Hybrid coronary revascularization versus total arterial revascularization for the treatment of left main coronary artery disease

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Background: Hybrid coronary revascularization (HCR) has a similar clinical outcome to coronary artery bypass grafting (CABG) in treating multivessel disease. However, the outcome of HCR in treating left main coronary artery (LM) disease is unclear. This study sought to compare the clinical outcome of HCR with total arterial revascularization (TAR) for treating LM disease.

Methods: Patients who underwent treatment for LM disease in our center between January 2009 and December 2019 were selected. Of these, 33 patients underwent HCR, and 70 patients underwent TAR. The primary efficacy outcome of this study was mid-term major adverse cardiac and cerebrovascular events (MACCE). The primary safety outcome was perioperative MACCE.

Results: The incidence of postoperative outcomes was comparable between the two groups after adjustment with inverse probability weighting (IPW) (P>0.05). The median follow-up time was 47 (interquartile range, 20 to 85) months. There was no significant difference in the incidence of all mid-term outcomes and the freedom of MACCE between the two groups after adjustment (P>0.05). The Cox proportional hazard model demonstrated that HCR was not a significant determinant for MACCE [hazard ratio (HR) =3.516, 95% confidence interval (CI): 0.835 to 14.813].

Conclusions: HCR may be safe and effective for the treatment of LM disease compared with TAR.

Keywords: Hybrid coronary revascularization (HCR); total arterial revascularization (TAR); left main coronary artery disease (LM disease)

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Introduction

More than two-thirds of left ventricular perfusion is provided by the left main coronary artery (LM) (1), and untreated LM disease often leads to poor prognosis (2,3). Coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are the two main options for treating LM disease. There have been several multicenter randomized controlled trials (RCTs) comparing CABG and PCI for patients with LM disease. The Nordic-Baltic-British Left Main Revascularization Study (NOBLE study) (4) showed a higher incidence of major adverse cardiac and cerebrovascular events (MACCE) in a PCI group than in a CABG group at 5 years. In the Evaluation of XIENCE Everolimus Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization Study (EXCEL study) (5), CABG was superior to PCI for all-cause mortality at 5 years. CABG remains the standard treatment for LM disease.

Recent studies support the benefits of total arterial or multi-arterial revascularization (6,7). The application of multiple arterial grafts (7) and the avoidance of saphenous vein grafts (SVG) (8) led to a lower graft failure rate, which potentially decreased the risk of long-term death, myocardial infarction (MI), and repeat revascularization. In the European guidelines, total arterial revascularization (TAR) is now a Level IIA recommendation for patients with a long life expectancy (9). However, TAR is used to treat a minimal number of patients nowadays, for multifactorial reasons (10). For patients at high risk for sternal complications, TAR with the bilateral internal mammary artery (BIMA) should not be performed (11). A low degree of target stenosis and targets in RCA territory decrease the patency of arterial grafts (12). Moreover, harvesting multiple arterial grafts increases operation time.

Hybrid coronary revascularization (HCR) combines a minimally invasive left internal mammary artery (LIMA)-left anterior descending coronary artery (LAD) graft with PCI to non-LAD lesions. Contemporary drug-eluting stents (DES) were not inferior to SVG in restenosis and thrombosis rate (13), leading to a similar long-term clinical outcome of HCR to CABG in multivessel disease (14). However, HCR is only a Level IIB recommendation in specific patient subsets at experienced centers (15). Performing HCR requires close cooperation between cardiac surgeons and cardiologists and hardware, such as hybrid operating rooms. Also, randomized controlled studies and large sample clinical evidence on HCR are still very limited.

The non-inferiority of HCR to TAR has not, however, been verified, and the clinical results of HCR for the treatment of LM disease is unclear. This study sought to assess the safety and efficacy of HCR in comparison with TAR for treating LM disease. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-4224).

