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Traditional coronary artery bypass graft versus totally endoscopic coronary artery bypass graft or robot-assisted coronary artery bypass graft – meta-analysis of 16 studies

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Abstract. – BACKGROUND: Robot-assisted coronary artery bypass graft (RACAB) or totally endoscopic coronary artery bypass graft (TECAB) utilizing the da Vinci surgical system is increasingly used to treat coronary heart disease (CHD), although traditional coronary artery bypass graft (CABG) remains a classic treatment. The aim of the present study was to establish the advantages and disadvantages of TECAB (or RACAB) compared with traditional CABG.

METHODS: PubMed and EBSCO databases were searched for studies of TECAB (or RACAB) using the da Vinci surgical system and CABG for CHD. The meta-analysis included 16 studies (2290 patients).

RESULTS: Compared with traditional CABG, TECAB (or RACAB) had lower rates of major adverse cardiac or cerebrovascular events (MACCE) 12 months postprocedure (7.0% vs. 12.4%; odds ratio [OR], 0.53; confidence interval [CI], 0.38-0.74; $p < 0.05$). Subgroup analysis highlighted the differences between TECAB and RACAB as follows: TECAB decreased the rate of renal failure requiring hemofiltration (OR, 0.25; CI, 0.07-0.88), wound infection (OR, 0.11; CI, 0.11-1.99), and stroke (OR, 0.14; CI, 0.02-0.77) during follow-up, but increased the need for re-exploration for bleeding and MACCE (OR, 2.18; CI, 1.14-4.16; $p < 0.05$).

CONCLUSIONS: TECAB and RACAB are safe and feasible therapies for CHD. This meta-analysis supports TECAB(or RACAB)using the da Vinci surgical system to treat CHD with reduced MACCE after 12 months. In addition, TECAB and RACAB do not increase the rates of MACCE in hospital, graft stenosis (or occlusion), and the need for reintervention compared with CABG.

Key Words:
Coronary artery bypass graft, Totally endoscopic coronary artery bypass graft, Robot-assisted coronary artery bypass graft, Meta-analysis, Da Vinci surgical system.

Introduction

Coronary heart disease (CHD) is a serious cardiovascular disease that can cause disability and death. The therapeutic methods include conservative treatment with drugs, percutaneous coronary intervention (PCI)[1], and coronary artery bypass graft (CABG) surgery[2]. Until now, CABG has been regarded as an established, safe, and efficient procedure. In addition, it has been proved many times that it reduces morbidity, mortality, and rates of graft occlusion[3-5]. However, traditional CABG often carries a high operation risk requires a large incision, and has a long recovery time. CABG through mini-thoracotomy (or minimally invasive direct coronary artery bypass (MIDCAB)) has been developed to improve on the disadvantages of traditional CABG[6]. With robot and endoscopy technologies being implemented in medicine, the robot-assisted coronary artery bypass graft (RACAB) has received growing attention.

In recent years, the da Vinci surgical system has become the most widely used robot-assisted operation system in the world, and is being employed for CABG in some cardiac centers. RACAB is thought to have many advantages over traditional CABG such as a low operation risk, the need for only a small incision, and a short recovery time. More recently, totally endoscopic coronary artery bypass graft (TECAB) surgery has been developed which is an advanced form of MIDCAB and RACAB[7]. Patients can undergo cardiac surgery without thoracotomy with the da Vinci surgical system. Some previous studies have suggested that TECAB (or RACAB) using the da Vinci surgi-

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cal system has advantages over traditional CABG[8,9], but most were single-center, and there has been no high-quality randomized, controlled trial or meta-analysis until now.

In this meta-analysis, we aimed to establish the advantages and disadvantages of TECAB (or RACAB) compared with traditional CABG, using information from published papers.

Methods

Eligibility Criteria and Information Sources

The eligibility criteria were broad to enable more articles to be included in our analysis, because there were not many published articles about TECAB (or RACAB). Indeed, the only papers were clinical trials and these were included based on the following criteria: (1) trials about TECAB (or RACAB), (2) sample size of ≥ 40 patients, (3) complete preoperative information of patients, (4) extensive perioperative data, and (5) follow-up for as long as possible.

