Clinical Effect and Prognosis of Off-Pump Minimally Invasive Direct Coronary Artery Bypass

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Background: Coronary artery bypass grafting (CABG) is a common procedure to circumvent the obstruction of coronary arteries when stents are unsuitable. CABG is a very traumatic surgery that requires redirecting blood flow to an external pump. Thus, this procedure has many risks during and after surgery, and minimizing these risks would greatly benefit the patients.

Material/Methods: We selected 126 patients with coronary artery syndrome and who were unsuitable for stent percutaneous coronary intervention. The observation group received minimally invasive direct coronary artery bypass (MIDCAB), while the control group was treated with off-pump CABG.

Results: Blood markers and echocardiography before and after treatment improved equally in both groups. Neither group exhibited obvious adverse reactions, or liver and kidney function damage. However, surgical bleeding and postoperative observation days were significantly reduced in the MIDCAB group. Death and cardiac shock at the end of follow-up were significantly lower in the MIDCAB group.

Conclusions: Overall, the clinical benefits of MIDCAB and OP-CABG were similar, but MIDCAB significantly reduced postoperative hospital stay and intraoperative blood transfusion, and improved clinical prognosis.

MeSH Keywords: Coronary Artery Bypass • Coronary Artery Bypass, Off-Pump • Surgical Procedures, Minimally Invasive

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Background

Coronary artery bypass grafting (CABG) is a common procedure to circumvent the obstruction of coronary arteries when stents are unsuitable. CABG is a very traumatic surgery that requires redirecting blood flow to an external pump. Minimally invasive direct coronary artery bypass (MIDCAB) in the left chest is a type of CABG [1]. Bypass from the internal mammary artery (IMA) to the left anterior descending coronary artery (LAD) is an effective technique for the treatment of simple anterior descending artery disease. This surgery is especially recommended for patients with multiple lesions that are not suitable for percutaneous coronary intervention (PCI) or stent stenosis. One of the main advantages of MIDCAB is that there is no need for cardiac arrest and cardiopulmonary bypass (CPB) transfer during surgery [2–4]. MIDCAB patients also benefit from the neurological protection associated with this minimally invasive procedure. According to the methods previously reported in the literature, we analyzed patients with CABG in the Heart Surgery Department in our hospital to further explore the clinical advantages of MIDCAB in the left chest.

Material and Methods

Inclusion and exclusion criteria

Inclusion criteria: 1) All patients enrolled complied with the ACS diagnostic criteria of the American Heart Association (AHA) [5]; 2) All patients enrolled were diagnosed with different degrees of pain or discomfort in the anterior region, and the diagnosis of ACS was confirmed by ECG, myocardial markers, and cardiac troponin; 3) Emergency intravenous thrombolysis in patients undergoing PCI; 4) Patients and their families were willing to accept relevant laboratory tests and signed informed consent [1]; and 5) Patients without other cardiovascular disease. This study was approved by the Ethics Committee of Cangzhou City Central Hospital.

Exclusion criteria were: 1) Application of immunosuppressive agents; 2) Acute and chronic bacterial and/or viral infections; 3) Autoimmune disease; 4) Patients with connective tissue disease; 5) Malignant tumor; 6) Liver or kidney insufficiency; 7) Chronic muscle disease; 8) Allergy to rosvastatin; 9) Peripheral vascular disease, chronic heart failure, thyroid disease, liver or renal insufficiency, tumor, major trauma in the past 6 months, surgical history; 10) Recent use of adrenal cortex hormone or other immune modulators; and 11) Patients and their families cannot cooperate with doctors and staff, or history of mental illness (6).

Clinical data

We identified 126 cases of acute coronary syndrome as the research objects from March 2014 to January 2015 at the Cangzhou City Central Hospital, including 78 males and 48 females, ages 28–87 years old (Table 1). Patients were randomly divided into the experimental and control groups. The experimental group received MIDCAB while the control group received off-pump coronary artery bypass grafting (OP-CABG). We found no significant differences in age and sex between the 2 groups (Table 1).

Heart rate

We used a diving YX301 finger clip type oximeter to record heart rate at 1, 6, and 12 weeks after PCI. Measurement was performed in a quiet state, each count for 1 minute, measured 3 times, and we calculated the average heart rate.

