Revascularization among patients with severe left ventricular dysfunction: a meta-analysis of observational studies

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Aims

Coronary artery bypass graft (CABG) surgery is the standard of care for the management of patients with severe three-vessel and left main coronary artery disease (CAD). However, the optimal strategy for management of patients with CAD and severe left ventricular (LV) dysfunction [ejection fraction (EF) $\leq 35\%$] is not clear. A meta-analysis of observational studies was performed to determine the operative mortality and long-term (5-year actuarial survival) outcomes among patients with severe LV dysfunction undergoing CABG.

Methods and results

A systematic computerized literature search was performed and observational studies consisting of patients undergoing isolated CABG for CAD and severe LV dysfunction were included. Studies that did not report operative mortality, long-term (≥ 1 year) survival data, or pre-operative EF and multiple studies from the same group were excluded. In total, 4119 patients from 26 observational clinical studies were included. The estimated mean age was 63.9 years and 82.4% of patients were men. The mean (estimate) pre-operative EF was 24.7% (95% CI 22.5–27.0%). The operative mortality among patients (26 studies, $n = 3621$) who underwent on-pump CABG was 5.4%, $n = 189$ (95% CI 4.5–6.4%). The 5-year actuarial survival among patients (13 studies, $n = 1980$) who underwent on-pump CABG was 73.4%, $n = 1483$ (95% CI 68.7–77.7%). Patients who underwent off-pump CABG (7 studies, $n = 498$) tended to have reduced operative mortality of 4.4%, $n = 20$ (95% CI 2.8–6.4%). The mean (estimate) post-operative EF was 35.19% (95% CI 31.95–38.43%).

Conclusion

The present meta-analysis demonstrates that based on data from available observational clinical studies, CABG can be performed with acceptable operative mortality and 5-year actuarial survival in patients with severe LV dysfunction.

Keywords

Coronary artery bypass surgery • Revascularization • Coronary artery disease • Meta-analysis • Observational studies

Introduction

Coronary artery bypass graft (CABG) surgery is the standard of care for the management of patients with severe three-vessel and left main stem coronary artery disease (CAD), based on reduced rates of major cardiovascular and cerebrovascular events at 1 year.¹ Although there has been a significant reduction in mortality following acute myocardial infarction (MI), there has also been an increase in the incidence of heart failure. Coronary artery disease has become the single most important cause of heart failure among Western populations. Among patients with

heart failure and severe left ventricular (LV) dysfunction, the risk of sudden death, ventricular arrhythmias, and worsening heart failure due to recurrent ischaemia is increased.

Recently, the STICH trial (Surgical Treatment for Ischemic Heart Failure) demonstrated that surgical LV reconstruction among patients undergoing CABG in the setting of severe LV dysfunction [ejection fraction (EF) $\leq 35\%$] was not associated with reduction in death from any cause or hospitalization due to cardiac causes at 2 years compared with CABG alone. Although disadvantaged by limitations such as small sample size in single centres, several observational studies have demonstrated reduced operative

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Table I Observational studies included in the meta-analysis

