Interactive CardioVascular and Thoracic Surgery (2022) 1–8
https://doi.org/10.1093/icvts/ivac095 Advance Access publication 21 April 2022

ORIGINAL ARTICLE

Cite this article as: Brynjarsdottir HB, Johnsen A, Heimisdottir AA, Heidarsdottir SR, Jeppsson A, Sigurdsson MI *et al.* Long-term outcome of surgical revascularization in patients with reduced left ventricular ejection fraction—a population-based cohort study. Interact CardioVasc Thorac Surg 2022; doi:10.1093/icvts/ivac095.

Long-term outcome of surgical revascularization in patients with reduced left ventricular ejection fraction—a population-based cohort study

Helga B. Brynjarsdottir[a], Arni Johnsen[a], Alexandra A. Heimisdottir [a], Sunna Rún Heidarsdottir[a], Anders Jeppsson[b,c], Martin I. Sigurdsson[d,e] and Tomas Gudbjartsson[a,e,*]

[a] Department of Cardiothoracic Surgery, Landspitali University Hospital, Reykjavik, Iceland
[b] Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[c] Department of Cardiothoracic Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden
[d] Department of Anesthesia and Intensive Care, Landspitali University Hospital, Reykjavik, Iceland
[e] Faculty of Medicine, University of Iceland, Reykjavik, Iceland

* Corresponding author. Department of Cardiothoracic Surgery, Landspitali University Hospital, Eiriksgata 5, 101 Reykjavik, Iceland. Tel: +354-825-5016; e-mail: tomasgud@landspitali.is (T. Gudbjartsson).

Received 2 February 2022; received in revised form 16 March 2022; accepted 19 April 2022

Key question

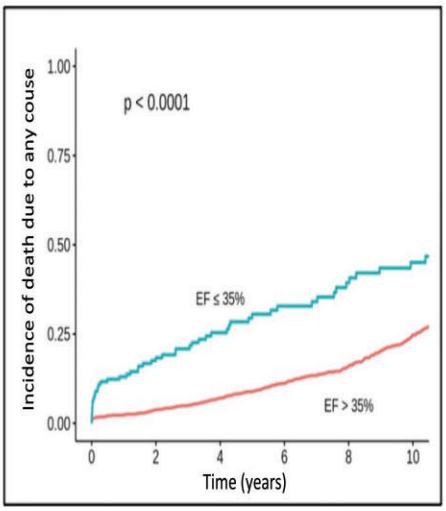
Does heart failure have a significant effect on long-term outcomes after CABG surgery?

Key finding(s)

The rate of death at 5 years was 31% for patients with LVEF ≤ 35 % versus 9% for patients with LVEF > 35%.

Take-home message

LVEF ≤ 35% was the strongest predictor for mortality in our cohort with a hazard ratio of 2.0.



Abstract

OBJECTIVES: Surgical revascularization is an established indication for patients with advanced coronary artery disease and reduced left ventricular ejection fraction (LVEF). Long-term outcomes for these patients are not well-defined. We studied the long-term outcomes of patients with ischaemic cardiomyopathy who underwent surgical revascularization in a well-defined nationwide cohort.

MATERIALS AND METHODS: A retrospective study on 2005 patients that underwent isolated coronary artery bypass grafting in Iceland between 2000 and 2016. Patients were categorized into two groups based on their preoperative LVEF; LVEF ≤35% (n = 146, median LVEF

30%) and LVEF >35% ($n = 1859$, median LVEF 60%). Demographics and major adverse cardiac and cerebrovascular events were compared between groups along with cardiac-specific and overall survival. The median follow-up was 7.6 years.

RESULTS: Demographics were similar in both groups regarding age, gender and most cardiovascular risk factors. However, patients with LVEF ≤35% more often had diabetes, renal insufficiency, chronic obstructive pulmonary disease and a previous history of myocardial infarction. Thirty-day mortality was 4 times higher (8% vs 2%, $P < 0.001$) in the LVEF ≤35%-group compared to controls. Overall survival was significantly lower in the LVEF ≤35%-group compared to controls, at 1 year (87% vs. 98%, P < 0.001) and 5 years (69% vs. 91%, P < 0.001). In multivariable analysis LVEF ≤35% was linked to inferior survival with an adjusted hazard ratio of 2.0 (95%-CI 1.5 - 2.6, p<0.001).

CONCLUSIONS: A good long-term outcome after coronary artery bypass grafting can be expected for patients with reduced LVEF, however, their survival is still significantly inferior to patients with normal ventricular function.

Keywords: Surgical revascularization • Coronary artery bypass grafting • Reduced left ventricular ejection fraction • Risk factors • Long-term outcome • Survival

ABBREVIATIONS

AKI	Acute kidney injury
CABG	Coronary artery bypass grafting
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
DM	Diabetes mellitus
eGFR	Estimated glomerular filtration rate
LVEF	Left ventricular ejection fraction
MACCE	Major adverse cardiac and cerebrovascular event
MI	Myocardial infarction
NYHA	New York Heart Association
PCI	Percutaneous coronary intervention

INTRODUCTION

Heart failure with reduced left ventricular ejection fraction (LVEF) as a result of coronary atherosclerosis is a major health burden, with a prevalence that is estimated to increase over the next decades [1]. Optimal treatment has not been well established and whether these patients should undergo myocardial revascularization with coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI) or receive medical therapy only is still under debate. So far, the available data comparing these treatment strategies are mostly observational [2], as many of the randomized studies on the outcome of CABG versus PCI excluded patients with severely reduced LVEF [3,4].

