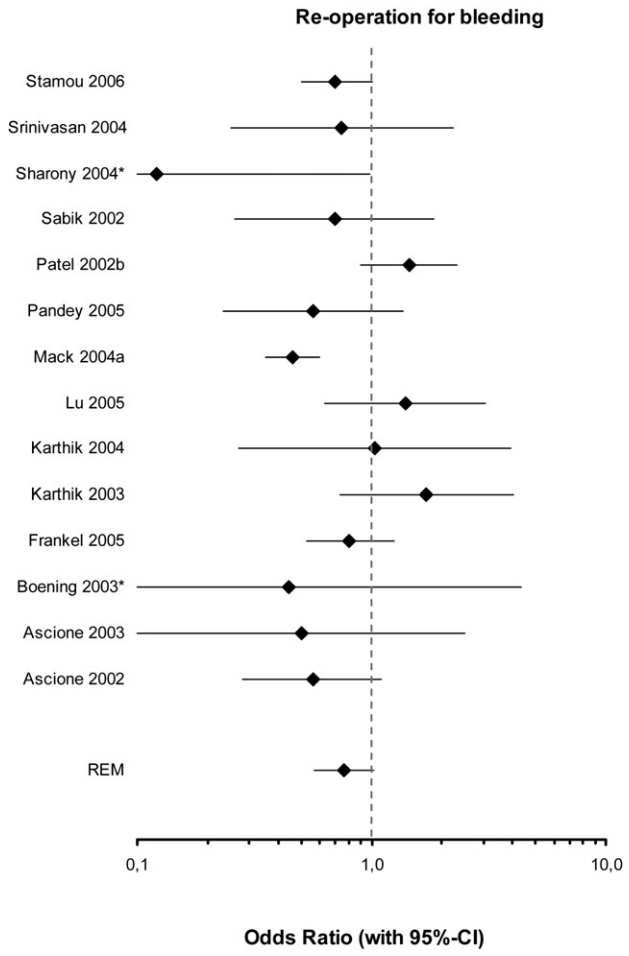


FIGURE E1. Continued



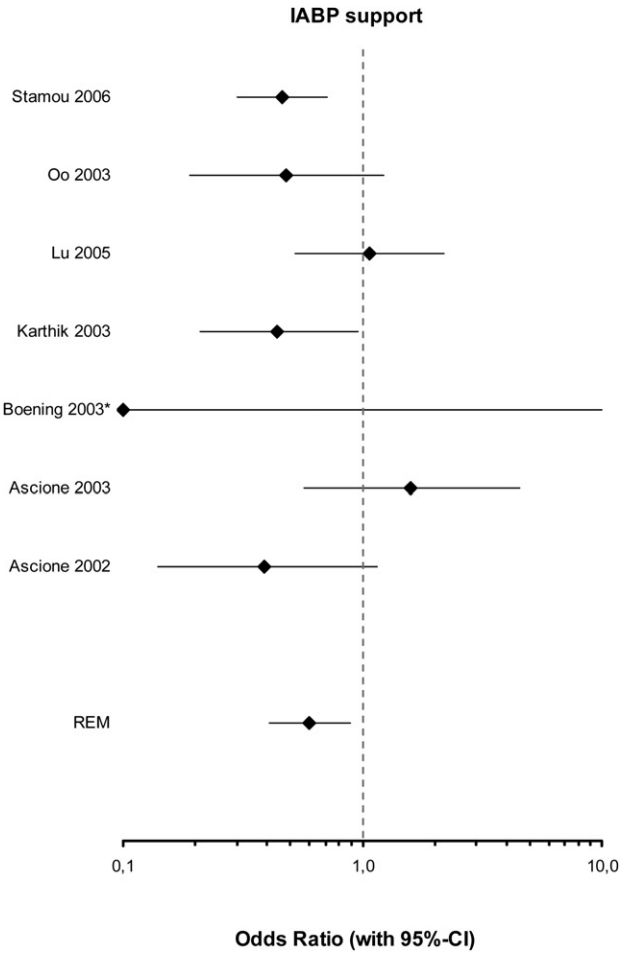


FIGURE E1. Continued

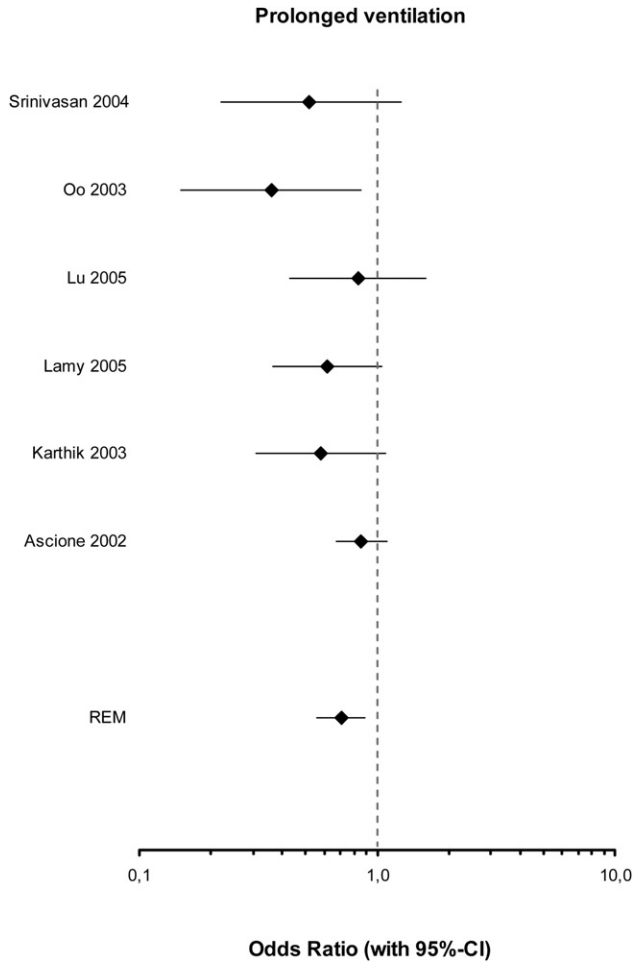