Imaging diagnosis

Patients in each group were diagnosed by coronary angiography before surgery. Coronary angiography in 1 patient is shown in Figure 1. After surgery, we used a Philips IE33 (probe frequency 2.5 MHZ) color Doppler ultrasound to measure LVEDD, LVESD, LVEDV, LVESV and LVEF at 1, 6, and 12 weeks after the treatment.

Serological detection

After fasting for 6–8 h, we extracted 4–6 ml of venous blood from each patient to assess CK-MB, hs-CRP, pro-BNP, matrix metalloproteinase 9 (MMP-9), and other biochemical indicators.

Table 1. Comparison of clinical data between the 2 groups.

| Group             | # of cases | Male/female | Age (years) | Course of disease (years) | BMI (kg/m²) |
|-------------------|------------|-------------|-------------|---------------------------|-------------|
| Observation group | 63         | 34/29       | 61.8±4.6    | 1.7±1.4                   | 22.1±0.3    |
| Control group     | 63         | 38/25       | 57.8±6.4    | 2.3±1.8                   | 21.5±0.7    |
| t/X2 value        | –          | 0.17        | 0.85        | 0.82                      | 0.37        |
| P                 | –          | 0.72        | 0.18        | 0.13                      | 0.61        |

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at 6 and 12 weeks after surgery [3]. At 1 and 12 weeks after treatment, we used 2 ml of blood for detection of pro-BNP levels by rapid fluorescence immunoassay (triage tester); 2–4 ml were centrifuged for 10 min at 1200 rpm, stored at –80°C, and detected hs-CRP, pro-BNP, and MMP-9 levels by enzyme-linked immunosorbent assay (ELISA).

Surgical procedures

We used general anesthesia and double-lumen endotracheal intubation. Patients were in supine position, with left chest pad high at 30°. The front right and left chest wall automatic defibrillation electrode plate was connected with the automatic external defibrillator. We made a 6–8 cm incision in the left chest fourth or fifth intercostal space, with single-lung ventilation in the chest. We suspended the internal mammary artery with a pull-open system (Germany Fehling, State Food and Drug Administration Machinery) with rib retraction, applied moderate stretch, and raised the chest wall, thus providing good visualization. Under direct vision, we moved the left internal mammary artery (LIMA) up to the first rib upper edge, down to the fifth rib. We used titanium clips to cut off the LIMA branch, and washed the LIMA free end with papaverine saline rinse to prevent spasms. After identifying the phrenic nerve, we cut the pericardium, determined the left anterior descending (LAD) artery anastomosis site, estimated that the length of free LAD was sufficient, added heparin (1 mg/kg), and kept intraoperatively activating clotting time ACT over 300 s. We observed the LIMA blood flow in the distal end of the LIMA, placed the rib retractor, and suspended the pericardium. Using a heart stabilizer to fix the LAD after coronary incision, we placed a coronary artery shunt, and used 8-0 PROBLEN line to complete LIMA and LAD anastomosis. We used ultrasonic flowmetry to measure LIMA bridge blood flow after completion of anastomosis. After treatment with protamine-neutralized heparin, we placed a thoracic drainage tube and closed chest. For the prevention and treatment of postoperative incision pain, we use ropivacaine hydrochloride to block the intercostal nerve when closing the chest. For patients with LCX and RCA pathological changes, we started PCI treatment of LCX and (or) RCA at 1 week after surgery.

Statistical methods

We used SPSS19.0 for statistical analysis and processing. Qualitative data were tested by $\chi^2$, and for 4-fold table data that did not meet the conditions, we used the Fisher’s exact probability test. Quantitative data were compared and tested by ANOVA. $p<0.05$ indicated that differences were statistically significant.

Results

Comparison of surgery data

We found no significant differences between the 2 groups in time of admission to the hospital ($p>0.05$). The surgery time (65.2±12.6 min), the amount of bleeding (56.4±4.7 ml), and the postoperative observation time (6.8±1.3 days) for the MIDCAB group were all significantly lower than for the control group ($p<0.05$) (Table 2). These results support the benefits of MIDCAB during surgery.

| Group         | Number of cases | Operation time (min) | Bleeding during operation (V/ml) | Postoperative observation (t/d) | Interval of admission to operation (t/min) |
|---------------|----------------|----------------------|---------------------------------|---------------------------------|-------------------------------------------|
| Observation group | 63            | 65.2±12.6            | 56.4±4.7                        | 6.8±1.3                        | 120.5±63.6                                |
| Control group  | 63            | 170.3±12.9           | 258.3±13.9                     | 12.4±4.2                       | 127.4±52.1                                |
| $T$ value     |                | 30.14                | 11.88                           | 20.11                           | 0.24                                      |
| $P$ value     |                | 0.008                | 0.005                           | 0.002                           | >0.05                                     |