Despite scarce long-term data, surgical revascularization is recommended (Class 1) over medical therapy alone by current guidelines for patients with ischaemic cardiomyopathy and 3-vessel coronary disease [5]. These recommendations are mainly based on the results of the STICH trial, the largest randomized trial to date comparing CABG to medical therapy alone in patients with ischaemic heart failure [6]. The STICH trial was first published in 2011 with a 5-year follow-up but did not identify a difference in all-cause mortality between CABG versus medical therapy alone. In 2016, an extended 10-year follow-up was published and the results showed a 7% absolute reduction in overall mortality after CABG compared to medical therapy alone [7]. Furthermore, a more recent analysis of the STICH trial has confirmed a more favourable outcome in the CABG group compared with medical therapy alone for other long-term outcomes like death from cardiovascular causes and cardiovascular hospitalization [8].

With a paucity of randomized trials available, observational studies can provide important data that can help clinicians in their decision-making. We therefore decided to study the outcome of CABG procedures in patients with coronary artery disease and ischaemic heart failure with LVEF of 35% or less in a well-defined whole-nation population. Our focus was on long-term outcomes, primarily overall (all-cause) mortality but also cardiac-specific mortality along with major adverse cardiac and cerebrovascular events (MACCE). By this, our goal was to provide information on the long-term outcome of surgical revascularization in patients with reduced LVEF in a well-defined population with thorough centralized follow-up.

MATERIALS AND METHODS

Ethics statement

The study was approved by the Icelandic National Bioethics Committee and the Data Protection Commission (1/10/20, VSN-19–04). Formal consent from patients was not needed due to anonymity.

Study design

This was a retrospective study that spanned 16 years between 1 January 2001 and 31 December 2016. The study group consisted of consecutive patients that underwent first time, isolated CABG in Iceland, excluding all patients undergoing concomitant procedures such as valve surgery. Patients with missing information on preoperative LVEF were excluded ($n = 55$), leaving 2005 patients for further analysis. All operations were performed at Landspitali University Hospital, the sole cardiothoracic center that serves all of Iceland, with a current population of 380 000 inhabitants. The patients were categorized into two groups based on their preoperative LVEF; LVEF ≤ 35% and LVEF > 35% as controls.

Data collection and demographics

To identify patients, we searched a digital diagnostic and operation registry using operative codes. When all patients had been identified, clinical information was gathered retrospectively from hospital charts at Landspitali. For long-term follow-up data, we also retrospectively reviewed medical records from all other hospitals in Iceland where patients are potentially admitted with cardiovascular disease. This made it possible to obtain thorough data on long-term complications for almost all patients. Furthermore, information on CABG and PCI

could be obtained and checked from centralized registries, with information on survival being collected from the centralized registry Statistics Iceland for all patients.

Information on preoperative LVEF was obtained from echocardiographic reports. Most often, the preoperative ultrasound was done by an experienced cardiologist with the patient in stable condition, but in some acute or semi-acute cases, the echocardiography was done in less controlled situations. If more than one preoperative echocardiograph existed for the same patient the one closest to surgery was used. In a few cases where emergency surgery was needed, there was no preoperative ultrasound on record so the intraoperative ultrasound was used to evaluate LVEF.

Preoperative demographics included gender, age, cardiovascular risk factors such as hypertension, diabetes mellitus (DM) and smoking; chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) and a previous history of myocardial infarction (MI) and/or PCI. CKD was defined as estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2 [9]. The New York Heart Association (NYHA) functional classification [10] was used to classify heart failure symptoms and the Canadian Cardiovascular Society grading system was used to grade angina [11]. Patient symptoms were classified into stable angina, unstable angina or new MI (indication for treatment) based on presenting symptoms in the same hospital stay the surgery was performed. Euroscore II [12] was then calculated for all patients to estimate the risk for 30-day mortality. All patients had a preoperative angiogram to evaluate the severity and distribution of the coronary artery disease.

Intraoperative variables included the operative technique, the urgency of the surgery (elective versus non-elective surgery with emergency surgery being defined as surgery within 24 h from hospital admission and semi-acute surgery being in the same hospital stay), use of cardiopulmonary bypass, duration of surgery (both skin–skin time and cross-clamp time) and the number of distal anastomoses performed. Postoperative bleeding (ml) in the first 24 h after surgery was documented, as well as the rate of re-exploration for bleeding.