FIGURE E1. Continued

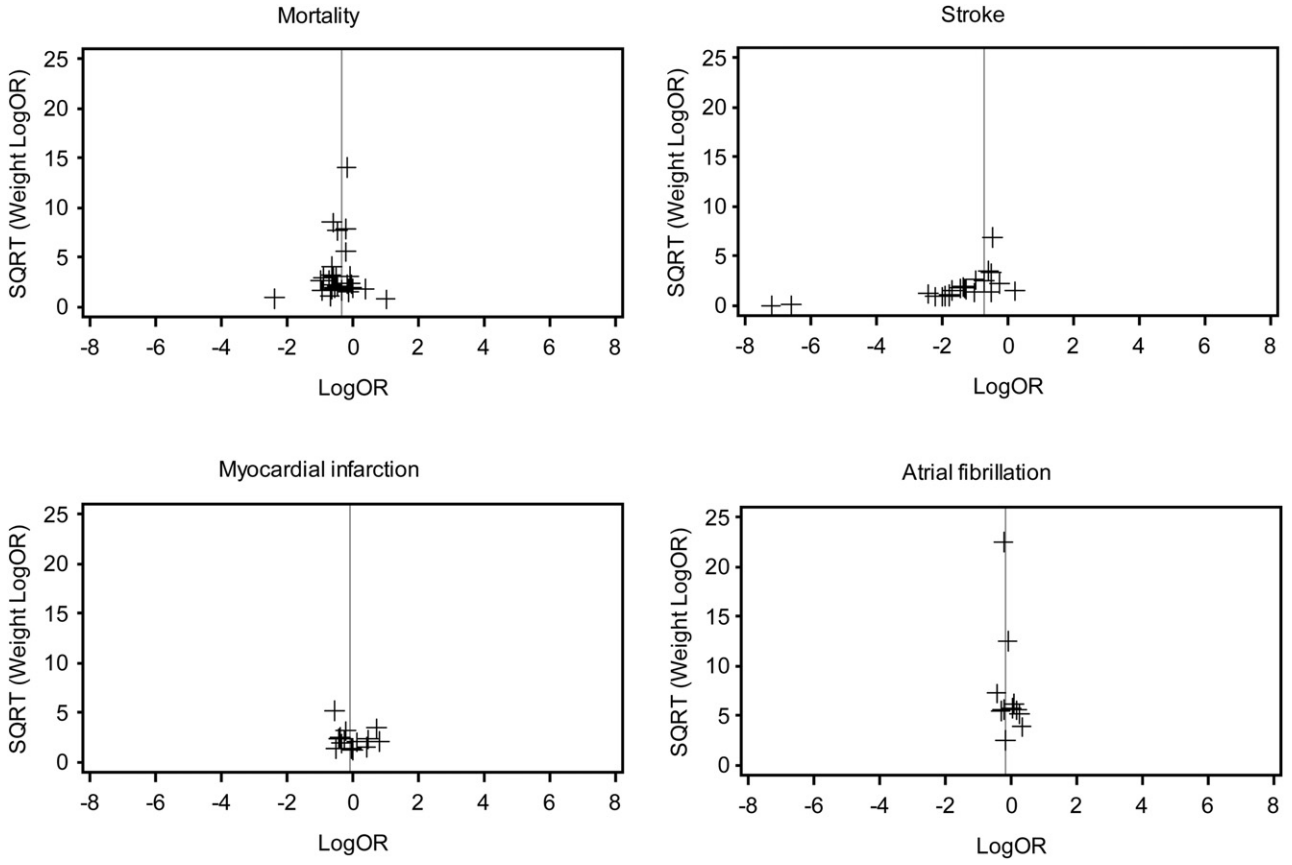


FIGURE E2. Funnel plots for all outcomes. *SQRT*, Square root; *OR,* odds ratio; *IABP,* intraaortic balloon pump.

