Original Article

Beating-heart on-pump coronary artery bypass grafting *vs.* off-pump coronary artery bypass grafting: a systematic review and meta-analysis

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Background: Beating-heart on-pump coronary artery bypass grafting (CABG), otherwise known as BH-ONCAB, can reduce myocardial injury by preserving native coronary blood flow while maintaining hemodynamic stability by the effective support of cardiopulmonary bypass (CPB). This study aimed to identify whether BH-ONCAB confers a survival, mortality, or morbidity benefit over off-pump CABG (OPCAB).

Methods: A systematic literature review identified 18 studies incorporating 5,615 patients (1,548 BH-ONCAB and 4,067 OPCAB cases) who satisfied the inclusion criteria. Outcome measures were meta-analyzed using random-effects modeling. Between-study heterogeneity was investigated through quality assessment and risk of bias analysis.

Results: The results demonstrated comparable early mortality and long-term survival between BH-ONCAB and OPCAB coronary revascularization with no significant statistical differences. The incidences of stroke, renal failure, blood loss, and arrhythmias were significantly higher in patients who underwent BH-ONCAB than patients who underwent OPCAB. However, BH-ONCAB conferred lower rates of incomplete revascularization and greater numbers of distal anastomoses.

Conclusions: BH-ONCAB is a safe and comparable alternative to OPCAB in terms of early mortality and late survival. BH-ONCAB may confer particular advantages in preventing incomplete revascularization and allowing more distal anastomoses compared to OPCAB. However, BH-ONCAB was associated with more postoperative complications due to the use of CPB. Future work should focus on larger matched studies and multicenter randomized controlled trials to optimize our surgical revascularization strategies.

Keywords: Coronary artery bypass grafting (CABG); on-pump; off-pump; beating-heart; meta-analysis

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Introduction

Coronary artery disease is a common condition that seriously endangers human health. In recent years, there has been an increasing application of percutaneous myocardial revascularization in managing this disease. To date, conventional on-pump coronary artery bypass

grafting (C-ONCAB) remains the gold standard for surgical coronary artery revascularization (1). However, this established technique is often associated with adverse effects such as systemic inflammation, neurological dysfunction, renal dysfunction, and other postoperative complications (2). The application of cardiopulmonary bypass (CBP) and cardioplegic arrest is significant triggers for these adverse perioperative events. Off-pump CABG (OPCAB) is an alternative technology that avoids the use of CPB, aortic cross-clamping, and cardioplegic arrest, and may reduce the incidences of adverse events, especially in high-risk and elderly patients. However, other adverse events have been associated with OPCAB. According to the Randomized On/Off Bypass (ROOBY) trial, OPCAB was associated with a higher rate of incomplete revascularization and an inferior long-term outcome (3).

In the mid-1990s, beating-heart on-pump CABG (BH-ONCAB) was firstly introduced for clinical application. This technique combines the advantages of OPCAB and conventional CABG. Theoretically, BH-ONCAB would cause less myocardial injury by preserving native coronary blood flow while maintaining hemodynamic stability with effective support from CPB (4). It may also provide higher perfusion pressure and avoid aortic cross-clamping, which may lead to less stroke, renal dysfunction, and perioperative myocardial ischemia, all of which are particularly beneficial for high-risk group patients (5).

There have been abundant studies comparing OPCAB and C-ONCAB, but there is a paucity of data on BH-ONCAB. This meta-analysis assessed the clinic outcomes of BH-ONCAB compared with OPCAB in the short- and long-term postoperative period.

We present the following article in accordance with the PRISMA reporting checklist (available at https://dx.doi.org/10.21037/jtd-21-268).

Methods

Literature search

A literature search was performed in the Cochrane Central, MEDLINE (PubMed), Web of Science, EMBASE (OVID Interface), and CNKI databases using the key terms, "cardiopulmonary bypass", "coronary artery bypass", "beating heart", and "off the pump", either alone or in combination. Studies published with an abstract between 1990 and 1st August 2020 were considered. There were no limitations on the language of publication. A summary of the literature selection strategy is described in *Figure 1*.