Data on postoperative complications within 30 days from surgery were collected. These variables were perioperative MI (defined as isolated ST-segment changes or a new left bundle branch block on electrocardiogram, along with elevation of creatine kinase MB of ≥70 μg/l); stroke, poststernotomy mediastinitis, acute kidney injury (AKI) requiring dialysis, new-onset atrial fibrillation, pneumonia and pleural effusion. Operative mortality was defined as death within 30 days of surgery.

Outcome and follow-up

The long-term endpoints collected and used in this study were MI (more than 30 days after surgery), stroke (neurological signs that persisted for more than 24 h), PCI or repeated CABG, and death. All endpoints were then combined into MACCE. The diagnostic criteria for new MI were the presence of an elevation in cardiac biomarkers, in addition to one of the following: symptoms of myocardial ischaemia, new significant changes on electrocardiogram (ST-segment changes, new left bundle branch block or development of Q-waves), new wall motion abnormalities or intracoronary thrombus detected on diagnostic imaging. Patients who had a cardiovascular event and died during the follow-up period were included in each endpoint.

Follow-up was completed for all patients on 1 June 2017 with the median follow-up being 7.6 years (range 0.1–16.4).

Statistical methods

Statistical analysis was performed with Microsoft Excel (2011) and R version 3.3.3. Categorical variables are presented as number (percentage). Continuous variables are presented as mean ± standard deviation if normally distributed, and as median [range] if not. Categorical variables were compared using the Chi-square test, except in cases where any expected count was less than 5; then Fisher's exact test was used. Normally distributed continuous variables were compared using the *t*-test. Non-normally distributed continuous variables were compared using the Wilcoxon rank-sum test. The normal distribution was visually assessed using kernel density estimation. Statistical significance was set to $P < 0.05$ for the primary hypothesis and for other analyses that were considered explanatory. Missing data on demographic and intraoperative variables were excluded from statistical analysis. In all cases, there were fewer than 25 missing values out of all 2005 patients except for body mass index (51 patients), CKD (29 patients), smoking history (38 patients) and skin–skin time (56 patients). There was 100% follow-up and no missing data on overall mortality and other long-term endpoints except for missing data on cause of death and therefore cardiac mortality in 294 patients (13% in the LVEF ≤35% group and 15% in the LVEF >35% group). Those patients were excluded from the analysis of cardiac mortality but included in all-cause survival analysis.

Univariable logistic regression was used to compare the frequency of postoperative complications between groups. Overall, cardiac-specific and MACCE-free survival was compared between groups using the log-rank test. A Cox proportional hazards model was then used to identify predictors for mortality. Univariable models were created with variables that were plausible to affect mortality (LVEF, hypertension, age, DM, current smoking, COPD, CKD, previous PCI, NYHA class III and IV, emergency procedure, off-pump surgery, number of distal anastomoses and operation length). Statistically significant variables ($P < 0.2$) in the univariable analysis were then combined in a multivariable model.

Additionally, we performed a propensity score matching between the two groups, using the following variables to construct the propensity score: (age, sex, hypertension, DM, COPD, off-pump surgery, body mass index, previous PCI, current smoking and emergency operation). Those variables were used based on plausibility to affect mortality. We used the nearest neighbour method, using MatchIT in R statistics. Balance of matching was assessed by comparing standardized mean difference of cases and controls before and after. All matching variables had a standardized mean difference <0.1 following matching. The aforementioned statistical methods were used to compare the matched groups. All patients were matched but 9 patients in the study group had to be excluded due to missing data. The total number of matched patients in each group was 137.

RESULTS

Preoperative LVEF for all the 2005 patients is shown in Fig. 1. Just over 7% of the cohort had an LVEF of 35% or less ($n = 146$).

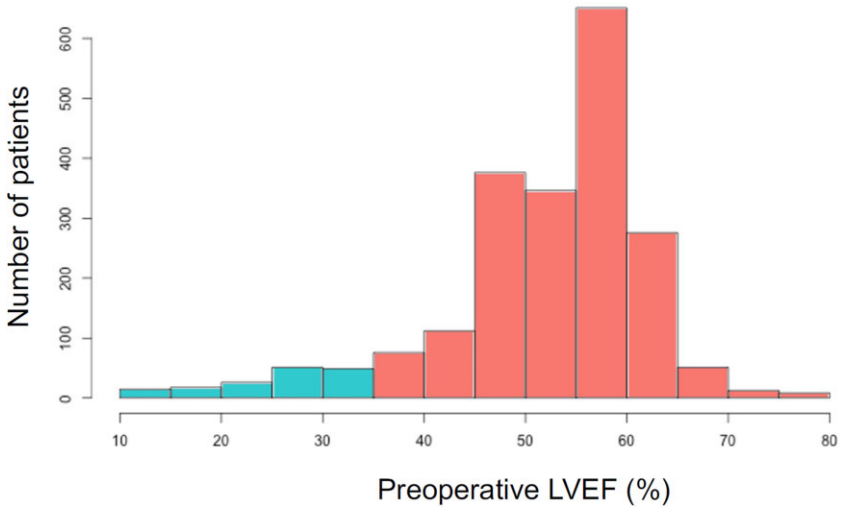


Figure 1: Distribution of preoperative left ventricular ejection fraction. LVEF: left ventricular ejection fraction.