Methods

Study design

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Ruijin Hospital (No. 2020-21) and individual consent for this retrospective analysis was waived. Data of patients attending the hospital between January 2009 and December 2019 were used. The inclusion criteria were as follows: (I) the patient underwent HCR or TAR; (II) the patient had LM disease; (III) the surgeons performed LIMA-to-LAD anastomosis. The exclusion criteria were as follows: (I) the operation was emergent; (II) the operation was a redo surgery.

We divided patients into an HCR group and TAR group according to the revascularization therapy used. HCR in our unit was completed in two-stages, combining minimally invasive direct coronary artery bypass (MIDCAB) and PCI with DES. In the first year after surgery, all patients received aspirin 100 mg and clopidogrel 75 mg per day. Following this, patients continued to take aspirin 100 mg daily.

Data collection

Two researchers independently collected the preoperative characteristics according to a specific form. A supervisor reviewed discrepancies. Preoperative characteristics included gender, age, body mass index (BMI) (which was calculated based on the height and weight at admission), hypertension history, diabetes mellitus (DM) history, hyperlipoidemia history, family history, smoking status, MI history (which was previous clinical MI or documented by electrocardiogram or echocardiogram), stroke history (which was previous clinical stroke or documented by computed tomography), chronic obstructive pulmonary disease (COPD) history (which was documented by clinical manifestation and pulmonary function test), chronic kidney disease (CKD) history (which was diagnosed previously or documented by serum creatinine level and glomerular filtration rate), and ejection fraction (EF). EuroSCORE II (16) was calculated based on the original methodology and score algorithm.

Outcome measures

This study's primary outcome was mid-term MACCE, defined as the composite of death, MI, stroke, or target vessel revascularization (TVR). The primary safety outcome was perioperative MACCE. We measured the clinical outcomes, including perioperative and mid-term clinical outcomes.

"Perioperative" was defined as within 30 days after surgery. The perioperative clinical outcomes were as follows: (I) death, defined as death from any cause (cardiovascular and non-cardiovascular mortality); (II) MI, defined as MI type 5 according to the *Fourth Universal*

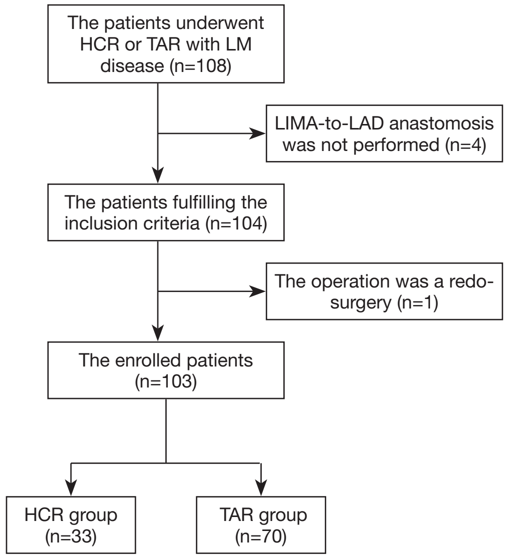


Figure 1 Flow diagram. HCR, hybrid coronary revascularization; TAR, total arterial revascularization; LM, left main coronary artery; LIMA, left internal mammary artery; LAD, left anterior descending coronary artery.

Definition of Myocardial Infarction (17); (III) stroke; (IV) TVR, defined as the target vessels needing PCI or redo surgery; (V) MACCE; (VI) the length of stay (LOS) in hospital.

The mid-term clinical outcomes were as follows: (I) death; (II) MI; (III) stroke; (IV) TVR; (V) MACCE.

The researchers reviewed adverse events during the study and adjudicate them to ensure the events met the definitions given. Two researchers independently adjudicated each event. A third researcher was called to adjudicate an event if the agreement was not reached. These assessments were blind to the knowledge of which group the patients were placed in.

Follow-up

Follow-up of patients within the unit is completed via an annual telephone interview. For the patients in this study, we performed an additional telephone interview. The incidence of death, MI, stroke, and TVR were recorded.

Inverse probability weighting (IPW)

A multivariate logistic regression model was employed to calculate propensity scores (PS), which estimated the probability that the patients would be selected for HCR, using all of the preoperative characteristics. We used IPW based on PS to adjust for differences between the two groups. This approach, which was implemented to create balance, weighted each patient by a stabilized weight, according to the study of Hernan (18).