Selection criteria

The inclusion criteria were as follows: (I) direct comparison of BH-ONCAB *vs.* conventional OPCAB; and (II) the study provided at least one of the following major clinical outcomes: early mortality, long-term survival, myocardial infarction, low output symptoms, the incidence of incomplete revascularization, and renal dysfunction.

The exclusion criteria were as follows: (I) use of concomitant interventions; (II) use of miniaturized CPB or other modifications of OPCAB *vs.* BH-ONCAB; (III) data inconsistencies prohibiting valid data extraction; and (IV) studies that contained duplicate data, in which case the more credible and recently published data set was selected.

Literature with a Newcastle Ottawa Scale (NOS) score of 6 or higher were regarded as high-quality studies. Two reviewers used the selection criteria to assess all eligible articles based on title, and abstract review, followed by a full-text article review, and the final selection was determined. Any disagreements were resolved by discussion and/or arbitration with a senior author.

Data collection

The investigators independently extracted data from each study using a standardized spreadsheet based on publication year, first author, place of study, study design, period of patient enrollment, number of participants treated with OPCAB and BH-ONCAB, study population, inclusion/exclusion criteria, and outcome measures.

Study variables

The primary outcome measure was the early mortality rate in hospitals and the long-term survival rate after surgery. The secondary outcomes were major postoperative complications, including myocardial infarction, low output syndrome, stroke, dialysis, arrhythmias, intra-aortic balloon pump (IABP) use, inotrope use, incomplete revascularization and renal dysfunction.

Quality scoring

Two reviewers used the Jadad composite scale to assess the quality of the randomized controlled trial (RCTs) (6), and

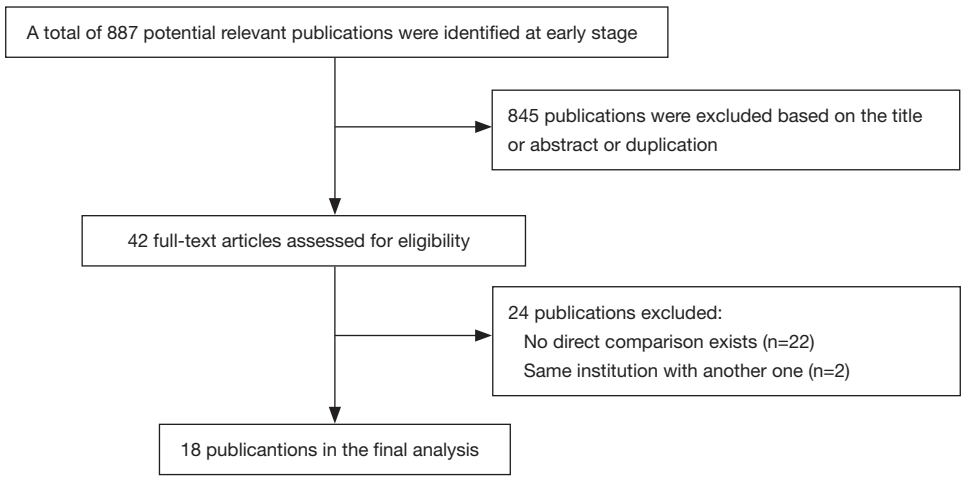

Figure 1 Search strategy.

the modified Newcastle-Ottawa Quality Assessment Scale Score (NOS) was used to assess the quality of observational studies (7). Studies with a Jadad score of no less than 2 (maximum score 5) or a modified NOS score of no less than 5 (maximum score 9) were considered high-quality studies.

Risk of bias analysis

According to the Cochrane guidelines, the risk of bias was evaluated (Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0). Two authors reviewed all the studies, marking "yes", "no", or "unclear" to the following parts: (I) allocation concealment (selection bias); (II) random sequence generation (selection bias); (III) blinding of outcome assessment (detection bias); (IV) blinding of participants and personnel (performance bias); (V) selective reporting (reporting bias); (VI) incomplete outcomes data (attrition bias); and (VII) other bias.