Table 2. Comparison of operations between the 2 groups.
Blood markers before and after surgery

At 6 and 12 weeks after surgery, the serum levels of CK-MB, hs-CRP, pro-BNP, and cTnl were significantly improved by both treatments (Table 3). However, we found no statistically significant differences between the 2 treatments (p>0.05), suggesting that both treatments confer similar clinical benefits.

Echocardiography indexes before and after surgery

Comparing echocardiography in the 2 groups before and after treatment, we found significant effects in LVEDD, LVESD, LVEF, and other indicators for both treatments (Table 4). However, we found no statistically significant differences when we compared the 2 groups (p>0.05) (Table 4). This result showed that the clinical benefits of the 2 groups were basically the same.

Prognosis

Neither treatment group showed obvious adverse reactions or liver and kidney function damage. In the MIDCAB group, death at the end of follow-up (1 year after treatment) was significantly lower than in the control group (χ²=24.79, p=0.003) (Table 5). Also, there were significantly fewer patients with cardiac shock in the MIDCAB group than in the control group (χ²=32.45, p=0.002). However, there was no significant difference in congestive heart failure at the end of follow-up between the 2 groups (χ²=1.39, p=0.357) (Table 5).

Discussion

CABG consists of using the patient's own vein or artery to connect the distal end of the affected coronary artery, bypassing the narrow coronary artery, and restoring the blood supply of the ischemic myocardium [6]. CABG is one of the main methods used to treat coronary heart disease and myocardial infarction [7]. The traditional CABG requires cardiopulmonary bypass, with produces major trauma, requires a long recovery time, and has a high incidence of death and complications, including arrhythmia and bleeding [8,9]. MIDCAB grafting is done through median sternotomy or intercostal incision, without cardiopulmonary bypass or stopping the beating of the heart, and finishes with coronary artery anastomosis. This procedure increases patient safety, and greatly reduces the operative mortality and postoperative complications [10,11].

MIDCAB and TECAB (totally endoscopic coronary artery bypass) technologies can significantly improve clinical outcomes, especially for patients not suitable for coronary stents, and can significantly reduce the surgery rate of CABG. MIDCAB surgery has been gradually accepted by most cardiac surgeons throughout the world [12–15]. MIDCAB treatment of LAD lesions with LIMA has a good long-term patency compared with bare stents and vein grafts [16], does not increase the mortality rate or the incidence of myocardial infarction, and the revascularization rate of the MID group was lower than in the PCI group [17].

Table 3. Comparison of blood markers between the 2 groups before and after surgery.

| Index   | Group        | # of cases | Before treatment | 6 weeks after treatment | 12 weeks after treatment |
|---------|--------------|------------|------------------|-------------------------|-------------------------|
| pro-BNP (ng/dl) | Observation group | 63         | 587.8±41.8       | 198.7±23.1              | 157.8±10.2              |
|         | Control group | 63         | 617.4±54.5       | 198.2±16.5              | 165.4±19.2              |
| T value |              |            | 0.76             | 0.62                    | 0.81                    |
| P value |              |            | 0.527            | 0.33                    | 0.18                    |
| CK-MB (UI/L) | Observation group | 63         | 1.29±0.32       | 0.33±0.11               | 0.24±0.12               |
|         | Control group | 63         | 1.22±0.47       | 0.38±0.44               | 0.21±0.38               |
| T value |              |            | 1.87             | 1.31                    | 0.41                    |
| P value |              |            | 0.20             | 0.29                    | 0.71                    |
| cTnI (UI/L) | Observation group | 63         | 1.05±0.33       | 0.46±0.11               | 0.97±0.04               |
|         | Control group | 63         | 1.18±0.12       | 0.87±0.14               | 0.96±0.31               |
| T value |              |            | 1.23             | 1.68                    | 0.28                    |
| P value |              |            | 0.11             | 0.33                    | 0.72                    |
| CRP (μg/L) | Observation group | 63         | 287.4±49.8      | 181.7±11.2              | 108.4±13.6              |
|         | Control group | 63         | 292.5±24.5      | 194.5±23.2              | 101.4±11.4              |
| T value |              |            | 0.42             | 1.27                    | 1.81                    |
| P value |              |            | 0.87             | 0.14                    | 0.12                    |
In our study, the 2 groups had a similar time of admission to the hospital, but MIDCAB improved operation time, bleeding, and postoperative observation time compared to the control group. These results are similar to a previous report showing that MIDCAB surgery had good outcomes in elderly patients with coronary artery stenosis or occlusion who did not qualify for stent interventional therapy, with the largest benefits coming from avoiding cardiac arrest and cardiopulmonary bypass [18]. MIDCAB reduces surgery time and bleeding, is well tolerated by elderly patients, and demonstrates better postoperative recovery [18].