Study	Sample size	Study period	Mean age $\pm$ SD (year)	Mean pre-operative EF (%)	Mean post-operative EF (%)	Surgical technique	Operative mortality (%)	Five-year survival unless specified (%)
1. Trachiotis	156	01/81–12/95	60 $\pm$ 10	19 $\pm$ 4	N/A	C	3.4	64
2. Mickleborough	125	01/82–09/97	59 $\pm$ 9	18 $\pm$ 5	N/A	C	4	72
3. Bouchart	141	01/88–12/98	63 $\pm$ 8	$\leq$ 25	N/A	C	7	70 $\pm$ 4
4. Chan	57	06/89–06/94	67 $\pm$ 8	28 $\pm$ 4	30 $\pm$ 9	C	1.7	73
5. Shah	57	06/89–06/94	67 $\pm$ 8	28 $\pm$ 4	30 $\pm$ 9	C	1.7	55.7
6. Lorusso	120	02/89–04/00	60 $\pm$ 9	28 $\pm$ 9	33 $\pm$ 9	C	1.6	80 $\pm$ 6
7. Carr	86	01/90–12/99	65 $\pm$ 10	18 $\pm$ 3	29 $\pm$ 8	C	11	59
8. Lee	120	08/90–05/05	60.3 $\pm$ 7.3	23.5 $\pm$ 4.2	32.8 $\pm$ 8.6	C	11.1	80.9
9. Sternik	117	01/91–07/94	N/A	$<$ 35	N/A	O, C	O 3.1, C13	O 86, C 65 (2 years)
10. Moshkovitz	75	12/91–12/94	60 $\pm$ 10	28 $\pm$ 6	N/A	C	2.7	73 (4 years)
11. Fukui	78	01/91–11/06	66.1 $\pm$ 9.4	28.2 $\pm$ 5.1	34.4 $\pm$ 8.4	C,O	7.7	73.1 $\pm$ 5.7 (10 years)
12. Nardi	302	01/93–12/03	62 $\pm$ 8.7	19 $\pm$ 4	43 $\pm$ 9	C	5.3	80 $\pm$ 2.5
13. Nishi	42	04/94–05/02	66 $\pm$ 9.3	23.8 $\pm$ 4.5	35.3 $\pm$ 8.5	C	2.4	83.1
14. de Carlo M	80	01/94–05/96	65 $\pm$ 9	27.1 $\pm$ 3.8	N/A	C	6.3	82 $\pm$ 5 (2 years)
15. Lslamoglu	273	01/95–11/00	61.02 $\pm$ 8.15	26.5 $\pm$ 3.6	39.6 $\pm$ 5.4	C	5.13	77.7
16. Selim Isbir	212	01/96–02/01	55.7 $\pm$ 10.6	25.1 $\pm$ 3.7	N/A	C	5.6	73 (4 years)
17. Appoo	430	01/96–12/01	64.5	$<$ 30	N/A	C	4.6	77.7
18. Ascione	250	04/96–08/06	65	$<$ 30	33.5	C,O	4	87 (3 year)
19. Hamad	75	07/97–03/99	64 $\pm$ 13	32.2 $\pm$ 6	44 $\pm$ 4	C	4	89.3 (8 years)
20. Filsofi	495	01/98–12/05	65 $\pm$ 11	30	N/A	C,O	3.6	75 $\pm$ 2.2
21. Toumpoulis	209	01/98–03/02	65 $\pm$ 10	O-16.1 $\pm$ 6.1 C-20.8 $\pm$ 5	N/A	O, C	O 5.1, C 6.8	O 66 C 68 (4 years)
22. Goldstein	210	01/99–31/01	67 $\pm$ 10.5	26 $\pm$ 4	N/A	C,O	7.1	C75 vs. O85 (1 year)
23. Youn	153	12/00–11/05	O-62.9 $\pm$ 8.8 C-62 $\pm$ 9.2	O 28.1 $\pm$ 5.9 C 27.9 $\pm$ 7	N/A	C,O	3	O-88.2 C-72.4 (6 years)
24. Chong	50	09/02–05/04	59 $\pm$ 9	19.7 $\pm$ 3.2	N/A	C	8	83 (2 year)
25. Elefteriades	135	N/A	66.5	23.6 $\pm$ 3.3	34	C	5.2	71 (4.5 years)
26. Oliveira	71	N/A	58	19.2 $\pm$ 7.9	27.1	C	2.8	62.8

C, on-pump; O, off-pump; EF, ejection fraction; SD, standard deviation; N/A, not available.

Identification

369 studies identified through the database search

Screening

59 studies screened

23 studies excluded due to lack of operative mortality data and same centre studies (1/23).

Eligibility

36 studies assessed for eligibility

10 studies excluded due to lack of long-term data

Included

26 studies included in the current meta-analysis

Figure 1 Study selection flow chart.

mortality and improved short- and long-term survival benefits following CABG among patients with severe LV dysfunction.^{2–27} Furthermore, advances in coronary artery bypass surgical techniques, improved targeted pharmacotherapy and the use of adjunct devices such as cardiac resynchronization therapy-defibrillators, have resulted in improved quality of life (QOL) and increased survival rates among patients with severe LV dysfunction.

The goal of this study was to perform a meta-analysis of observational studies to determine the operative mortality and 5-year actuarial survival outcomes among patients with severe LV dysfunction undergoing CABG.