Statistical analysis

This meta-analysis used a weighted fixed effects model to analyze the data. For primary outcomes, the odds ratio (OR) and the logarithm of the hazard ratio (HR) with 95% confidence intervals (CIs) were used to calculate survival differences. For secondary outcomes, categorical variables were assessed by the OR, and an OR of less than 1 would favor the treatment group. The point estimate of the OR would be considered statistically significant if the P value was less than 0.05 and the 95% CI did not equal the value of 1. Continuous data were analyzed by the weighted mean difference (WMD) as the summary statistic with the 95% CI, and the point estimate of the WMD was considered statistically significant if p was less than 0.05 and the 95% CI interval did not equal to the value 0. The Q-statistic and I^2 (index of inconsistency) tests were used to quantify the degree of heterogeneity in all studies. If statistically significant heterogeneity ($P<0.1$ or $I^2>50\%$) was detected in the included studies, random effects models were used for pooled analysis, and sensitivity analyses were performed to identify the source of heterogeneity. Sensitivity analyses were performed by omitting each study in sequence. Publication bias was assessed by visual inspection of funnel plots. Data were analyzed with the RevMan 5.3 software (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark).

Results

Literature search

A total of 22 articles were identified in the initial search, and 4 were excluded based on the selection criteria, including 2 articles with duplicate data and 2 studies that focused on mini-CPB with little comparative data. Finally, a total of 18 single-center studies (8-25) were enrolled in this meta-analysis, including a total of 5,615 patients, of which 1,548 had undergone BH-ONCAB, and 4,067 were treated with OPCAB. There were 5 RCTs (9,10,12,14,22), and 13 retrospective observational studies (8,11,13,15-21,23-25). A summary of the basic characteristics of the 18 included

studies is presented in *Table 1*.

Early mortality

Early mortality was defined as death occurring within 30 days after surgery or in-hospital death at any time. 17 of all 18 studies (8-25) provided information on early mortality (*Table 2*, *Figure 2*). Analysis of 18 included studies demonstrated that there were no differences in the overall early mortality between BH-ONCAB and OPCAB patients (OR 1.28; 95% CI: 0.91 to 1.80; Z=1.40, P=0.16), and there was no significant heterogeneity (I^2=0; *Figure 2A*).

Long-term survival

Data for long-term survival were available for 5 studies (15,18,21,23,24), and no significant differences were found in overall survival between the two groups (HR 0.86; 95% CI: 0.51 to 1.45; Z=0.57, P=0.57). There was no significant heterogeneity (I^2=0; *Figure 2B*; *Table 2*).

Secondary outcomes

A synopsis of the secondary endpoints is shown in *Table 2* and *Figure 2*.

A total of 12 studies (8,11,13,15-19,21,23-25) were included in the analysis of postoperative stroke. The summary OR suggested that patients treated with BH-ONCAB had a higher incidence of postoperative stroke (OR 1.67; 95% CI: 1.08 to 2.58; Z=2.32, P=0.02), with no significant heterogeneity (I^2=0; *Figure 2B*).

Data for postoperative renal failure was available for 9 studies (8,11,13,15-17,21,23,25). However, there was significant heterogeneity among the studies (I^2 = 42%, P=0.09). Heterogeneity (I^2=6%; P=0.38) was acceptable after removing the study by Edgerton *et al.* (15), and exclusion of this study did not influence the overall results.

Data from 13 studies were used for analysis of postoperative arrhythmias (8,10,12-15,17-19,21,23-25). The heterogeneity (I^2=45%, P=0.04) is significant and the removal of the study by Velioglu *et al.* (25) makes the heterogeneity acceptable (I^2=0%, P=0.48). The total OR suggested that OPCAB patients were less likely to have arrythmias compared to BH-ONCAB patients (OR 1.30; 95% CI: 1.06 to 1.60; Z=2.47, P=0.01).