Baseline characteristics of the patient population can be seen in Table 1. Demographics were similar for the LVEF ≤35% group and controls regarding age, gender and the proportion of patients with hypertension. However, patients in the LVEF ≤35% group were more likely to have other comorbidities such as DM, renal insufficiency, COPD and a previous history of MI. Patients in the LVEF ≤35% group were also more symptomatic with higher NYHA scores, and also had a higher calculated Euroscore II (4.2 vs 1.4, $P < 0.001$).

In the LVEF ≤35% group, 93 patients (64%) presented with MI compared to 476 patients (26%) in the control group ($P < 0.001$).

Operative details are shown in Table 2. Almost a third of the patients in the LVEF ≤35% group had elective surgery, 52% underwent a semi-acute surgery and 17% an emergency surgery. In both groups, around 80% of patients had conventional CABG where cardiopulmonary bypass was used, the rest being operated off-pump. The number of distal anastomoses was higher in the LVEF ≤35% group (median 4 vs 3 for controls) and the surgeries were longer (skin–skin time 215 min vs 200 min, $P < 0.001$) compared to those of controls.

Overall complications were more common in the LVEF ≤35% group. Table 3 shows the number of cases for each complication. The rates of perioperative MI (2% vs 4%, $P = 0.2$) and stroke (3% vs 1%, $P = 0.06$) were similar between the groups, while new-onset atrial fibrillation (43% vs 31%, $P = 0.002$) was more common in the LVEF ≤35% group. The total chest tube output for the first 24 h after surgery was similar between groups, but re-exploration was more common in the LVEF ≤35% group (11% vs 5%, $P = 0.003$).

Thirty-day mortality was around 4 times higher in the LVEF ≤35%-group compared to controls (8% vs 2%, $P < 0.001$).

Figure 2 shows long-term outcomes, both for death and MACCE. Overall survival was 87% and 69% for the LVEF ≤35%-group at 1 and 5 years, compared to 98% and 91% for patients with LVEF >35%. As can be seen in the figure, the lines separate most in the first few months but later on they run practically parallel. In the same groups, respectively, MACCE-free survival was 83% and 62% at 1 and 5 years compared to 94% and 82%. The rate of long-term MI was similar between groups, the rate being 2–4% at 5 years postoperatively. The need for long-term PCI was also similar between groups, being 9–11% after 10 years of follow-up. The rate of stroke at 5 years was 9% for patients with LVEF ≤35% compared to 4% for controls, the difference not being statistically significant ($P = 0.2$).

Table 1: Comparison of demographic characteristics

	LVEF ≤ 35% $n = 146$	LVEF >35% $n = 1859$	*P*-value
Age (years)	67 ± 10	66 ± 9	NS (0.6)
Male	126 (86)	1531 (82)	NS (0.3)
Hypertension	88 (61)	1218 (66)	NS (0.4)
Diabetes mellitus	34 (23)	308 (17)	0.04
Chronic kidney disease[a]	33 (23)	275 (15)	0.02
Previous myocardial infarction	62 (43)	429 (23)	<0.001
Previous PCI	30 (21)	417 (22)	NS (0.7)
Cardiac valve disease[b]	13 (9)	55 (3)	<0.001
History of smoking	102 (71)	1309 (70)	NS (0.8)
Current smoker	51 (35)	410 (22)	<0.001
Chronic obstructive pulmonary disease	18 (13)	127 (7)	0.02
Body mass index, kg/m^2	27 ± 4	28 ± 5	NS (0.08)
Euroscore II	4.2 [0.7–37]	1.4 [0.5–36]	<0.001
NYHA score III or IV	116 (80)	1109 (60)	<0.001
CCS score III/IV	110 (75)	1360 (73)	NS (0.6)
Number of diseased vessels			
Three-vessel disease	121 (83)	1497 (81)	NS (0.6)
Left main stenosis	63 (43)	771 (41)	NS (0.8)
3vd and/or left main	129 (88)	1658 (89)	NS (0.9)
Myocardial infarction as presenting symptom	93 (64)	476 (26)	<0.001

Mean ± SD, median [range] or number (%).
[a]eGFR < 60 ml/min/1.73 m^2.
[b]In most cases mild to moderate aortic stenosis or mild to moderate mitral regurgitation, not haemodynamically significant and not requiring surgery.
CCS: Canadian Cardiovascular Society; eGFR: estimated glomerular filtration rate; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; SD: standard deviation.

The risk factors for overall survival are shown in Table 4. Independent predictors of long-term mortality in the multivariable model were advanced age, DM, CKD, COPD, current smoking, NYHA classification III or IV, emergency procedure and longer skin-to-skin time. Importantly, LVEF ≤35% was also linked to inferior survival (adjusted hazard ratio 2.0, 95% confidence interval 1.5–2.6, $P < 0.001$).