Methods

Data extraction

A systematic computerized literature search was performed using the search terms 'poor left ventricle', 'coronary artery bypass surgery', 'revascularization', 'LV dysfunction', and 'heart failure'. Observational studies consisting of patients undergoing isolated CABG (on-pump and off-pump) for CAD and severe LV dysfunction ($EF \leq 35\%$) were included in this meta-analysis. Studies that did not report operative mortality, long-term survival (≥ 1 year) data and pre-operative LVEF were excluded. Multiple studies from the same study group were also excluded from the analysis. All abstracts were independently reviewed by two authors (V.K. and W.Q.) and papers that met the inclusion criteria were included. Internal validity and quality of the selected studies were evaluated as per the recommendations for meta-analysis on observational studies published by the MOOSE study group (see Supplementary material online for full reference).

Baseline characteristics including age, sex, past medical history (prior MI, diabetes, hypertension, heart failure, and EF), diagnosis at the time of procedure and outcome measures (operative mortality and 5-year survival rates) were recorded from all studies where this information was available by two reviewers (W.Q. and V.K.).

Table 2 Baseline characteristics of the study population

Variables	Pooled estimate	95% CI low	95% CI upper
Age (mean years)	63.9	63.7	64.1
Male (%)	82.4	79.4	85.3
Hypertension (%)	56.2	50.7	61.6
Diabetes (%)	31.3	25.7	37.2
Prior MI (%)	57.6	46.3	68.5
Hypercholesterolaemia (%)	52.2	37.6	66.7
Heart failure (%)	55.5	47.1	63.8
COPD (%)	10.9	8.3	13.7
Ejection fraction (%)	24.7	22.5	27.0
Three vessel disease (%)	78.0	71.3	84.1
Diagnosis at the time of surgery			
Stable angina (%)	66.3	49.9	80.9
Unstable angina (%)	38.6	25.7	52.5
Cardiogenic shock (%)	5.7	3.7	8.1

MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; CI, confidence interval.

The meta-analyses for all variables show strong heterogeneity. Hence, results based on the random effects models were reported. No publication bias was detected except for the variable diabetes. For diabetes, the reported meta-analysis result was after adjustment for publication bias by using the trim-and-fill method.

Outcome measures

The primary outcome measure was operative mortality and 5-year actuarial survival rate among patients with severe LV dysfunction ($EF \leq 35\%$) undergoing on-pump CABG. The secondary outcome measure was operative mortality among patients with severe LV dysfunction undergoing off-pump CABG (OPCAB). Studies of patients undergoing OPCAB did not report 5-year survival; hence these data were not available for the secondary outcome analysis. Other

Figure 2 (A) Meta-analysis of operative mortality—on-pump coronary artery bypass graft, (B) funnel plot for operative mortality—on-pump coronary artery bypass graft, (C) meta-analysis for five-year survival—on-pump coronary artery bypass graft, and (D) funnel plot for five-year survival—on-pump coronary artery bypass graft.

Table 3 Total operative mortality: on-pump coronary artery bypass graft

Study	Total number	Total death	Operative mortality ^a	95% CI low ^b	95% CI upper ^b
Appoo	430	20	0.047	0.029	0.071
Ascione	176	5	0.028	0.009	0.065
Bouchart	141	10	0.071	0.035	0.127
Carr	86	9	0.105	0.049	0.189
Chan	57	1	0.018	0.000	0.094
Chong	50	4	0.080	0.022	0.192
de Carlo M	80	5	0.063	0.021	0.140
Elefteriades	135	7	0.052	0.021	0.104
Filsoufi	424	17	0.040	0.024	0.063
Fukui	62	6	0.097	0.036	0.199
Goldstein	110	12	0.109	0.058	0.183
Hamad	75	3	0.040	0.008	0.113
Lee	120	13	0.108	0.059	0.178
Lorusso	120	2	0.017	0.002	0.059
Lslamoglu	273	14	0.051	0.028	0.085
Mickleborough	125	5	0.040	0.013	0.091
Moshkovitz	75	2	0.027	0.003	0.093
Nardi	302	16	0.053	0.031	0.085
Nishi	42	1	0.024	0.001	0.126
Oliveira	71	2	0.028	0.003	0.098
Selim Isbir	212	12	0.057	0.030	0.097
Shah	57	1	0.018	0.000	0.094
Sternik	53	7	0.132	0.055	0.253
Toumpoulis	136	7	0.052	0.021	0.103
Trachiotis	156	6	0.039	0.014	0.082
Youn	53	2	0.038	0.005	0.130
Total Fixed effect	3621	189	0.0531	0.0460	0.0606
Total Random effects	3621	189	0.0544	0.0453	0.0643

^aOperative mortality is the proportion of the number of in-hospital deaths: [Total death/the number of subjects at baseline (total number)].