The total OR for the incidence of incomplete revascularization (8,10,11,13,21,22,24,25) suggested that BH-ONCAB patients were less likely to experience incomplete revascularization compared to OPCAB patients (OR, 0.67; 95% CI: 0.49 to 0.92; Z=2.49, P=0.01), with no significant heterogeneity (I^2=0, P=0.53).

Analysis of 8 studies (8,13,14,16,20,21,24,25)revealed that BH-ONCAB patients experienced more blood loss compared to OPCAB patients (8,13,14,16,20,21,24,25) (MD 111.56; 95% CI: 42.94 to 180.18; Z=3.19, P=0.001).

Fourteen studies (8-15,17,20,21,23-25) provided details related to distal anastomoses and showed that OPCAB patients had significantly less distal anastomoses compared to BH-ONCAB patients (MD 0.45; 95% CI: 0.29 to 0.61; Z=5.51; P<0.00001; studies (8-15,17,20,21,23-25).

No differences were observed for the other postoperative events including myocardial infarction (8,10,12,13,15-19,21,23) (OR 1.23, 95% CI: 0.76 to 1.97; Z=0.85, P=0.40), dialysis (11,13,15,23,25) (OR 1.53; 95% CI: 0.83 to 2.80; Z=1.37, P=0.17), low output syndrome (13,16,17,23-25) (OR 0.81; 95% CI: 0.51 to 1.28; Z=0.91, P=0.36), IABP use (8,11-13,15,16,21-25) (OR 1.32; 95% CI: 0.92 to 1.88; Z=1.51, P=0.13; removal of the study by Edgerton *et al.* (15) due to the higher heterogeneity), and inotropic use (8,13,19,21,25) (OR 0.97; 95% CI: 0.67 to 1.39; Z=0.19, P=0.85, removal of the study by Darwazah *et al.* (8) due to the higher heterogeneity).

Discussion

This meta-analysis compared the clinical outcomes between BH-ONCAB and OPCAB in patients undergoing coronary artery bypass surgery. The results demonstrated comparable early mortality and long-term survival between BH-ONCAB and OPCAB coronary revascularization with no significant statistical differences. No heterogeneity was observed when analyzing the early mortality and long-term survival. Furthermore, advantages observed in BH-ONCAB patients included lower incidences of incomplete revascularization and greater numbers of distal anastomoses. However, BH-ONCAB patients experienced an increased risk of stroke, renal failure, arrhythmia, and drainage.

To date, conventional ON-CABG is still the gold standard for surgical coronary artery revascularization. However, it has been associated with severe postoperative complications due to the use of cardiac, pulmonary bypass. In the 1990s, OPCAB was developed to be used without cardioplegia, aortic cross-clamping, or hypothermia to avoid adverse events such as systematic inflammation and renal failure (26). Previous studies have demonstrated that