Table 2: Operative and postoperative variables

	LVEF ≤ 35% *n* = 146	LVEF >35% *n* = 1859	*P*-value
Off-pump surgery	22 (15)	366 (20)	NS (0.2)
Elective surgery	46 (32)	885 (48)	<0.001
Non-elective surgery	100 (68)	974 (52)	<0.001
Emergent	25 (17)	69 (4)	<0.001
Semi-acute	75 (52)	905 (49)	NS(0.5)
Skin–skin time, min	215 [128–630]	200 [85–555]	<0.001
Time on CPB, min	99 [38–366]	85 [25–319]	<0.001
Cross-clamp time, min	49 [16–191]	45 [10–204]	0.02
Intraoperative inotropes	109 (76)	946 (51)	<0.001
Perioperative use of IABP	44 (30)	56 (3)	<0.001
Intraoperative defibrillation	20 (14)	269 (14)	NS (0.7)
Number of distal anastomoses	4 [1–6]	3 [1–6]	0.02
LIMA used	129 (88)	1767 (95)	0.001
Postoperative bleeding 24 h, ml	820 [115–3835]	760 [100–31 820]	NS (0.08)
Re-exploration for bleeding	16 (11)	92 (5)	0.003
ICU days	2 [1–32]	1 [0–42]	<0.001
Total ward days	8 [0–75]	7 [0–75	<0.001

Median [range] or number (%).

CPB: cardiopulmonary bypass; IABP: intra-aortic balloon pump; ICU: intensive care unit; LIMA: left internal mammary artery.

Table 3: Postoperative complications

	LVEF ≤35% *n* = 146	LVEF >35% *n* = 1859	OR (95% CI)	*P*-value
New-onset atrial fibrillation	63 (43)	579 (31)	1.7 (1.2, 2.4)	0.003
Pneumonia	17 (12)	107 (6)	2.2 (1.2, 3.6)	0.005
Pleural effusion	24 (16)	220 (12)	1.5 (0.9, 2.3)	NS (0.1)
Leg wound infection	16 (11)	176 (9)	1.2 (0.7–2.0)	NS (0.7)
Perioperative MI	3 (2)	77 (4)	0.5 (0.1, 1.3)	NS (0.2)
Stroke	4 (3)	18 (1)	2.9 (0.8, 7.9)	NS (0.06)
Poststernotomy mediastinitis	3 (2)	14 (1)	2.8 (0.6, 8.6)	NS (0.1)
Postoperative dialysis	2 (1)	7 (0.5)	3.7 (0.5, 15.3)	NS (0.1)
Thirty-day mortality	11 (8)	28 (2)	5.3 (2.5, 10.7)	<0.001

Number (%).

CI: confidence interval; MI: myocardial infarction; OR: odds ratio.

In the propensity-matched cohort (*n* = 137), the findings of both long-term complications and mortality were similar to our analysis that was performed without matching, with the outcomes being significantly inferior for patients with LVEF ≤35% **(**5-year survival for LVEF ≤35% was 69% vs 91% for controls, $P < 0.001$, Table 5). The difference in surgical mortality was, however, not statistically significant between groups (7% vs 4% for the LVEF ≤35% group vs controls, respectively, $P = 0.2$). Patient variables and standardized mean differences after matching can be seen in Supplementary Material, Table S1 and Fig. S1.

DISCUSSION

This whole-nation study reports long-term outcomes for patients with LVEF ≤35%, in a well-defined nationwide cohort, reporting both all-cause survival and the rate of MACCE.

Compared to similar studies, the long-term outcomes on myocardial revascularization in this subgroup of patients in the present study can be regarded as generally good, albeit significantly worse for patients with lower left ventricular function, as should be expected. We observed a 30% five-year mortality after CABG for patients with LVEF ≤35%, compared to 36% in the STICH trial [6] and 21–23% at 4–5 years in 2 recently published observational studies that compared CABG to PCI in patients with reduced LVEF [13, 14]. We also reported rates of MACCE that were significantly higher in the LVEF ≤35% group, primarily driven by the difference in mortality observed in the groups. There was no significant difference in the rate of stroke, MI or revascularization with PCI in the two groups. That could indicate that the technical aspect of the surgery is similar between groups with similar results in revascularization.

New-onset atrial fibrillation and pneumonia were the only short-term complications that were more common in the LVEF ≤35% group versus controls. Low LVEF is a known risk factor for new-onset atrial fibrillation after cardiac surgery so that did not come as a surprise [15, 16]. Total time in the intensive care unit was longer in the LVEF ≤35% group so that could explain the higher rate of pneumonia due to longer time on invasive ventilation.