^b95% CIs were constructed by first performing the averaged angular transformation to the proportions, then applying normal approximation to obtain 95% CIs for the transformed proportions and finally transform the 95% CIs back to the original scale.

CI, confidence interval.

secondary outcomes included improvement in EF, stroke rate, length of hospital (LOH) stay following CABG, post-operative respiratory failure rate, intra- or post-operative intra-aortic balloon pump (IABP) use, and intra- or post-operative inotrope use.

Operative mortality was defined as any death, occurring: (i) within 30 days after surgery in or out of the hospital, and (ii) after 30 days during the same hospitalization subsequent to the operation as recommended by the European Association of Cardiac and Thoracic Surgeons (EACTS) and the Society of Thoracic Surgeons (STS).

Statistical analysis

DerSimonian and Laird's random effects model was utilized to pool the parameter estimates (operative mortality and 5-year survival rate) from individual observational studies to form weighted parameter estimates, this takes into account heterogeneity among individual observational studies. The weights reflect the relative 'value' of the information provided in a study (measured by variance of the estimated parameters) and also reflect the between-study variation. For proportions (e.g. operative mortality), the average angular transformation proposed by Freeman and Tukey was used to stabilize variance. Cochran's Q test was used to evaluate heterogeneity. The I^2 statistic ($I^2 = \chi^2 - (k-1)/$

χ^2) proposed by Higgins and Thompson was used to measure inconsistencies in the meta-analysis. Light and Pillemer's funnel plot and Begg and Mazumdar's rank-correlation test were used to assess publication bias. Duval and Tweedie's trim-and-fill method was used to adjust for any observed publication bias via imputing the numbers of unpublished trials, if any, and their treatment effects. Finally, the weighted parameter estimate and its variance based on the filled funnel plot were calculated. All *P*-values were reported as two sided and values <0.05 were considered statistically significant. For continuous variables (e.g. age and height), standard deviation was approximated by range/6 when it was not directly available from the literature. All analyses were undertaken in statistical software R.

Results

In total, 369 peer reviewed published articles on CABG in the setting of severe LV dysfunction were reviewed. Of these, 26 observational clinical studies, which included 4119 patients, were identified and were included in the analysis (Table 1). The remaining 343 studies that did not provide operative mortality data

Table 4 Meta-analysis of 5-year survival: on-pump coronary artery bypass graft

Study	Total number	Total survival	Five-year survival ^a	95% CI low ^b	95% CI upper ^b
Appoo	430	334	0.777	0.734	0.815
Bouchart	141	99	0.702	0.619	0.776
Carr	86	51	0.593	0.482	0.698
Chan	57	42	0.737	0.603	0.845
Lee	120	105	0.875	0.802	0.928
Lorusso	120	96	0.800	0.717	0.868
Lslamoglu	273	212	0.777	0.722	0.825
Mickleborough	125	90	0.720	0.633	0.797
Nardi	302	242	0.801	0.752	0.845
Nishi	42	35	0.833	0.686	0.930
Oliveira	71	45	0.634	0.511	0.745
Shah	57	32	0.561	0.424	0.693
Trachiotis	156	100	0.641	0.560	0.716
Total Fixed effect	1980	1483	0.7508	0.7315	0.7695
Total Random effects	1980	1483	0.7335	0.6874	0.7773

^aFive-year survival is the proportion of the number of survival in 5 years: [Total survival/the number of subjects at baseline (total number)].

^b95% CIs were constructed by first performing the averaged angular transformation to the proportions, then applying normal approximation to obtain 95% CIs for the transformed proportions and finally transform the 95% CIs back to the original scale.
CI, confidence interval.

(or those studies that did not meet the STS/EACTS operative mortality definition), did not provide long-term (≥ 1 year) follow-up data, and those that did not report pre-operative EF (and studies with EF $>35\%$) were excluded (Figure 1). Of the 26 included studies, 13 provided 5-year actuarial survival rates among patients undergoing on-pump CABG.