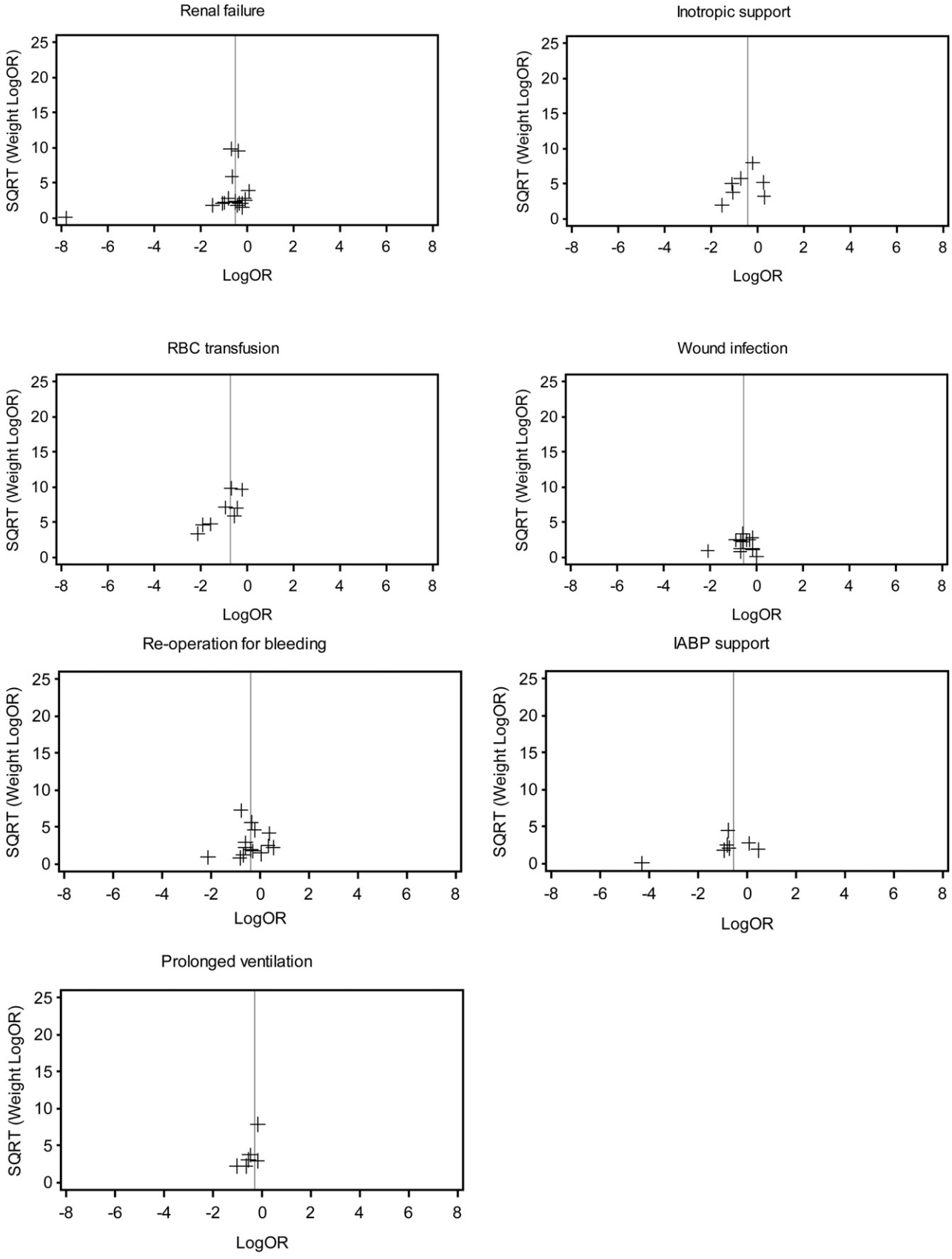


FIGURE E2. Continued

TABLE E1. List of included articles

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Table E1. Continued

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TABLE E2. Results from the single studies

Mortality

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.37 (0.18–0.77)	2.29	1.32
Ascione 2003	1.45 (0.51–4.17)	1.15	0.63
Boening 2003	2.74 (0.24–30.9)	0.23	0.12
Calafiore 2003a	0.41 (0.21–0.79)	2.77	1.63
Calafiore 2003b	0.52 (0.28–0.96)	3.04	1.82
Calafiore 2005	0.63 (0.24–1.64)	1.38	0.77
Chukwuemeka 2005	0.90 (0.24–3.31)	0.76	0.41
Ivanov 2006	0.71 (0.22–2.26)	0.96	0.52
Karthik 2003	0.83 (0.36–1.93)	1.76	0.99
Karthik 2004	0.98 (0.35–2.75)	1.20	0.66
Lamy 2005	0.90 (0.48–1.69)	2.96	1.76
Lu 2005	0.95 (0.41–2.18)	1.77	1.00
Mack 2004a	0.54 (0.43–0.68)	12.35	13.25
Mack 2004b	0.81 (0.63–1.04)	11.39	11.29
Magee 2002	0.53 (0.32–0.83)	4.73	3.07
Magee 2003	0.83 (0.72–0.96)	17.83	35.88
Meco 2004	0.09 (0.01–0.83)	0.28	0.15
Oo 2003	0.57 (0.21–1.56)	1.26	0.69