The independent predictors of mortality identified with multivariable logistic regression were similar to those reported in

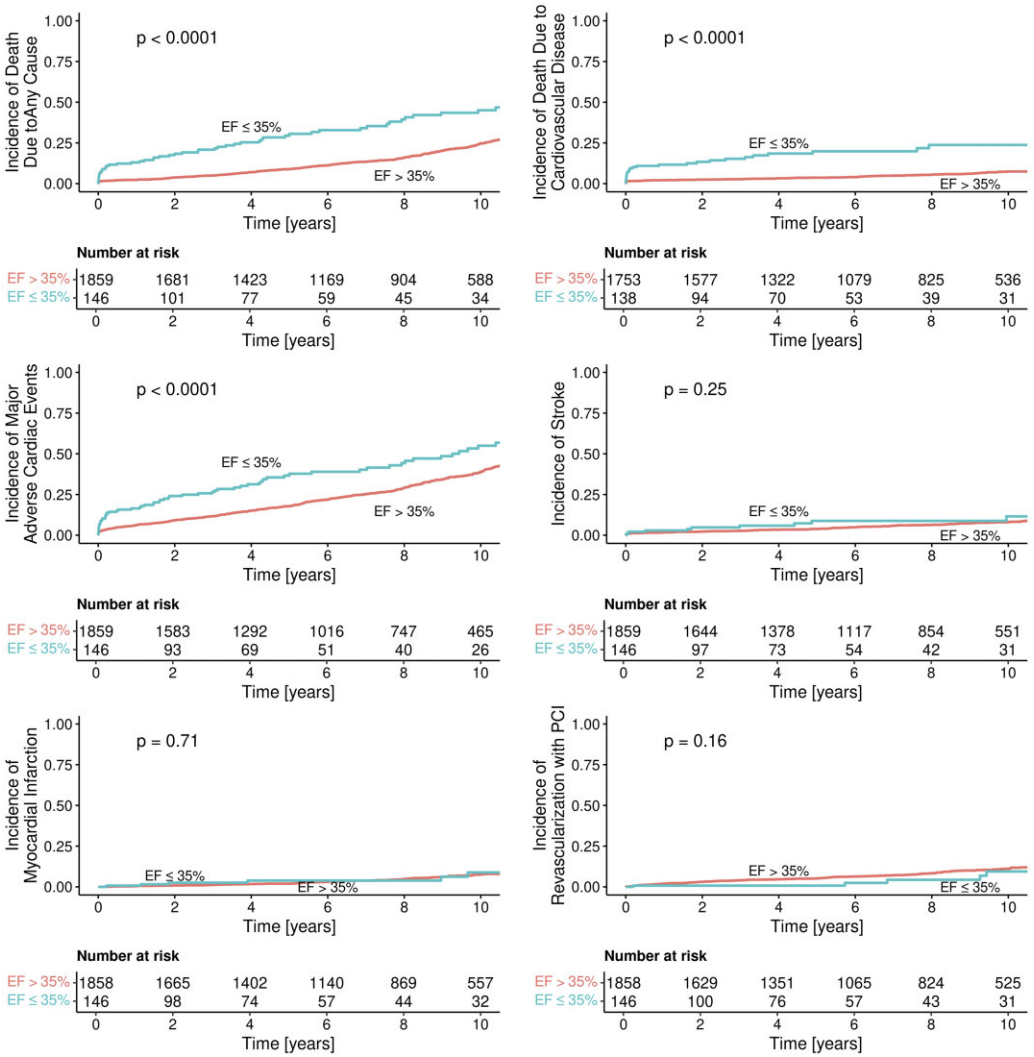


Figure 2: Long-term incidence of death (top-left), cardiovascular death (top-right), major adverse cardiac and cerebrovascular events (middle-left), stroke (middle-right), myocardial infarction (bottom-left) and revascularization with PCI (bottom-right) in both groups. EF: ejection fraction; PCI: percutaneous coronary intervention.

Table 4: Cox regression analysis showing risk factors predicting for death with unadjusted and adjusted HR

	Unadjusted HR	95% CI	*P*-value	Adjusted HR	95% CI	*P*-value
LVEF ≤35	2.6	(1.9, 3.4)	<0.001	2.0	(1.5, 2.6)	<0.001
Age	2.2	(2.0, 2.5)	<0.001	1.08	(1.06, 1.09)	<0.001
HTN	1.1	(0.9, 1.4)	NS(0.2)			
DM	1.7	(1.4, 2.2)	<0.001	1.9	(1.5, 2.3)	<0.001
CKD	2.8	(2.2, 3.5)	<0.001	1.6	(1.3, 2.0)	<0.001
Current smoking	1.2	(1.0, 1.4)	0.1	1.5	(1.2–1.8)	<0.001
COPD	2.4	(1.8, 3.1)	<0.001	1.6	(1.2, 2.2)	<0.001
Previous PCI	1.1	(0.8, 1.3)	NS (0.4)			
NYHA 3 or 4	1.5	(1.2, 1.8)	<0.001	1.3	(1.1, 1.6)	0.007
Emergency procedure	2.2	(1.5, 3.1)	<0.001	1.5	(1.0, 2.2)	0.03
Off-pump surgery	0.8	(0.7, 1.0)	0.1	0.8	(0.6–1.0)	0.06
Distal anastomoses	1.0	(0.9, 1.1)	NS (0.6)			
Operation length (skin–skin time)	1.003	(1.001, 1.004)	0.001	1.002	(1.000, 1.004)	0.006

CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; HR: hazard ratio; HTN: hypertension; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention.