We searched the PubMed and EBSCO host databases between October 2002 and October 16, 2013. The terms used for the Boolean search were (heart OR coronary AND surgery) AND (Da Vinci OR Davinci OR robotics OR robot), with results limited to humans, and English language.

Exclusion Criteria

To reduce the possibility of bias, we defined some exclusion criteria as follows: (1) trials with a significant lack of preoperative, perioperative, or follow-up information, (2) data presented as medians without mean values, and (3) data used in previous trials.

Data Collection Process

After the preliminary selection, the titles and abstracts of the articles were checked. If the article was selected, it was rescreened by examining the full text. Our predefined eligibility and exclusion criteria were added for the third screening. To guarantee that all data were extracted uniformly, the articles were examined by the same reviewer.

The data included baseline characteristics of patients (age, sex, body mass index [BMI], smoking, hypertension, diabetes mellitus, dyslipidemia, angina, previous myocardial infarction [MI], cerebrovascular disease [CVD], peripheral vascular disease [PVD], and chronic obstructive pulmonary disease [COPD]), perioperative outcomes (total procedure time, time in an intensive care unit [ICU], postprocedure hospital stay, perioperative MI, perioperative cerebral vascular accident [CVA], pneumonia, renal failure, wound infection, anastomotic stenosis, re-exploration for bleeding, and hospital mortality), and follow-up (major adverse cardiac or cerebrovascular events [MACCE]).

Statistical Analysis

We performed fixed effects meta-analyses using odds ratios (ORs) for dichotomous data and weighted mean difference for continuous data. In the present analysis, a statistically significant p value of < 0.05 suggests that differences in patient characteristics may have affected the results of some of the studies in the meta-analysis. We had planned to perform some subgroup analysis according to, for example, sex, and age. However, as TECAB and RECAB are new treatments, there was insufficient data for this to be possible. In our analysis, we separated the robot-assisted CABG into 2 groups: RACAB through mini-thoracotomy and TECAB. RACAB through mini-thoracotomy (referred to as RACAB) was defined as robotic internal mammary artery harvesting, followed by completion of a minimally invasive direct CABG without a robot through a lateral thoracic incision. TECAB was performed on the arrested heart or on the beating heart.

Adjustment for Differences Between Groups

We anticipated that different studies would focus on different preprocedural characteristics. Therefore, we collected data on the variables that were available in both groups. When values of a particular characteristic in a study were absent, the study was eliminated from the statistical analysis of that characteristic. If a study had several variables absent, it was excluded from the meta-analysis to prevent bias.

Results

Study Selection

The flow diagram of study selection is given in Figure 1. The literature search initially produced 832 articles published between October 2002 and October 2012. After screening, 16 studies with a total of 2290 patients were included in our meta-

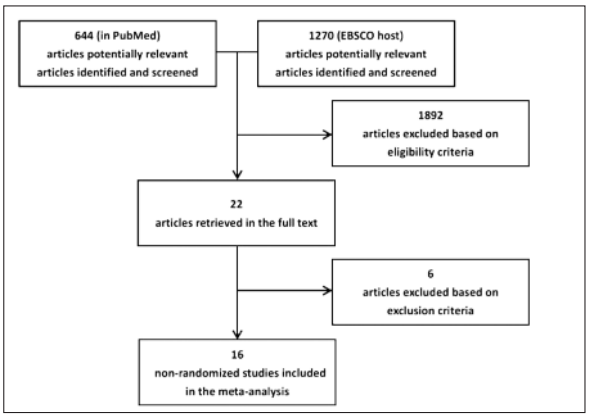

Figure 1. Flow diagram of article selection.

analysis. Of these, 1414, 632, and 876 patients underwent TECAB, RACAB, and other surgical methods, respectively. Details of the included studies are listed in Table I. Due to the lack of a high-quality control study, we selected a study of 897 patients who underwent CABG that was published in the New England Journal of Medicine as a control group[10].