Table 1 Study design and patients characteristics

Study	Country	Study period	Total patients	Study design	Number of patients		Age, years		Male, %		Mean LVEF%		BMI, kg/m^2	
					BH-ONCAB	OPCAB	BH-ONCAB	OPCAB	BH-ONCAB	OPCAB	BH-ONCAB	OPCAB	BH-ONCAB	OPCAB
Ahmad K. Darwazah 2010	Israel	1999–2009	137	RO	39	98	58±8	57±10	82.05	85.71	28 ± 6	26 ± 5	27.6±4.5	28.2±4.5
Anjum Jalal 2007	Kingdom of Saudi Arabia	2003.2–2004.4	45	RCT	15	15	63.13±10.16	54.6±11.06	53.33	6.67	40±8.63	45±8.01	–	–
Ardawan Julian Rastan 2005	Germany	–	40	RCT	21	19	65.3±3.9	63.0±6.0	80.00	0.00	63±14.2	66.1±6.7	29.9±3.2	27.4±2.5
Chien-Chao Lin 2010	China Taiwan	2006.8–2008.2	319	RO	132	88	64±11	64±8	75.00	78.41	54±17	57±16	–	–
Chih-Yuan Lin 2010	China Taiwan	2007.1–2008.12	37	RCT	13	12	63.38±4.94	62.58±6.49	61.54	58.33	50.46±7.94	54.67±5.79	27.49±2.65	27.70±2.25
Emmanuel Munos 2011	France	2008.1–2010.1	214	RO	51	57	72.9±7.8	73.7±9.9	68.63	68.42	35±11.6	33.56±10.1	>30, 16 patients	>30, 19 patients
Innes Y. P. Wan 2004	China Hong Kong	–	37	RCT	19	18	65.37±9.08	63.61±10.47	57.89	83.33	50.42±12.04	52.93±13.58	–	–
James R. Edgerton 2003	USA	2000.1–2002.12	4,604	RO	364	1908	63.4±10.3	64±11.3	74.73	69.34	45.6±12.5	51±13.1	–	–
Jinqiang Shen 2018	China	2010.1–2014.12	216	RO	88	128	66±7.9	65.2±8.2	79.55	78.91	31±2.8	31±2.9	–	–
Ki-Bong Kim 2001	Korea	1998.1–1999.7	206	RO	19	122	59±6	61±6	63.16	71.31	47±16	55±13	–	–
Matthew sKanCKe 2018	USA	2004.1–2015.3	756	RO	60	696	65.467±1.218	65.629±0.353	98.33	98.42	–	–	30.376±0.651	29.773±0.233
Miguel Sousa Uva 2003	Portugal	2001.1–2001.7	221	RO	47	108	66.2±9.7	65±9.3	76.60	69.44	–	–	27±3.1	27.5±4.2
Mostafa A. Sabban 2007	Kingdom of Saudi Arabia	2005.1–2006.1	127	RO	33	21	63.8±10.3	55.9±12.7	–	–	40.1±11.2	45.8±10.9	29.9±4.9	29.5±6.9
OrcunGurbuz 2016	Turkey	2003.1–2009.10	398	RO	181	217	61.17±9.02	60.16±8.8	81.22	82.49	–	–	>30, 53patients	>30, 48 patients
Tomohiro Mizuno 2016	Japan	2006.9–2012.3	74	RCT	37	37	69.2±9.6	73.7±8.2	72.97	89.19	–	–	–	–
Weitie Wang 2019	China	2013.1–2017.12	112	RO	44	68	60.48±9.44	61.22±9.59	70.45	70.59	34.92±4.49	–	>30, 25 patients	>30, 40 patients
Yi-Ting Tsai 2012	China Taiwan	2002.1–2010.1	186	RO	48	56	62.7±11.9	68.3±12	64.58	64.29	40.9±12.6	55.2±12.6	25.4±3.0	24.9±3.6
Yusuf Velioglu 2019	Turkey	2011.1–2018.1	736	RO	337	399	63.81±9.56	63.3±9.85	52.23	46.37	51.3±8.99	52.1±9.87	27.7±3.89 (>30.69)	27.5±4.01 (>30.70)

BH-ONCAB, beating-heart on-pump coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting; LVEF, left ventricular ejection fraction.