Table 5: Long-term survival and MACCE after propensity score matching

	LVEF ≤ 35% (95% CI) *n* = 137	LVEF > 35% (95% CI) *n* = 137	*P*-value
Survival, years			
1	88% (0.8, 0.9)	98% (0.9, 1.0)	<0.001
5	69% (0.6, 0.8)	91% (0.9, 1.0)	
10	55% (0.5, 0.7)	73% (0.6, 0.8)	
Freedom from MACCE, years			
1	84% (0.8, 0.9)	96% (0.9, 1.0)	0.002
5	62% (0.5, 0.7)	84% (0.8, 0.9)	
10	45% (0.4, 0.6)	63% (0.5, 0.7)	

CI: confidence interval; LVEF: left ventricular ejection fraction; MACCE: major adverse cardiac and cerebrovascular events.

previous CABG studies [17] and included advanced age, DM, COPD, acute operation and extended operative times. Furthermore, and as expected LVEF ≤35% showed an inferior long-term survival compared to that of patients with LVEF >35%. However, the greatest part of the survival difference is likely explained by higher mortality in the early postoperative period as can be seen in Fig. 2.

We decided to use an LVEF ≤35% as a cut-off for low LVEF and heart failure, as was done in the STICH trial [6] and other more recent trials comparing CABG and PCI in patients with heart failure [13, 14]. However, in a new definition and classification of heart failure published by the Heart Failure Society of America (HFSA), the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) and the Japanese Heart Failure Society (JHFS) the cut-off of LVEF <40% is used to define heart failure with reduced LVEF [18]. The rational for this is the helpfulness of this cut-off for applying therapies that have been shown to work in patients with reduced LVEF. Whether it is better to use the cut-off of 40% in LVEF can be debated, however, many studies still use the cut-off of 35%, calling it either reduced LVEF or severely reduced LVEF, which then makes comparison to the literature more convenient. As for surgical mortality, the European system for cardiac operative risk evaluation (*Euro*SCORE) categorizes patients with LVEF <30% in a three-fold higher-risk group compared to patients with LVEF 30–50% [12, 19].

Our propensity-matched analysis showed that 30-day mortality was not statistically different between the LVEF groups when matched for patients with similar comorbidities; this in contrast to our unmatched analysis. However, in line with our unmatched cohort analysis, the long-term survival of patients with LVEF ≤35% was inferior to that of those with normal ventricular function, which supports the main findings of the study. The fact that 30-day mortality was not significantly inferior for patients with lower LVEF in our study when matched for other comorbidities could be explained by insufficient statistical power (type 2 error). It is also possible that a low LVEF is not a key factor when it comes to surgical mortality in patients with comorbidities, where surgical mortality already is high. Finally, it is plausible that reduced LVEF only affects surgical mortality significantly for those patients with the lowest LVEF, but our database was not of sufficient size to evaluate this concept further.

Limitations and strengths

A clear strength of this study is the fact that it includes all patients who underwent CABG in a well-defined population-based cohort; the findings therefore being less affected by potential selection bias. Our database is very detailed and the survival data exact, especially with regards to mortality, where information was gained from a centralized death registry in Iceland, with a follow-up of 100%. With a median follow-up of 7.6 years and 100% follow-up for overall mortality, we now have a great insight into long-term prognosis for this subgroup of patients with LVEF ≤35% that has not been studied before in Iceland.

The major limitation is the retrospective design and, therefore, inevitable missing data on factors which rely on the accuracy of registration. Our postoperative long-term data are also limited to factors and events that are registered in hospital files (MACCE and death). We do not have data on postoperative medical therapy because most patients are followed up at private clinics after surgery. We therefore cannot draw any conclusions to whether patients were on optimal medical therapy. However, all patients at the cardiac surgery department at Landspitali are discharged on medications according to current guidelines. Another limitation is the possibility that ejection fraction was falsely estimated as too low in some patients that underwent acute surgery. The current study included both patients with stable and unstable angina, including those with acute MI and requiring urgent surgery. This is in contrast to the STICH trial in which patients with recent acute MI, the most common cause for left ventricular dysfunction, were excluded [6]. Acute ischaemia can cause a transient state of mechanical cardiac dysfunction which leads to temporarily reduced LVEF. This might result in miscategorization to LVEF ≤35% for patients with acute MI. We expect this would decrease the difference in outcome between the study group and controls. A postoperative ultrasound would be helpful to evaluate plausible mis-grouped patients with temporarily reduced LVEF. However, data on postoperative ultrasound were not available, as most patients were followed up at private cardiology clinics in Iceland and the data too often missing.

In a retrospective study like ours, it is important not to make too strong conclusions, as the heterogenic cohort only includes 2005 patients. We decided to include all patients that underwent isolated CABG surgery; even those with a recent MI or severe comorbidities. Preoperatively, the patients in the LVEF ≤35% group were sicker, and by using a Cox regression model we tried to take this into account. Nevertheless, this is a limitation of the study. In future studies, it would, for example, be interesting to discriminate between patients with recent or chronically reduced LVEF as there is so much difference here in our cohort, with a recent MI rate of 64% vs 26% in the LVEF ≤35% vs controls, respectively.