Table II shows the baseline characteristics of the study patients. The mean age of the TECAB (or RACAB) group (61.6 ± 4.1 years) was less than that of the control group (65.0 ± 9.8 years). There was no statistically significant difference in BMI between the 2groups (28.2 ± 1.7 vs. 27.9 ± 4.5, respectively). A much higher proportion of patients smoked in the TECAB (or RACAB) group, and more patients had hypertension, diabetes, and CVD than in the CABG group. The percentage of patients with angina was lower in the TECAB (or RACAB) group (68.3%) than in the CABG group (85.2%). In addition, 24.1% and 33.8% of patients in the TECAB (or RACAB) and CABG groups, respectively, had previous MI. More than half of the patients (60.5%) in the TECAB (or RACAB) group met the criteria of dyslipidemia, and 5.7% and 10.9% had PVD and COPD, respectively. There was no unified and clear standard to define dyslipidemia in the CABG group; therefore, no relevant data could be obtained. Furthermore, there were no PVD and COPD data for the CABG group.

Primary Outcomes

To assess the feasibility of a new surgical method, the procedure time and postoperative recovery time were examined. In this study, the mean total procedure time of the TECAB (or RACAB) group was 3.9 h, the mean time in the ICU was 27.7 h, and the mean postprocedure hospital stay was 6.7 d. In the CABG group, the mean total procedure time was 3.4 h, which was a little shorter than in the TECAB (or RACAB) group. However, the postprocedure hospital stay was much greater (9 d) than the TECAB (or RACAB) group.

The follow-up period was 1-5 years. The main follow-up events were MACCE. The rates of MACCE in hospital were 4.1% (46/1126) and 5.4% (47/870) in the TECAB (or RACAB) and CABG groups, respectively (Figure 2). Patients who were followed up for < 1year were eliminated

Table I. Features of trials included after full-text inspection.

Author and reference	Year	Location	Cases	Age	Male	Major method
Dogan S, et al 10	2002	Germany	45	63	32	All cases TECAB
Mishra YK, et al 11	2004	India	268	56.2	213	254 cases RACAB
Turner WF, et al 12	2006	USA	70	65.9	22	67 cases RACAB
Srivastava S, et al 13	2006	USA	150	67.2	99	All cases TECAB
Bonatti J, et al 14	2006	Austria	40	59	28	85 cases TECAB
Argenziano M, et al 15	2006	USA	98	58.2	69	72 cases TECAB
Schachner T, et al 16	2007	Austria	85	58 (m)	66	72 cases TECAB
de Canniere D, et al 17	2007	Belgium	228	59.2	NA	164 cases TECAB
Kiaii B, et al 18	2008	Canada	60	59.9	47	58 cases RACAB
Nikolaos B, et al 19	2009	Austria	56	64	49	All cases TECAB
Bonatti J, et al 20	2009	USA	100	59 (m)	81	89 cases TECAB
Srivastava S, et al 21	2010	USA	214	67.9	111	187 cases TECAB
Wiedemann D, et al 22	2011	USA	325	62 (m)	240	279 cases TECAB
Balkhy HH, et al 23	2011	USA	120	66.3	86	117 cases TECAB
Schachner T, et al 24	2011	Austria	326	60	243	280 cases TECAB
Gao C, et al 25	2011	China	105	59	77	All cases RACAB

TECAB: totally endoscopic coronary artery bypass graft; RACAB: robot-assisted coronary artery bypass graft; m: mean; NA: not available.

Table II. Baseline characteristics of TECAB/RACAB and CABG patients.

Characteristic	TECAB/RACAB	CABG
Age	61.6 ± 4.1	65.0 ± 9.8
Male sex	70%	72.30%
BMI	27.9 ± 4.5	27.9 ± 4.5
Smoking	39.90%	22.00%
Hypertension	66.40%	64.00%
Diabetes mellitus	25.40%	24.60%
Dyslipidemia	60.50%	NA
Angina	68.30%	85.20%
Previous MI	24.10%	33.80%
CVD	9.20%	8.40%
PVD	5.70%	NA
COPD	10.90%	NA