Pandey 2005	0.39 (0.12–1.27)	0.94	0.51
Patel 2002b	0.59 (0.31–1.12)	2.86	1.69
Sabik 2002	0.50 (0.09–2.73)	0.45	0.24
Saunders 2006	0.87 (0.30–2.47)	1.16	0.64
Sharony 2004	0.54 (0.29–1.03)	2.86	1.70
Srinivasan 2004	0.53 (0.18–1.55)	1.10	0.60
Stamou 2004	0.63 (0.50–0.83)	11.08	10.72
Stamou 2005	0.48 (0.23–0.98)	2.29	1.32
Stamou 2006	0.81 (0.57–1.15)	7.48	5.67
Williams 2005	0.53 (0.22–1.24)	1.66	0.93

Stroke

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Calafiore 2003a	0.26 (0.09–0.80)	4.21	2.68
Calafiore 2003b	0.18 (0.05–0.63)	3.48	2.14
Calafiore 2005	1.25 (0.33–4.69)	3.12	1.89
Chukwuemeka 2005	0.00 (0.00–>100)	0.00	0.00
Grunkemeier 2002	0.37 (0.17–0.77)	7.64	5.86
Ivanov 2006	0.11 (0.01–0.87)	1.37	0.77
Karthik 2003	0.36 (0.08–1.53)	2.56	1.51
Karthik 2004	0.09 (0.02–0.50)	2.19	1.27
Lamy 2005	0.49 (0.23–1.06)	7.43	5.63
Lee 2006	0.14 (0.02–1.13)	1.33	0.74
Lu 2005	0.17 (0.02–1.31)	1.35	0.75
Mack 2004a	0.64 (0.48–0.85)	18.56	40.44
Oo 2003	0.17 (0.03–0.93)	1.94	1.11
Pandey 2005	0.00 (0.00–>100)	0.00	0.00
Patel 2002a	0.24 (0.08–0.74)	4.16	2.64