Blood markers and echocardiography were similarly improved before and after treatment in both groups. The blood markers showed no obvious adverse reactions or liver and kidney function damage. Heart function and multiple organ function were not severely damaged after the operation. These results indicate that MIDCAB and OP-CABG surgery had basically the same benefits, but 1 year after treatment, number of deaths at the end of follow-up and incidence of cardiac shock were significantly lower in the MIDCAB group. We found no significant differences in congestive heart failure at the end of follow-up between the 2 groups. We think that this result was due to the reduced trauma in minimally invasive surgery. Due to the poor tolerance for surgery in elderly patients, minimally invasive surgery effectively avoids inflammation reaction following the surgical trauma of OP-CABG surgery, especially the effect of inflammatory cytokines IL-6 and IL-10, TNF-α, and autoimmune reactions on postoperative recovery. Especially, patients with coronary heart disease often have abnormalities of blood lipid and glucose metabolism, and the effect of major trauma after median sternotomy on the immune neural system and the endocrine system further aggravates the existing basic diseases [19–21].

### Conclusions

In summary, our data support that although the effect of MIDCAB and OP-CABG surgeries is basically similar, MIDCAB significantly reduces postoperative in-hospital stay and intraoperative blood transfusion volume, and effectively improve the clinical prognosis.

### Table 4. Comparison of echocardiography indexes between the 2 groups before and after treatment.

| Index  | Group                  | # of cases | Before treatment | 6 weeks after treatment | 12 weeks after treatment |
|--------|------------------------|------------|------------------|-------------------------|-------------------------|
|        | Observation group      | 63         | 61.4±15.3        | 56.2±12.0               | 51.3±5.1                |
|        | Control group          | 63         | 59.4±12.5        | 59.0±11.8               | 52.2±7.6                |
|        | T value                | –          | 0.38             | 0.52                    | 2.48                    |
|        | P value                | –          | 0.37             | 0.51                    | 0.71                    |
|        | LVEDD (mm)             | Observation group | 63 | 42.3±7.7        | 38.5±4.3               | 34.2±2.6                |
|        | Control group          | 63         | 40.8±3.2        | 41.6±3.8               | 39.5±5.8                |
|        | T value                | –          | 0.22             | 0.36                    | 1.82                    |
|        | P value                | –          | 0.39             | 0.42                    | 0.28                    |
|        | LVESD (mm)             | Control group | 63 | 43.4±5.6        | 50.3±4.8               | 57.5±2.6                |
|        | Observation group      | 63         | 44.9±7.2        | 48.2±5.5               | 59.2±5.8                |
|        | T value                | –          | 1.23             | 2.47                    | 1.73                    |
|        | P value                | –          | 0.45             | 0.25                    | 0.49                    |
|        | LVEF (%)               | Control group | 63 | 43.4±5.6        | 50.3±4.8               | 57.5±2.6                |
|        | Observation group      | 63         | 44.9±7.2        | 48.2±5.5               | 59.2±5.8                |
|        | T value                | –          | 1.23             | 2.47                    | 1.73                    |
|        | P value                | –          | 0.45             | 0.25                    | 0.49                    |

### Table 5. Comparison of follow-up data of patients of the 2 groups.

| Item                         | # of follow-up | Control group | Observation group | χ²   | P       |
|------------------------------|----------------|---------------|-------------------|------|---------|
| Death at the end of follow-up| 126            | 9 (0.12)      | 2 (0.03)          | 24.79| 0.003   |
| Cardiac shock                | 126            | 12 (0.16)     | 4 (0.05)          | 32.45| 0.002   |
| Congestive heart failure     | 126            | 1 (0.02)      | 0 (0.00)          | 1.39 | 0.357   |
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