Baseline characteristics

The baseline characteristics of patients are shown in Table 2. The mean (estimate) age was 63.9 years [95% confidence interval (CI) 63.7–64.1 years] and 82.4% of patients (95% CI 79.4–85.3%) were men. Diabetes was reported in 31.3% of patients (95% CI 25.7–37.2%) and 78% (95% CI 71.3–84.1%) had three-vessel disease. The diagnosis at time of CABG surgery was stable angina in 66.3% (95% CI 49.9–80.9%) of patients and cardiogenic shock in 5.7% (95% CI 3.7–8.1%) of patients. The mean (estimate) EF prior to CABG was 24.7% (95% CI 22.5–27.0%).

Operative mortality: on-pump coronary artery bypass graft surgery

The operative mortality among patients who underwent on-pump CABG in the setting of severe LV dysfunction is shown in Figure 2A and Table 3. The weighted estimate of operative mortality was 5.31% (95% CI 4.6–6.06%) using the fixed effect model and 5.44% (95% CI 4.53–6.43%) using the random effects model. Cochran's Q value was 37.1 with 25 degrees of freedom (df) and a P-value of 0.0569. The I^2 value was 32.6% (95% CI 0–58.2%). This suggests that there was no significant evidence for heterogeneity. Furthermore, the funnel plot for operative mortality (Figure 2B) shows no obvious asymmetry. Begg and Mazumdar's rank-correlation test of funnel plot asymmetry was not significant (P-value = 0.675). Hence, there was no significant

evidence to reject the hypothesis that the funnel plot was symmetrical, or equivalently there was no significant evidence for publication bias.

Five-year actuarial survival: on-pump coronary artery bypass graft surgery

The five-year actuarial survival among patients who underwent on-pump CABG in the setting of severe LV dysfunction is shown in Figure 2C and Table 4. Thirteen individual studies that included 1980 patients reported five-year actuarial survival rates. The weighted estimate of five-year survival was 75.08% (95% CI 73.15–76.95%) using the fixed effect model and 73.35% (95% CI 68.74–77.73%) using the random effects model. Cochran's Q value was 57.7 with df 12 and a P-value of <0.0001 . The I^2 value was 79.2% (95% CI 65.1–87.6%). This analysis demonstrates strong evidence for heterogeneity. Therefore, estimates based on the random effects model were used. The funnel plot for five-year survival showed no obvious asymmetry (Figure 2D). Begg and Mazumdar's rank-correlation test of funnel plot asymmetry was not significant (P-value = 0.1534). Hence, there was no significant evidence to reject the hypothesis that the funnel plot was symmetrical, or equivalently there was no significant evidence for publication bias.

Operative mortality: off-pump coronary artery bypass graft surgery

The operative mortality among patients who underwent OPCAB in the setting of severe LV dysfunction is shown in Figure 3A and Table 5. Seven of the 26 studies, consisting of 498 patients, utilized the OPCAB technique. The weighted estimate of operative mortality was 4.42% (95% CI 2.88–6.27%) using the fixed effect model and 4.4% (95% CI 2.8–6.4%) using the random effects model. Cochran's

Figure 3 (A) Meta-analysis for operative mortality—off-pump coronary artery bypass graft, (B) funnel plot for operative mortality—off-pump coronary artery bypass graft, (C) operative mortality off-pump coronary artery bypass graft vs. on-pump coronary artery bypass graft, and (D) funnel plot for operative mortality of off-pump coronary artery bypass graft vs. on-pump coronary artery bypass graft.

Table 5 Total operative mortality: off-pump coronary artery bypass graft

Study	Total number	Total death	Operative mortality ^a	95% CI low ^b	95% CI upper ^b
Ascione	74	5	0.068	0.022	0.151
Filsoufi	71	2	0.028	0.003	0.098
Fukui	16	0	0.000	0.000	0.206
Goldstein	100	3	0.030	0.006	0.085
Sternik	64	2	0.031	0.004	0.108
Toumpoulis	73	5	0.069	0.023	0.153
Youn	100	3	0.030	0.006	0.085
Total Fixed effect	498	20	0.0442	0.0288	0.0627
Total Random effects	498	20	0.044	0.028	0.064

^aOperative mortality is the proportion of the number of in-hospital deaths: [Total death/the number of subjects at baseline (total number)].

^b95% CIs were constructed by first performing the averaged angular transformation to the proportions, then applying normal approximation to obtain 95% CIs for the transformed proportions and finally transform the 95% CIs back to the original scale.

CI, confidence interval.