TECAB: totally endoscopic coronary artery bypass graft; RACAB: robot-assisted coronary artery bypass graft; CABG: coronary artery bypass graft; BMI: body mass index; MI: myocardial infarction; CVD: cerebrovascular disease; PVD: peripheral vascular disease; COPD: chronic obstructive pulmonary disease; NA:not available.

from the analysis. After 1 year, the MACCE rate was significantly lower in the TECAB (or RACAB) group than in the CABG group (7.0% [60/862] and 12.4% [105/849], respectively). The graft stenosis or occlusion rate was also lower in the TECAB (or RACAB) group (1.8% [20/1131]) than in the CABG group (2.5% [21/854]). However, the reintervention rates were similar (1.4% [16/1131] and 1.3%[11/849], respectively). From the forest plot (Figure 2), we concluded that, compared with traditional CABG, TECAB (or RACAB) had lower rates of MACCE 12 months post procedure (7.0% vs. 12.4%; OR, 0.53; confidence interval (CI), 0.38-0.74; $p < 0.05$).

Subgroup Outcomes

The TECAB (or RACAB) group was separated into 2 subgroups: TECAB and RACAB. The mean total procedure time and ventilation time were 3.9h and 10.4h, respectively, in the TECAB group (Table III), which were shorter than those in the RACAB group (5.0 hand 34.5 h, respectively). However, the time in the ICU and postprocedure hospital stay with TECAB were longer than with RACAB (25.6 h vs. 11.5 h, and 6.7 d vs. 5.9 d, respectively).

We also analyzed several perioperative events. Rates of CVA and hospital death were similar in the 2 groups (1.0% vs. 1.0%, and 0.30% vs. 0.30%, respectively). The rates of renal failure requiring hemofiltration, pneumonia, and wound infection were all lower in the TECAB than in the RACAB group (0.8% vs. 3.1%, 2.8% vs. 3.3%, and 0% vs. 0.7%, respectively). However, the rates of MI, anastomotic stenosis, and re-exploration for bleeding were higher in the TECAB than in the RACAB group (1.2% vs. 0.7%, 1.3%

Table III. Intraoperative and postoperative outcomes of TECAB and RACAB.

Outcome	TECAB	RACAB
Total procedure time (h)	3.9	5.0
Ventilation time (h)	10.4	34.5
ICU stay time (h)	25.6	11.5
Postprocedure hospital stay time (d)	6.7	5.9
Perioperative MI	1.20%	0.70%
Perioperative CVA	1.00%	1.00%
Pneumonia	2.80%	3.30%
Renal failure	0.80%	3.10%
Wound infection	0.00%	0.70%
Anastomotic stenosis	1.30%	0.20%
Reexploration for bleeding	4.10%	1.60%
Hospital death	0.30%	0.30%

TECAB: totally endoscopic coronary artery bypass graft; RACAB: robot-assisted coronary artery bypass graft; ICU: intensive care unit; MI: myocardial infarction; CVA: cerebral vascular accident; h: hours; d: days.

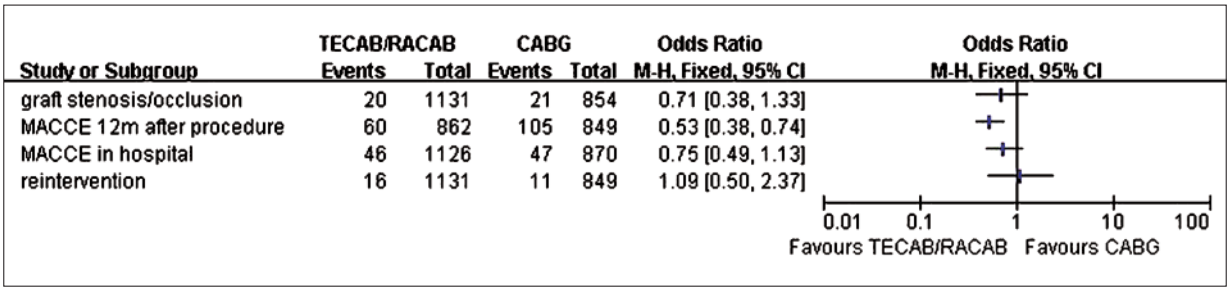

Figure 2. TECAB/RACAB and CABG follow-up outcomes. TECAB: totally endoscopic coronary artery bypass graft; RACAB: robot-assisted coronary artery bypass graft; MACCE: major adverse cardiac or cerebrovascular events; M-H: Mantel-Haenszel.