(Continued)

Table E2. Continued

Stroke

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Patel 2002b	0.26 (0.09–0.70)	4.77	3.12
Sabik 2002	0.60 (0.14–2.51)	2.68	1.59
Sharony 2004	0.27 (0.09–0.84)	4.09	2.59
Srinivasan 2004	0.15 (0.02–0.96)	1.56	0.88
Stamou 2002	0.56 (0.33–1.00)	11.09	10.69
Stamou 2006	0.60 (0.33–1.08)	10.28	9.35
Williams 2005	0.78 (0.33–1.87)	6.19	4.37

Myocardial infarction

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	2.29 (0.91–5.76)	6.59	4.86
Ascione 2003	1.61 (0.71–3.85)	7.38	5.79
Boening 2003	1.01 (0.22–4.66)	3.05	1.77
Calafiore 2003a	0.66 (0.30–1.48)	7.83	6.39
Calafiore 2003b	0.76 (0.33–1.76)	7.51	5.96
Calafiore 2005	1.51 (0.42–5.36) 4.14	2.57	
Chukwuemeka 2005	1.13 (0.43–2.94)	6.27	4.52
Karthik 2003	0.72 (0.26–1.98)	5.79	4.02
Karthik 2004	0.96 (0.24–3.92)	3.55	2.12
Lamy 2005	2.09 (1.18–3.69)	11.18	12.74
Mack 2004a	0.58 (0.40–0.85)	14.80	29.60
Patel 2002b	0.81 (0.44–1.51)	10.42	10.89
Sabik 2002	0.60 (0.14–2.51)	3.38	2.00
Srinivasan 2004	0.68 (0.31–1.48)	8.11	6.78

Atrial fibrillation

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.73 (0.51–1.04)	7.95	3.25
Ascione 2003	0.85 (0.39–1.87)	2.45	0.67
Calafiore 2003a	0.64 (0.49–0.84)	10.61	5.70
Calafiore 2003b	0.79 (0.56–1.12)	8.25	3.47
Karthik 2003	1.30 (0.89–1.88)	7.51	2.95
Karthik 2004	1.39 (0.84–2.30)	5.03	1.63
Lu 2005	1.11 (0.81–1.53)	9.03	4.08
Mack 2004a	0.79 (0.73–0.87)	17.64	54.44
Pandey 2005	1.03 (0.73–1.45)	8.43	3.60
Seif 2005	0.91 (0.78–1.07)	15.05	16.89
Srinivasan 2004	1.21 (0.85–1.72)	8.06	3.32

Renal failure

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.90 (0.44–1.85)	4.20	2.50
Ascione 2003	0.70 (0.28–1.79)	2.64	1.50
Calafiore 2003a	0.80 (0.31–2.03)	2.61	1.48

(Continued)

Table E2. Continued

Renal failure

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Chukwuemeka 2005	0.81 (0.22–2.96)	1.42	0.77
Karthik 2003	0.44 (0.22–0.90)	4.34	2.60
Karthik 2004	0.59 (0.26–1.34)	3.31	1.92
Lamy 2005	0.23 (0.08–0.69)	2.00	1.11
Lu 2005	0.92 (0.42–1.98)	3.66	2.14
Mack 2004a	0.50 (0.41–0.61)	22.42	32.79
Mack 2004b	1.07 (0.64–1.78)	7.48	4.99
Oo 2003	0.35 (0.14–0.89)	2.66	1.51
Pandey 2005	0.61 (0.25–1.48)	2.83	1.62
Sabik 2002	0.00 (0.00–>100)	0.00	0.00
Sharony 2004	0.66 (0.23–1.88)	2.10	1.17
Srinivasan 2004	0.38 (0.16–0.94)	2.88	1.64
Stamou 2006	0.52 (0.37–0.72)	13.57	11.63
Weerasinghe 2005	0.69 (0.56–0.85)	21.87	30.64

Inotropic support

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.81 (0.63–1.03)	16.71	35.80
Ascione 2003	0.22 (0.08–0.56)	9.33	2.29
Boening 2003	1.33 (0.71–2.47)	12.92	5.57
Chukwuemeka 2005	1.27 (0.87–1.85)	15.59	15.35
Lu 2005	0.49 (0.35–0.69)	15.93	18.78
Oo 2003	0.35 (0.21–0.59)	14.11	8.11
Pandey 2005	0.33 (0.23–0.49)	15.42	14.10