Table 6 Comparison of operative mortality: off-pump coronary artery bypass graft vs. on-pump coronary artery bypass graft

Study	Total (OPCAB)	Death (OPCAB)	Total (CABG) ^a	Death (CABG) ^a	Relative risk estimate	95% CI low	95% CI upper
Ascione	74	5	176	5	2.378	0.71	7.972
Filsoufi	71	2	424	16	0.747	0.175	3.177
Fukui	16	0	62	6	0.291	0.017	4.912
Goldstein	100	3	110	12	0.275	0.08	0.946
Sternik	64	2	53	7	0.237	0.051	1.091
Toumpoulis	73	5	136	7	1.331	0.438	4.045
Youn	100	3	53	2	0.795	0.137	4.611
Total Fixed effect	498	20	1014	55	0.672	0.410	1.102
Total Random effects	498	20	1014	55	0.708	0.351	1.426

CI, confidence interval; OPCAB, off-pump CABG.

^aConventional CABG.

Q value was 3.67, with df 6 and a *P*-value of 0.722. The *I*² value was 0% (95% CI 0–52.2%). This suggests that there was no significant evidence for heterogeneity. The funnel plot for operative mortality (OPCAB) showed no obvious asymmetry (Figure 3B). Begg and Mazumdar's rank-correlation test of funnel plot asymmetry was not significant (*P*-value >0.99). Hence, there was no significant evidence to reject the hypothesis that the funnel plot was symmetrical, or equivalently there was no significant evidence for publication bias.

Operative mortality: on-pump coronary artery bypass graft surgery vs. off-pump coronary artery bypass graft surgery

The operative mortality among patients who underwent OPCAB vs. on-pump CABG is displayed in Figure 3C and Table 6. Seven studies compared operative mortality utilizing the on-pump CABG technique in 1014 patients and the OPCAB technique in 498 patients. The weighted relative risk estimate (OPCAB vs.

on-pump CABG) was 0.672 (95% CI 0.410–1.102) using the fixed effect model and 0.708 (95% CI 0.351–1.426) using the random effects model. Cochran's Q value was 9.84 with df 6 and a *P*-value of 0.132. The *I*² value was 39% with 95% CI (0–74.3%). Hence, there was no significant evidence for heterogeneity. The funnel plot comparing operative mortality of OPCAB with that of on-pump CABG demonstrates symmetry (Figure 3D). Begg and Mazumdar's rank-correlation test of funnel plot asymmetry was not significant (*P*-value = 0.453). Hence, there was no significant evidence to reject the hypothesis that the funnel plot was symmetrical, or equivalently, there was no significant evidence for publication bias.

Other secondary analyses

In total, 14 studies provided data on post-operative EF and demonstrated improvement in post-operative EF following CABG. The mean estimated post-operative EF was 35.19% (95% CI 31.95–38.43%) (Table 1 and Figure 4A). The mean (standard deviation)

Figure 4 (A) Meta-analysis of post-operative left ventricular ejection fraction; (B) meta-analysis of stroke rate; (C) meta-analysis of length of hospital stay; and (D) meta-analysis of respiratory failure rate. TE, estimate of treatment effect; seTE, standard error of treatment estimate. Filled data indicates that corresponding studies were based on trim and fill method correcting the asymmetry of funnel plot due to publication bias.

of the differences in mean EF (mean post-operative EF—mean pre-operative EF) was 8.6% (4.4%). Eleven studies provided information on post-operative stroke rate and the mean estimated stroke rate was 3% (95% CI 2–4%) (Figure 4B, Table 7). Eight studies provided information on LOH stay and the meta-analysis based on the random effect model showed that the mean estimated LOH was 8.8 days (95% CI 6.46–11.15 days) (Figure 4C, Table 7). Five studies provided information on post-operative respiratory failure rate and the mean estimated respiratory failure rate was 11% (95% CI 9–13%) (Figure 4D, Table 7). Nine studies provided data on the use of intra- or post-operative IABP and the mean IABP use was 8% (95% CI 6–11%) (Figure 5A, Table 7). Four studies provided information on inotrope use and the mean estimated inotrope use was 43% (95% CI 20–67%) (Figure 5B, Table 7).

Discussion

The present meta-analysis of contemporary observational clinical studies involving a large cohort of patients demonstrates that CABG can be performed with acceptable operative mortality and 5-year actuarial survival among patients with severe LV dysfunction.