Statistical analysis

Continuous variables were summarized as mean ± standard deviation (SD) or median (the 25th percentile, the 75th percentile), and categorical variables were categorized as percentages. Continuous variables were compared using a two-tailed Student's *t*-test. Categorical variables were compared using the χ^2 test or Fisher exact test. The time to the first occurrence of MACCE was described by the unadjusted Kaplan-Meier curve (K-M curve) and the adjusted K-M curve with the use of IPW, and the comparison of K-M curves was performed with the log-rank analysis. The adjusted K-M curve was obtained using R package IPW survival (F. Le Borgne and Y. Foucher, 2017). Using estimated freedom from MACCE among patients undergoing HCR and those undergoing TAR, we calculated risk ratios at specific time points and used bootstrap methods to obtain 95% confidence intervals (CIs). The hazard ratio (HR) was calculated by a Cox proportional hazards model and adjusted via the PS. The HR was estimated with the TAR group as the control group. All analysis was performed with SPSS version 22.0 (Chicago, IL, USA) and R version 3.4.3. A P value of <0.05 was considered to be statistically significant.

Results

Patients characteristics

We identified 33 patients in the HCR group and 70 patients in the TAR group fulfilling the inclusion and exclusion criteria (*Figure 1*). *Table 1* demonstrates the baseline characteristics of patients before and after adjustment with the use of IPW. Before adjustment, patients in the HCR group were older (P<0.001) and had a higher risk of surgery (P<0.001). The adjustment achieved an adequate balance between the groups for all covariates (P>0.05).

Perioperative outcomes

Table 2 demonstrates the perioperative results of the two

Table 1 Preoperative characteristics of patients undergoing HCR and TAR before and after adjustment with the use of IPW

Variables	Unadjusted data			Data adjusted with the use of IPW		
	HCR group (n=33)	TAR group (n=70)	P value	HCR group (n=34)	TAR group (n=59)	P value
Male (%)	75.8	90.0	0.107	90.9	89.5	0.886
Age (yrs)	71.2±9.9	53.8±9.9	<0.001*	61.8±9.4	57.6±10.4	0.055
BMI (kg/m^2)	24.6±3.2	25.0±2.6	0.501	25.0±3.4	25.0±2.5	1.000
Hypertension (%)	81.8	60.0	0.028*	41.2	56.3	0.161
DM (%)	39.4	27.1	0.210	33.5	25.1	0.383
Hyperlipoidemia (%)	12.1	25.7	0.116	24.4	22.5	0.837
Family history (%)	0.0	4.3	0.563	0.0	3.4	0.732
Smoker (%)	30.3	67.1	<0.001*	50.6	60.7	0.344
MI (%)	36.4	28.6	0.425	14.7	25.8	0.213
Stroke (%)	9.1	2.9	0.378	3.5	3.2	0.603
COPD (%)	3.0	4.3	0.811	1.5	4.1	0.941
CKD (%)	18.2	2.9	0.021*	5.9	2.4	0.768
EF (%)	61.9±10.0	63.6±7.2	0.328	66.1±6.9	63.4±6.8	0.069
Euroscore II (%)	1.6 (1.1, 3.05)	0.7 (0.7, 0.9)	<0.001*	0.7 (0.6, 1.2)	0.8 (0.7, 1.1)	0.281

*, means there was significant difference between two groups (P<0.05). HCR, hybrid coronary revascularization; TAR, total arterial revascularization; IPW, inverse probability weighting; BMI, body mass index; DM, diabetes mellitus; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; EF, ejection fraction.