RBC transfusion

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.40 (0.30–0.52)	12.98	13.27
Calafiore 2003b	0.59 (0.42–0.81)	12.63	9.26
Frankel 2005	0.50 (0.39–0.58)	13.38	25.49
Oo 2003	0.12 (0.07–0.22)	10.72	3.06
Pandey 2005	0.15 (0.10–0.23)	11.93	5.56
Sabik 2002	0.64 (0.48–0.84)	12.97	13.05
Srinivasan 2004	0.21 (0.14–0.32)	12.02	5.88
Williams 2005	0.80 (0.66–0.99)	13.36	24.42

Wound infection

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.83 (0.42–1.66)	14.96	14.96
Ascione 2003	0.84 (0.16–4.55)	2.52	2.52
Boening 2003	1.00 (0.00–>100)	0.01	0.01

(Continued)

Table E2. Continued

Wound infection

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Chukwuemeka 2005	0.86 (0.18–4.16)	2.82	2.82
Karthik 2004	0.50 (0.11–2.33)	3.03	3.03
Lu 2005	0.73 (0.33–1.61)	11.25	11.25
Mack 2004a	0.54 (0.31–0.97)	21.33	21.33
Mack 2004b	0.50 (0.21–1.17)	9.78	9.78
Pandey 2005	0.41 (0.19–0.92)	11.17	11.17
Sabik 2002	0.12 (0.02–0.99)	1.63	1.63
Sharony 2004	0.50 (0.04–5.53)	1.22	1.22
Srinivasan 2004	0.65 (0.29–1.42)	11.20	11.20
Williams 2005	0.56 (0.23–1.34)	9.10	9.10

Reoperation for bleeding

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.56 (0.28–1.10)	8.50	5.12
Ascione 2003	0.50 (0.10–2.50)	2.66	0.92
Boening 2003	0.44 (0.04–4.33)	1.44	0.46
Frankel 2005	0.80 (0.53–1.24)	12.10	13.26
Karthik 2003	1.72 (0.73–4.04)	6.68	3.27
Karthik 2004	1.03 (0.27–3.95)	3.58	1.33
Lu 2005	1.39 (0.63–3.07)	7.30	3.82
Mack 2004a	0.46 (0.35–0.60)	14.39	32.94
Pandey 2005	0.56 (0.23–1.36)	6.45	3.08
Patel 2002b	1.45 (0.90–2.31)	11.41	10.78
Sabik 2002	0.69 (0.26–1.84)	5.67	2.52
Sharony 2004	0.12 (0.02–0.98)	1.69	0.55
Srinivasan 2004	0.74 (0.25–2.23)	4.85	2.00
Stamou 2006	0.70 (0.50–1.00)	13.29	19.94

IABP support

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.39 (0.14–1.15)	10.73	7.49
Ascione 2003	1.59 (0.57–4.55)	10.96	7.69
Boening 2003	0.01 (0.00–>100)	0.04	0.02
Karthik 2003	0.44 (0.21–0.96)	17.03	14.37
Lu 2005	1.07 (0.52–2.18)	18.33	16.16
Oo 2003	0.48 (0.19–1.23)	12.85	9.52
Stamou 2006	0.46 (0.30–0.71)	30.06	44.74

Prolonged ventilation

Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Ascione 2002	0.86 (0.67–1.10)	47.62	59.46
Karthik 2003	0.58 (0.31–1.08)	12.10	9.38
Lamy 2005	0.61 (0.36–1.04)	16.24	13.18
Lu 2005	0.83 (0.43–1.61)	10.94	8.39

(Continued)

Table E2. Continued

Prolonged ventilation			
Study	OR (95% CI)	Relative weight (%), RE	Relative weight (%), FE
Oo 2003	0.36 (0.15–0.86)	6.54	4.79
Srinivasan 2004	0.52 (0.22–1.26)	6.55	4.80

OR, Odds ratio; *CI,* confidence interval; *RE,* random effect; *FE,* fixed effect; *RBC,* red blood cell; *IABP,* intraaortic balloon pump. Given are the odds ratios (with 95% CI) and the relative weights (in %) with which the respective studies were weighted in the overall random effect or fixed effect estimator.