The results of the present study are consistent with large individual studies included in the current meta-analysis. The Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) registry of 430 patients with low EF (<30%) reported an operative mortality of 4.6% with a 5-year survival of 77.7%.² Filsoufi *et al.*¹² in their series of 495 patients with EF ≤30% undergoing CABG reported an operative mortality of 4%

(on-pump CABG) and 5-year survival rate of 75%. Likewise, in a series of 302 patients with EF ≤35%, Nardi *et al.*²¹ demonstrated an operative mortality of 5.3% and 10-year survival rate of 63%.

Left ventricular EF is a powerful determinant of operative mortality among patients undergoing open-heart surgery and is included as a variable when calculating the European System for Cardiac Operative Risk Evaluation score (EuroSCORE). In the EuroSCORE database study by Roques and colleagues (see Supplementary material online for full reference), operative mortality in the absence of identifiable risk factors was 3.4%. In the present analysis of patients with severe LV dysfunction (estimated mean EF of 24.7%) the overall operative mortality was 5.4% for on-pump CABG and 4.4% for off-pump CABG. Importantly, there was an improvement in EF following CABG with low rates of cerebrovascular accidents and with minimal need for cardiac support using IABP and/or inotropes.

A recent large-scale randomized trial by Shroyer and colleagues (see Supplementary material online for full reference) demonstrated that off-pump CABG compared with on-pump CABG was associated with non-superior 30 days (7 vs. 5.6%, $P = 0.19$) and long-term (1 year) outcomes (9.9 vs. 7.4%, $P = 0.04$) including death, non-fatal MI and repeat revascularization. In the present study of patients with severe LV dysfunction, utilizing the off-pump CABG technique had a hazard ratio of 0.71 (95% CI 0.351, 1.426, $P = 0.334$) for mortality when compared with the on-pump technique. This result needs to be interpreted with caution, given the small proportion of patients in this subgroup analysis that underwent OPCAB and the fact that the studies included in this meta-analysis were not randomized. Furthermore,

Table 7 Other secondary endpoints

Study	QOL	LOH stay (days)	Stroke rate (%)	Respiratory failure rate (%)	IABP use (%)	Inotrope use (%)
1. Appoo	N/A	N/A	N/A	N/A	N/A	N/A
2. Ascione	N/A	8 (6–11)	3	9	12	25
3. Bouchart	N/A	N/A	N/A	N/A	N/A	N/A
4. Carr	N/A	N/A	4	14	N/A	N/A
5. Chan	Yes	N/A	N/A	N/A	N/A	N/A
6. Chong	N/A	N/A	N/A	N/A	8	N/A
7. de Carlo M	N/A	N/A	N/A	N/A	N/A	N/A
8. Eleftheriades	N/A	N/A	N/A	N/A	N/A	N/A
9. Filsoufi	N/A	8 (6–13)	2	11	N/A	N/A
10. Fukui	N/A	N/A	0	N/A	N/A	N/A
11. Goldstein	Yes	N/A	N/A	N/A	8	N/A
12. Hamad	Yes	N/A	N/A	N/A	N/A	N/A
13. Lee	Yes	18.9 ± 14.2	N/A	N/A	N/A	N/A
14. Lorusso	Yes	N/A	N/A	N/A	N/A	N/A
15. Lslamoglu	Yes	N/A	N/A	N/A	N/A	N/A
16. Mickleborough	Yes	N/A	4	N/A	15	N/A
17. Moshkovitz	Yes	7 ± 3	1.3	N/A	2.7	20
18. Nardi	Yes	N/A	N/A	N/A	N/A	N/A
19. Nishi	Yes	N/A	7.14	N/A	4.76	N/A
20. Oliveira	Yes	N/A	N/A	N/A	N/A	N/A
21. Selim Isbir	Yes	N/A	N/A	N/A	N/A	N/A
22. Shah	Yes	N/A	N/A	N/A	N/A	N/A
23. Sternik	Yes	10 ± 6	6	N/A	7.5	57
24. Toumpoulis	N/A	11.8 ± 12.9	2.9	9.6	N/A	N/A
25. Trachiotis	Yes	9.2 ± 5.8	2.6	N/A	10.7	N/A
26. Youn		15.6 ± 10.3	3.8	13.2	1.9	39
Total	15 studies	8 studies	11 studies	5 studies	9 studies	4 studies

QOL, quality of life; LOH, length of hospital stay; IABP, intra-aortic balloon pump.

patients undergoing OPCAB usually have favourable baseline characteristics compared with patients undergoing on-pump CABG. This might in turn have a favourable effect on surgical mortality rates. Whether off-pump surgery might be beneficial among patients with severe LV dysfunction requires further evaluation.