Table 2 Postoperative outcomes of patients undergoing HCR and TAR before and after adjustment with the use of IPW

Variables	Unadjusted data			Data adjusted with the use of IPW		
	HCR group (n=33)	TAR group (n=70)	P value	HCR group (n=34)	TAR group (n=59)	P value
Death (%)	0.0	1.4	0.699	0.0	2.7	0.888
MI (%)	9.1	0.0	0.041*	6.1	0.0	0.228
Stroke (%)	3.0	0.0	0.699	0.9	0.0	0.240
TVR (%)	0.0	0.0	–	0.0	0.0	–
MACCE (%)	12.1	1.4	0.045*	7.4	2.7	0.599
LOS in hospital (days)	19.1±11.6	17.3±7.6	0.349	15.8±7.0	17.4±7.3	0.309

*, means there was significant difference between two groups (P<0.05). HCR, hybrid coronary revascularization; TAR, total arterial revascularization; IPW, inverse probability weighting; MI, myocardial infarction; TVR, target vessel revascularization; MACCE, major adverse cardiac and cerebrovascular events; LOS, length of stay.

groups. The perioperative MI rate (P=0.041) and MACCE rate (P=0.045) were significantly higher in the HCR group than in the TAR group before adjustment with the use of IPW. After adjustment, all of the perioperative results were comparable between the two groups (P>0.05).

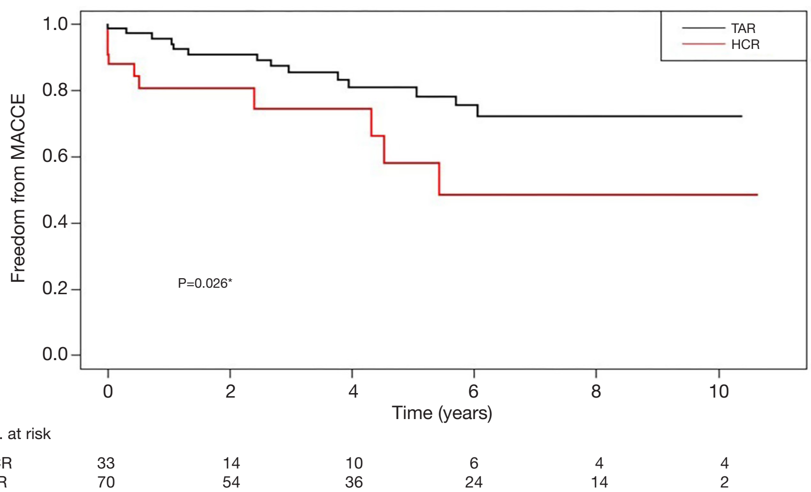
Mid-term outcomes

The median follow-up time was 47 (interquartile range, 20 to 85) months. The follow-up rates of the HCR and TAR groups were 90.9% and 90.0%, respectively. Before adjustment, the incidence of MI was significantly higher

Table 3 Mid-term outcomes of patients undergoing HCR and TAR before and after adjustment with the use of IPW

Variables	Unadjusted data			Data adjusted with the use of IPW		
	HCR group (n=33)	TAR group (n=70)	P value	HCR group (n=34)	TAR group (n=59)	P value
Death (%)	9.1	5.7	0.829	4.7	6.6	0.935
MI (%)	12.1	0.0	0.015*	7.6	0.0	0.133
Stroke (%)	3.0	2.9	0.563	0.9	2.5	0.824
TVR (%)	3.0	7.1	0.703	1.5	5.8	0.647
MACCE (%)	24.2	15.7	0.298	13.5	15.1	0.920

*, means there was significant difference between two groups (P<0.05). HCR, hybrid coronary revascularization; TAR, total arterial revascularization; IPW, inverse probability weighting; MI, myocardial infarction; TVR, target vessel revascularization; MACCE, major adverse cardiac and cerebrovascular events.