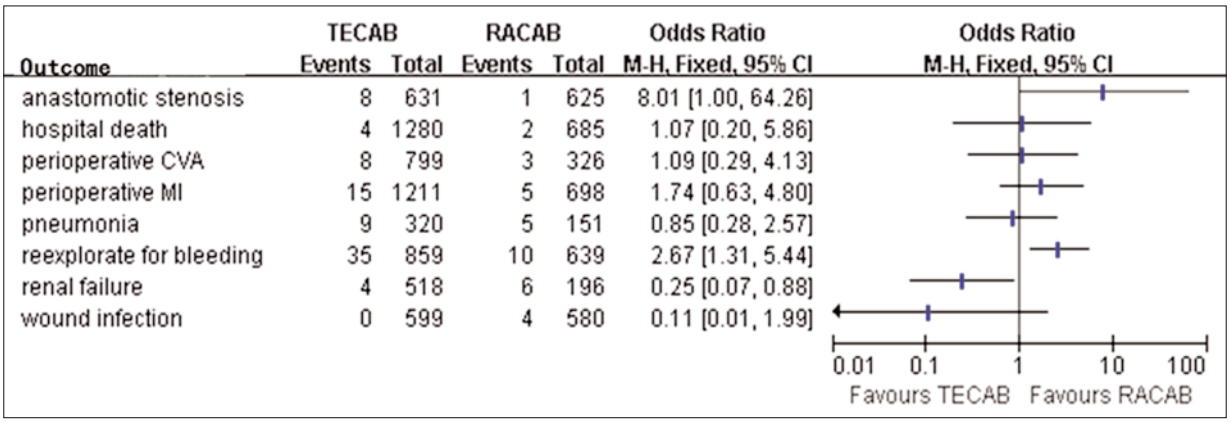

Figure 3. TECAB and RACAB perioperative outcomes. TECAB: totally endoscopic coronary artery bypass graft; RACAB: robot-assisted coronary artery bypass graft; CVA: cerebral vascular accident; MI: myocardial infarction; M-H: Mantel-Haenszel.

vs. 0.2%, and 4.1% vs. 1.6%, respectively). When these data were compared on a forest plot, it was concluded that TECAB was associated with a significant reduction in the rates of renal failure (OR, 0.25; CI, 0.07-0.88) and wound infection (OR, 0.11; CI, 0.11-1.99), but, in contrast, there was a 167% increase in the risk of reexploration for bleeding (OR, 2.67; CI, 1.31-5.44; Figure 3).

Unlike the front study, there were incomplete data on MACCE in hospital. In the TECAB group, the total rate of MACCE was 5.4% (66/1124) which included the death, stroke, and MI rates (0.2% [2/917], 0.6% [4/648], and 0.6% [7/1211], respectively; Figure 4). In the RACAB group, the total rate of MACCE was 2.6% (11/431). The rate of death was lower (but not significantly) than with TECAB (0.1%[1/749]), and the stroke rate was 4.3% (2/46). The risk of MACCE in the RACAB group was much lower than in the TECAB group (OR, 2.18; CI, 1.14-4.16), However, the risk of stroke was significantly higher (OR, 0.14; CI, 0.02-0.77). There was no significant difference between the groups in the MI rate (0.6% [7/1211] vs. 0.6%[2/326], respectively). During follow-up, the graft stenosis or occlusion rate was higher (but not significantly) in the TECAB than the RACAB group (1.8% [20/1131] vs. 0.8% [5/639], respectively), and the rates of reintervention (the need for repeated surgery or PCI) were0.8%(8/1030) vs. 1.1% (8/749), respectively.