Table 2 Results of meta-analysis for clinical outcomes

Outcome	Study numbers	BH-ONCAB		OPCAB		Overall effect		Heterogeneity			
		Total	Events	Total	Events	WMD/OR/HR	95% CI	P	λ	P	I^2(%)
Primary outcomes											
Early mortality	15	1,501	55	4,022	104	1.21	0.91–1.80	0.16	9.93	0.77	0
Long-term survival	5	–	–	–	–	0.86	0.51–1.45	0.57	3.60	0.46	0
Secondary outcomes											
MI	11	1046	35	3509	51	1.23	0.76–1.97	0.40	3.71	0.96	0
Stroke	12	1410	43	3945	51	1.67	1.68–2.58	0.02	2.62	0.99	0
Renal failure	9	1255	88	3085	85	2.68	1.94–3.70	<0.00001	13.85	0.09	42
Dialysis	5	928	28	2520	31	1.53	0.83–2.80	0.17	4.23	0.38	5
Low output syndrome	6	587	32	830	53	0.81	0.51–1.28	0.36	4.47	0.48	0
Arrhythmias	12	906	173	3379	443	1.30	1.06–1.60	0.01	10.58	0.48	0
IABP use	10	970	82	1160	76	1.32	0.92–1.88	0.13	14.36	0.11	37
Inotrope use	4	616	60	781	79	0.97	0.67–1.39	0.85	2.61	0.46	0
Incomplete revascularization	8	846	82	971	152	0.67	0.49–0.92	0.01	7.19	0.41	3
Drainage	7	796	–	994	–	111.56	42.94–180.18	0.001	3.19	<0.00001	83
distal anastomoses	14	1316	–	3098	–	0.45	0.29–0.61	<0.00001	80.34	<0.00001	84

BH-ONCAB, beating-heart on-pump coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting; LVEF, left ventricular ejection fraction.