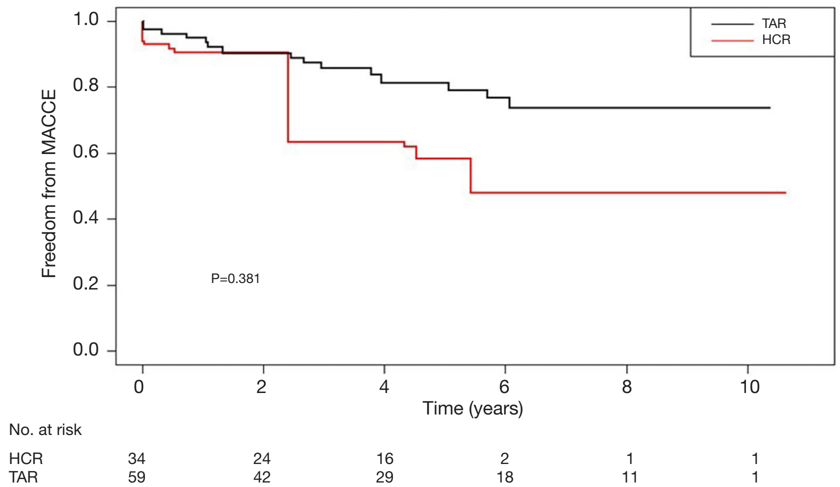
	30-day	1-yr	3-yr	5-yr	10-yr
MACCE rate after HCR, % (95% CI)	12.1 (0.9–23.3)	19.3 (5.4–33.2)	25.5 (8.1–42.9)	42.1 (17.8–66.4)	51.7 (25.0–78.4)
MACCE rate after TAR, % (95% CI)	1.4 (0.0–4.1)	4.4 (0.0–9.3)	14.6 (5.8–23.4)	19.2 (8.8–29.6)	27.9 (14.8–41.0)
Relative risk with HCR, (95% CI)	8.6 (0.2–17.9)	4.4 (0.6–66.4)	1.7 (0.3–7.4)	2.2 (0.6–7.5)	1.9 (0.6–5.3)

Figure 2 The K-M curves of freedom from MACCE before the adjustment with the use of IPW. K-M methods and the log-rank test were used to calculate and compare the freedom from MACCE before the adjustment with the use of IPW. The cumulative freedom from MACCE of the HCR group was significantly lower than that of the TAR group (P=0.026). *, means there was significant difference between two groups (P<0.05). K-M, Kaplan-Meier; MACCE, main adverse cardiovascular and cerebrovascular events; IPW, inverse probability weighting; HCR, hybrid coronary revascularization; TAR, total arterial revascularization; CI, confidence interval.

in the HCR group than in the TAR group (P=0.015). The incidences of the other mid-term outcomes were comparable between the two groups (P>0.05) (*Table 3*). After adjustment, there was no difference in the incidences of all mid-term outcomes between the two groups (P>0.05) (*Table 3*).

The freedom from MACCE was estimated by K-M curves and adjusted by IPW. The unadjusted K-M curves demonstrated significantly lower freedom from MACCE in the HCR group than in the TAR group (P=0.026) (*Figure 2*). However, there was no significant difference in the freedom of MACCE between the two groups after adjustment (P>0.05) (*Figure 3*).

The univariate Cox proportional hazard model



	30-day	1-yr	3-yr	5-yr	10-yr
MACCE rate after HCR, % (95% CI)	7.2 (0.0–15.8)	9.7 (0.0–19.9)	36.9 (18.7–55.1)	41.9 (22.5–61.3)	52.1 (0.2–100.0)
MACCE rate after TAR, % (95% CI)	2.7 (0.0–6.8)	5.3 (0.0–11.4)	14.4 (3.8–25.0)	18.7 (6.0–31.4)	26.4 (8.6–44.2)
Relative risk with HCR, (95% CI)	2.7 (0.2–11.2)	1.8 (0.0–25.6)	7.0 (0.7–14.5)	2.2 (0.7–10.2)	2.0 (0.0–11.6)

Figure 3 The K-M curves of freedom from MACCE after the adjustment with the use of IPW. K-M methods and the log-rank test were used to calculate and compare the freedom from MACCE after the adjustment with the use of IPW. There was no significant difference in the cumulative freedom from MACCE between the two groups (P=0.381). K-M, Kaplan-Meier; MACCE, main adverse cardiovascular and cerebrovascular events; IPW, inverse probability weighting; HCR, hybrid coronary revascularization; TAR, total arterial revascularization; CI, confidence interval.

demonstrated that HCR was not significantly associated with increased risks for MACCE (HR =2.391, 95% CI: 0.953 to 6.002). After being adjusted for PS, HCR was not a significant determinant for MACCE (HR =3.516, 95% CI: 0.835 to 14.813).