Discussion

There is no doubt that developments are tending towards minimally invasive surgery, and the

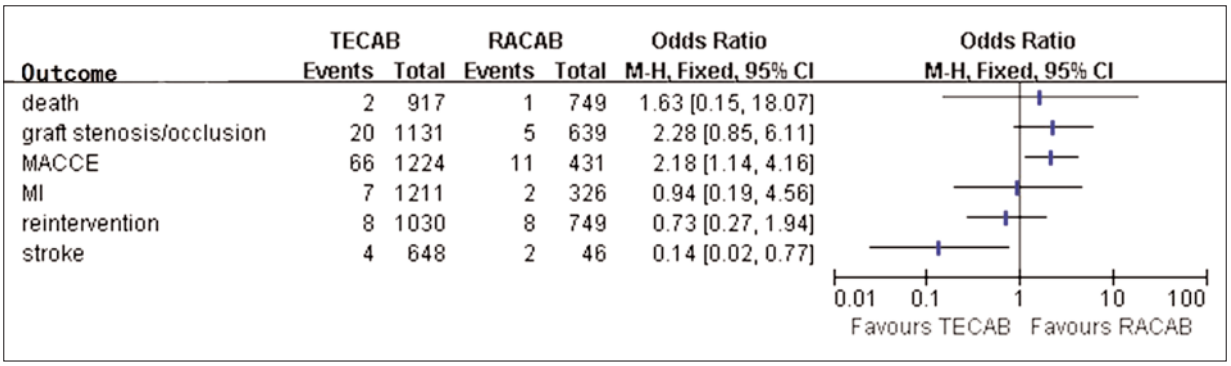

Figure 4. TECAB and RACAB follow-up outcomes. TECAB: totally endoscopic coronary artery bypass graft; RACAB: robot-assisted coronary artery bypass graft; MACCE: major adverse cardiac or cerebrovascular events; MI: myocardial infarction; M-H: Mantel-Haenszel.

da Vinci surgical system is an outstanding one. Since the da Vinci surgical system was authorized by the Food and Drug Administration (FDA) to be used for surgery in humans, more than 2585 da Vinci surgical systems have been installed in over 2025 hospitals worldwide[27,28]. The da Vinci surgical system enables surgeons to perform delicate and complex operations through a few tiny incisions with increased vision, precision, dexterity, and control. Minimally invasive surgery is also a development trend for coronary artery revascularization. Although CHD can be treated by PCI, CABG is still the first choice in CHD in the left main coronary artery or triple artery disease.

In our meta-analysis, comparisons were conducted not only between the robot-assisted CABG (TECAB or RACAB) and traditional CABG but also between TECAB and RACAB. In the 16 eligible studies, 11 mainly reported on TECAB, and 5 on RACAB. As previously described, since there were no satisfactory control groups in previous research, a control group was selected by searching the electronic database. The chosen control group, from a study on CABG and PCI published in the New England Journal of Medicine, was selected because there was comparability between the study and control groups.

The primary outcome of postoperative recovery time (postprocedure hospital stay) is a major consideration, and was significantly shorter in the TECAB (or RACAB) group than in the CABG group. This indicates that patients will recover faster after undergoing TECAB or RACAB. In addition, the rates of MACCE in hospital and 12 months postprocedure were lower in the TECAB (or RACAB) group, which demonstrated the feasibility and safety of the new methods.

For the subgroup outcomes, some perioperative events of TECAB and RACAB were compared in more detail. TECAB showed greater advantages in reducing total procedure time and ventilation time than RACAB. However, we noticed that the time in the ICU and postprocedure hospital stay were longer with TECAB than with RACAB. This was because the occurrences of anastomotic stenosis, re-exploration for bleeding, and perioperative MI were higher in the TECAB group than in the RACAB group. However, the above shortcoming may be improved with training and experience. The need for such a small incision with TECAB causes minimum trauma, and therefore, the rate of renal failure (requiring hemofiltration) and wound infection were satisfactory. Most of the time, TECAB was carried out with 1-lung ventilation, and the short ventilation time following the procedure, may lead to a lower rate of pneumonia.

The characteristics of study patients were compared between the TECAB (or RACAB) and CABG groups. Patients from the TECAB (or RACAB) group were usually young and had fewer diseases. This may have been related to the inclusion criteria. During the period of learning of a new therapy, surgeons tend to be more inclined to choose patients who are young with fewer baseline complications for inclusion in their studies.