CONCLUSIONS

This study shows that good long-term outcome can be obtained in CABG patients with reduced LVEF, although their survival is inferior to patients with normal ventricular function. Randomized studies are needed to evaluate the best treatment option for these patients.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

ACKNOWLEDGEMENTS

The results presented in this paper have not been published previously. Part of this work was presented at the 10th joint Scandinavian conference in Cardiothoracic surgery in Copenhagen, 2018.

Funding

This study was supported by the Research Fund of Landspitali University Hospital and the Research Fund of University of Iceland.

Conflict of interest: none declared.

Data Availability Statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Author contributions

Helga B. Brynjarsdottir: Data curation; Formal analysis; Writing—original draft. **Arni Johnsen:** Formal analysis; Writing—review & editing. **Alexandra A. Heimisdottir:** Data curation; Writing—review & editing. **Sunna Rún Heidarsdottir:** Data curation; Writing—review & editing. **Anders Jeppsson:** Writing—review & editing. **Martin I. Sigurdsson:** Formal analysis; Writing—review & editing. **Tomas Gudbjartsson:** Formal analysis; Project administration; Supervision; Writing—review & editing.

Reviewer information

Interactive CardioVascular and Thoracic Surgery thanks Marko Ivan Turina, Dominique Shum-Tim, Daniel Zimpfer and the other anonymous reviewer(s) for their contribution to the peer review process of this article.

REFERENCES

[1] Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW *et al.*; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2021 update: a report from the American Heart Association. Circulation 2021;143:e254–743.

[2] Wolff G, Dimitroulis D, Andreotti F, Kołodziejczak M, Jung C, Scicchitano P *et al.* Survival benefits of invasive versus conservative strategies in heart failure in patients with reduced ejection fraction and coronary artery disease: a meta-analysis. Circ Heart Fail 2017;10.

[3] Murphy ML, Hultgren HN, Detre K, Thomsen J, Takaro T. Treatment of chronic stable angina. A preliminary report of survival data of the randomized Veterans Administration cooperative study. N Engl J Med 1977;297:621–7.

[4] Killip T, Passamani E, Davis K. Coronary artery surgery study (CASS): a randomized trial of coronary bypass surgery. Eight years follow-up and survival in patients with reduced ejection fraction. Circulation 1985; 72(Pt 2):V102–9.

[5] Neumann F-J, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U *et al.*; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;40:87–165.

[6] Velazquez EJ, Lee KL, Deja MA, Jain A, Sopko G, Marchenko A *et al.* Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med 2011;364:1607–16.

[7] Velazquez EJ, Lee KL, Jones RH, Al-Khalidi HR, Hill JA, Panza JA *et al.* Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. N Engl J Med 2016;374:1511–20.

[8] Howlett JG, Stebbins A, Petrie MC, Jhund PS, Castelvecchio S, Cherniavsky A *et al.* CABG improves outcomes in patients with ischemic cardiomyopathy: 10-year follow-up of the STICH trial. JACC Heart Fail 2019;7:878–87.

[9] Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI *et al.*; for the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.

[10] Dolgin M; New York Heart Association, Criteria Committee. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. Boston: Little, Brown, 1994.

[11] Campeau L. The Canadian Cardiovascular Society grading of angina pectoris revisited 30 years later. Can J Cardiol 2002;18:371–9.

[12] Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR *et al.* EuroSCORE II. Eur J Cardiothorac Surg 2012;41:734–44; discussion 744–5.

[13] Sun LY, Gaudino M, Chen RJ, Bader Eddeen A, Ruel M. Long-term outcomes in patients with severely reduced left ventricular ejection fraction undergoing percutaneous coronary intervention vs coronary artery bypass grafting. JAMA Cardiol 2020;5:631–41.

[14] Bangalore S, Guo Y, Samadashvili Z, Blecker S, Hannan EL. Revascularization in patients with multivessel coronary artery disease and severe left ventricular systolic dysfunction. Circulation 2016;133: 2132–40.

[15] Taha A, Nielsen SJ, Bergfeldt L, Ahlsson A, Friberg L, Björck S *et al.* New-onset atrial fibrillation after coronary artery bypass grafting and long-term outcome: a population-based nationwide study from the SWEDEHEART registry. J Am Heart Assoc 2021;10:e017966.

[16] Ismail MF, El-Mahrouk AF, Hamouda TH, Radwan H, Haneef A, Jamjoom AA. Influencing postoperative atrial fibrillation in patients undergoing on-pump coronary artery bypass grafting, single center experience. J Cardiothorac Surg 2017;12:40.

[17] Wu C, Camacho FT, Wechsler AS, Lahey S, Culliford AT, Jordan D *et al.* Risk score for predicting long-term mortality after coronary artery bypass graft surgery. Circulation 2012;125:2423–30.

[18] Bozkurt B, Coats AJS, Tsutsui H, Abdelhamid CM, Adamopoulos S, Albert N *et al.* Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. Eur J Heart Fail 2021;23:352–80.

[19] Nashef SAM, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9–13.