Discussion

Patients with LM disease have a poor prognosis due to a large amount of myocardium at risk (19). Revascularization brings survival benefits to these patients in comparison to medical therapy alone (20). In the RCTs involving LM disease patients, CABG was associated with a lower mortality and MACCE rate at 5 years than PCI, making CABG a more reasonable option for LM disease (4,5). Graft selection influences the outcomes following CABG. Multiple studies demonstrate that a second arterial graft, such as a right internal mammary artery (RIMA) (6) or a radial artery (RA) (7), has incremental benefits, due to the more durable patency of these grafts compared with SVG (21,22). Performing CABG with TAR is a strategy to eliminate the impact of inferior SVG patency rates. TAR induced lower rates of graft failure, potentially decreasing the long-term incidence of death, MI, and TVR (23).

HCR combines the survival benefit of LIMA-LAD graft and the minimal invasion of PCI to non-LAD lesions (24). The greater freedom from atherosclerosis and long-term patency of LIMA-LAD graft make it the standard of care. An effectively revascularized LAD decreases the difficulty and risk of LM PCI and simplifies complex stent procedures to a single LM DES, reducing restenosis and TVR rates (25). The stent extending from the LM to the left circumflex coronary artery (LCX) does not block the flow to LAD due to LIMA-LAD graft. In this study, HCR was completed in two stages, and MIDCAB was performed first in most cases. Performing MIDCAB first avoids conflict between excellent surgical hemostasis and dual antiplatelet therapy for stent implantation (26). Moreover, two-stage HCR obviates the need for a hybrid operating room with specialized imaging systems.

In this study, the safety and efficacy of HCR were compared with that of TAR for treating LM disease. There was a significant difference in preoperative characteristics between the two groups. Surgeons rarely choose elderly patients for TAR because of the limited life expectancy, which reduces the survival benefit of TAR. However, for elderly patients with a high risk of traditional surgery, HCR, a minimally invasive procedure, is a reasonable option and often chosen by surgeons. In this study, IPW was used to eliminate the difference in baseline data between the two groups. After adjustment, the preoperative characteristics of the two groups were comparable.

Most reports comparing HCR with CABG involved patients with multivessel coronary artery disease and demonstrated similar in-hospital and mid-term outcomes (27-30). Halkos and colleagues reported favorable perioperative outcomes and comparable mid-term MACCE and TVR rates of HCR for treating LM disease compared with CABG (31). In this study, the perioperative outcomes of the two groups were comparable, which supports the safety of HCR in the treatment of LM disease. A similar LOS in hospital of the two groups showed that two-stage HCR did not extend the LOS in hospital. We found no differences between the two groups in mid-term outcomes, which further demonstrated that HCR effectively treats LM disease. The patients treated with HCR had higher perioperative and mid-term MI rates than those treated with TAR, but these were not statistically significant after adjustment. Most perioperative MI events happened when patients with high SYNTAX scores waited for PCI after MIDCAB. Performing one-stage HCR in patients with high SYNTAX scores may improve the clinical outcomes of HCR in treating LM disease.

The small sample size and retrospective design of this study are its main limitations. The results of this study should be interpreted as hypothesis-generating and used with caution. The patients undergoing HCR were carefully selected, so generalizing these results to a broader population of LM disease patients is limited by selection bias. Moreover, survival data is limited by the relatively small sample size and short follow-up.

Conclusions

In conclusion, the results of this study suggest that HCR may be safe and effective for treating LM disease compared with TAR.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/atm-20-4224

Data Sharing Statement: Available at http://dx.doi.org/10.21037/atm-20-4224

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-4224). 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Ruijin Hospital (No. 2020-21) and individual consent for this retrospective analysis was waived.

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