In order to overcome the differences in patients' characteristic which would reduce the comparability, we compared the TECAB and RACAB groups in detail as well as the robot-assisted and traditional CABG groups. The rates of perioperative MI, anastomotic stenosis, and re-exploration for bleeding were higher in the TECAB group than in the RACAB group. However, in contrast, occurrences of pneumonia, renal failure, and wound infection were lower. There were no significant differences between the 2 groups in perioperative CVA and death in hospital. MACCE were higher in the TECAB than in the RACAB group, and the rate of graft stenosis or occlusion was also higher. This might have been caused by inexperience. Bonatti et al[21] divided a series of 100 patients into 4 phases. With increasing numbers of operations completed by the surgeon, the operative times and hospital stays decreased significantly with each subsequent phase, and the occurrence rate of adverse events decreased correspondingly.

One of the criticisms of robot-assisted CABG (TECAB or RACAB) has been prolonged operative time compared with traditional CABG. In our study, the mean operative times were 3.9 h and 3.4 h with TECAB or RACAB and CABG, respectively. After analysis, some intraoperative technical problems were found that may have impacted operative times. Furthermore, inexperience affected every step of the procedures. Once this was overcome, the operative time clearly became shorter. In addition, anastomotic problems, re-exploration for bleeding and left thoracic aorta ITA injuries prolong operative times. When comparing TECAB with RACAB, we found that the operative time in the TECAB group was significantly shorter than that in the RACAB group. Because most researchers prefer to perform

RACAB only once they have fully mastered the robot-assisted procedure, TECAB has become more frequently adopted. Furthermore, opening and closing the incision of the mini-thoracotomy during the RACAB procedure would prolong the operative time.

In our study, we found that the rate of graft stenosis or occlusion was lower with robot-assisted CABG than with traditional CABG during follow-up. However, the rate of reintervention was slightly (but not significantly) higher in the robot-assisted CABG group. When the MACCE were compared, the rate with TECAB after 12 months was lower than with CABG; however, this did not reach statistical significance. This outcome demonstrated that the efficacies between the TECAB (or RACAB) and traditional CABG groups were similar, which suggests that the new methods of CABG are feasible. Furthermore, there were fewer MACCE > 12 months postprocedure with robot-assisted CABG, demonstrating a clear advantage for these procedures because of the outstanding outcomes of long-term follow-up.

Our study has demonstrated that robot-assisted CABG using the daVinci surgical system is feasible and safe. This assumption was drawn from not only a single study but also a multicenter and synthetic analysis. Many variables were compared in this study, especially between TECAB and RACAB, and these abundant data provide a foundation for future progress, and may help in the choices made with respect to surgery and perioperative management.

However, in our report, there is a lack of high-quality randomized controlled trials. This is perhaps partly because the da Vinci surgical system is expensive and few hospitals are equipped with it. Furthermore, it is a new technology within cardiac surgeries, which are difficult and high precision compared with other surgeries. The utilization of the da Vinci surgical system in cardiac surgeries is, therefore, in the initial stages. This limits the number of cases that can be included within even a single center; thus, designing a randomized controlled trial is very difficult.

Moreover, the clinicians are inexperienced in the technology. Different doctors have different surgical skills in different centers, and da Vinci robot-assisted minimally invasive surgery requires many new skills. Therefore, many centers are still learning the skills needed, which may cause an unsatisfactory bias in the outcome of the surgery.

In addition, a factor that cannot be ignored is patient selection. Large centers or hospitals are usually those equipped with the da Vinci robot systems, and these institutions often care for patients with more serious illnesses than other centers. This selection bias in patients' characteristics may affect the results of the new therapeutic methods; the rate of MACCE maybe increased and the outcomes more negative.

Conclusions

TECAB and RACAB using the da Vinci surgical system are safe and feasible therapies for CHD, and reduce the rate of MACCE after 12 months. Furthermore, they do not increase the rates of MACCE in hospital, graft stenosis (or occlusion), and reintervention compared with CABG. However, more evidence is needed to further investigate and support TECAB and RACAB for CHD.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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