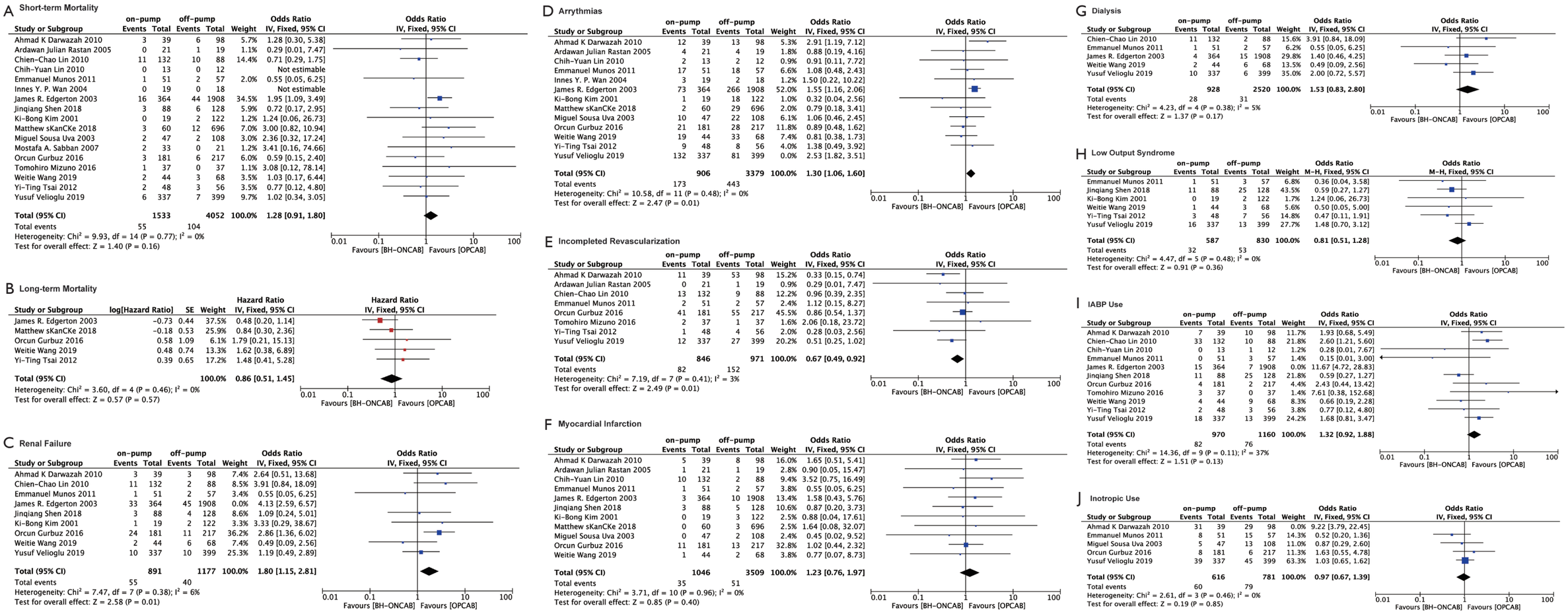

Figure 2 Meta-analysis for clinical outcomes between BH-ONCAB and OPCAB. (A) Short-term mortality; (B) long-term mortality; (C) renal failure; (D) arrythmias; (E) incomplete revascularization; (F) myocardial infarction; (G) dialysis; (H) low output syndrome; (I) IABP use; (J) inotropic use. BH-ONCAB, beating-heart on-pump coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting; IABP, intra aortic ballon pump.

compared with conventional CABG, OPCAB showed decreased morbidity and mortality and is favorable for severe coronary disease patients, especially for those with contraindications for CPB (27,28). However, despite those advantages, OPCAB still has inherent defects compared with conventional CABG, such as incomplete revascularization and inferior long-term graft patency (3). In addition, one of the most severe problems is that OPCAB sometimes requires emergent conversion to conventional CABG in certain high-risk patients with unstable hemodynamics, which might lead to high morbidity and mortality (29). Thus, BH-ONCAB has been developed to overcome these issues. BH-ONCAB allows coronary artery flow during surgery, thereby eliminating the cross-clamping of the aorta and reducing the time of CBP. It is safe and suitable for the most unwell and unstable patients (15). This current analysis demonstrated that early mortality and long-term survival of BH-ONCAB patients was similar to that of OPCAB patients, which suggested that short-term cardiopulmonary bypass without avoiding cardiac arrest and aortic clamping did not increase the mortality of BH-ONCAB patients.

Although the CPB time for cardiac manipulation is limited in BH-ONCAB, the CPB support itself still led to some complications. This might account for the higher rate of certain postoperative complications in BH-ONCAB patients, such as renal failure, stroke, arrhythmia, and increased drainage or blood loss compared to OPCAB patients. Thus, non-CPB techniques may be better suited to patients at high risk for those complications instead of BH-ONCAB, which may aggravate the condition. However, patients with cardiac dysfunction usually cannot tolerate prolonged intraoperative maneuvers and position shifts with non-CPB-support heart beating. The support of CPB could provide a better surgical visual field and allow the surgeon to operate more efficiently in BH-ONCAB surgery. This may explain the improved revascularization and greater number of distal anastomoses in BH-ONCAB patients. In conclusion, the BH-ONCAB technique may provide more efficient hemodynamic support than OPCAB while reducing the side effects of conventional CABG with shortened CPB time.

The risk of myocardial infarction in BH-ONCAB patients was similar to that of OPCAB patients. The reasons for this remain unclear but may be affected by multiple factors, such as myocardial ischemia caused by CPB and improved revascularization. Future investigations with a larger cohort are required to understand further the mechanisms involved.

There were several limitations in this research. This meta-analysis compared BH-ONCAB with OPCAB, including 18 studies and 5,615 patients. Only 5 of these 18 studies were RCTs. The other 13 studies were small observational studies, and it may have been difficult to accumulate data prospectively, and there may be a high level of selection bias. Furthermore, some outcomes had a small number of events, leading to a higher risk of Type I error. Finally, the period of the included studies was 19 years, and the results may not reflect the improvements in surgical techniques over that period.

Conclusions

In conclusion, BH-ONCAB and OPCAB were comparable in terms of early mortality and long-term survival. However, each technique had its pros and cons regarding the risk of secondary outcomes. BH-ONCAB was associated with fewer incidences of incomplete revascularization and more distal anastomoses, while OPCAB was associated with a lower risk of stroke, renal failure, arrhythmia, and drainage. There were no statistically significant differences in the incidences of myocardial infarction and low output syndrome. Future work should focus on larger matched studies and multicenter randomized controlled trials, and this will allow us to further optimize our surgical revascularization strategies in these patients.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/jtd-21-268). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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