Myocardial viability and LV dyssynchrony are also important predictors of operative mortality among patients with severe LV dysfunction. A meta-analysis by Allman and colleagues (see Supplementary material online for full reference) demonstrated a strong association between myocardial viability on non-invasive testing and improved survival following revascularization among patients with CAD and impaired LV dysfunction (EF 32 ± 8%). Interestingly, only four studies^{9,15,17,24} included in the present meta-analysis performed myocardial perfusion scanning to assess viability prior to revascularization. Nevertheless, the present meta-analysis demonstrates acceptable operative mortality and 5-year survival among patients who underwent CABG without routine evaluation for myocardial viability and reversible ischaemia. Identification of myocardial viability and LV dyssynchrony prior to surgery might be beneficial particularly in the present era of device therapy and advanced pharmacotherapy to further improve long-term clinical outcomes.

The present study included 82.4% men and the diagnosis at the time of surgery was stable angina in 66% of patients. A previous study by Kwon and colleagues (see Supplementary material online for full reference) demonstrates that women with severe LV dysfunction tend to have poorer survival outcomes compared with men. Given the small proportion of women in the present study, the results cannot be generalized to men and women with severe LV dysfunction undergoing CABG.

The Heart Failure Revascularization Trial (HEART), although overcome by the limitation of study discontinuation prior to complete patient enrolment, demonstrated that a conservative strategy may not be inferior to invasive management of patients with CAD and severe LV dysfunction.²⁸ Soran et al.²⁹ in a recent state-of-the-art review, provided a current perspective on the use of percutaneous coronary intervention (PCI) and CABG among patients with multivessel CAD. Observational studies comparing PCI with CABG among patients with severe LV dysfunction have demonstrated comparable long-term (≥1 year) survival benefit albeit with an increase in the need for repeat revascularization in the PCI group.³⁰ Further randomized studies are planned within the United Kingdom comparing medical therapy vs. PCI among patients with CAD and severe LV dysfunction.

Figure 5 (A) Meta-analysis of intra-aortic balloon pump use and (B) meta-analysis of inotrope use.

Limitations

The number of patients, the inclusion and the exclusion criteria, the type of surgery (off-pump and on-pump), the indication for CABG and the definition of severe LV dysfunction varied across the studies. Nevertheless, the results of this study demonstrate a favourable outcome among patients with severe LV dysfunction across several centres with several surgeons and across a varied patient cohort. In addition, the studies utilized different methods for the assessment of LV function (echocardiography, cardiac catheterization, and scintigraphy).

The present study remains subject to the inherent caveats of a meta-analysis including publication bias, however, in-depth statistical analysis was performed to account for these limitations. Given the fact the present meta-analysis included patients over a long study period (1981–2006) and from different organizations around the world, patient level data were not available and the results were obtained from published pooled data. Medical therapy in addition to revascularization is beneficial for patients with CAD particularly in patients with severe LV dysfunction; however, information about drug therapy was not available in our analysis.

In the present meta-analysis, 78% of patients had three-vessel disease. Details of the number of grafts used would have provided useful information about the completeness of the revascularization procedure; however, since not all of the studies provided this information, it cannot be reported here. Nevertheless, the present study demonstrates encouraging 5-year survival rates among patients with severe LV dysfunction undergoing on-pump CABG. In view of the increasing proportion of patients with

CAD and severe LV dysfunction encountered in day-to-day clinical practice, optimal treatment strategies for this population are worthy of extensive evaluation in future randomized controlled clinical trials, in order to improve QOL and survival.

Conclusions

The present meta-analysis that included a large cohort of patients demonstrates that based on currently available observational clinical studies, CABG surgery can be performed with acceptable operative mortality and 5-year actuarial survival in patients with severe LV dysfunction. Further randomized clinical trials are now required to determine the best strategy for the management of patients with CAD and severe LV dysfunction.

Supplementary material

Supplementary material is available at *European Journal of Heart Failure* online.

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