VIEWPOINT

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Could minimally invasive surgical revascularization procedures become the gold standard for ischemic heart disease?

¿Podrían los procedimientos quirúrgicos de revascularización mínimamente invasivos convertirse en el estándar de oro para la cardiopatía isquémica?

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ABSTRACT

Ischemic heart disease is the most common and deadliest heart disease and is a huge health burden costing billions of dollars. The current optimal treatment for this disease is myocardial revascularization and the gold standard method in the medium- and long-term management is coronary bypass surgery. This surgery is a highly invasive operation due to the use of a cardiopulmonary bypass machine and open sternotomy technique; however, at the same time, it has a short-term increase in morbidity and complication rate. Off-pump coronary artery bypass grafting surgery, minimally invasive direct coronary artery bypass surgery, and minimally invasive cardiac surgery-coronary artery bypass grafting were introduced in the past years. However, these treatments have not yet become the widespread gold standard, and discussions on durability and survival are still ongoing. In this review, we will discuss

RESUMEN

La cardiopatía isquémica es la enfermedad cardíaca más común y más mortal, y es una enorme carga para la salud que cuesta miles de millones de dólares. El tratamiento óptimo actual para esta enfermedad es la revascularización miocárdica y el método estándar de oro en el manejo a mediano y largo plazo es la cirugía de bypass coronario. Esta cirugía es una operación altamente invasiva debido al uso de una máquina de derivación cardiopulmonar y técnica de esternotomía abierta; sin embargo, al mismo tiempo, tiene un aumento a corto plazo en la tasa de morbilidad y complicaciones. La cirugía de revascularización coronaria sin circulación extracorpórea y la cirugía mínimamente invasiva con bomba o sin bomba se han introducido en los últimos años. No obstante, estos tratamientos aún no se han convertido en el estándar de oro generalizado y las discusiones sobre la durabilidad y la supervivencia aún están en curso. En esta revisión,

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minimally invasive coronary artery bypass grafting techniques in terms of survival and durability.

Keywords: ischemic heart disease, minimally invasive surgery, myocardial revascularization, off-pump coronary artery bypass.

analizaremos las técnicas de injerto de derivación de arteria coronaria mínimamente invasivas en términos de supervivencia y durabilidad.

Palabras clave: *cardiopatía isquémica, cirugía mínimamente invasiva, revascularización miocárdica, cirugía de revascularización coronaria sin bomba.*

INTRODUCTION

Cardiovascular disease accounts for one-third of all deaths worldwide, with the most common subgroup being ischemic heart disease (IHD), that accounts for more than 9 million deaths annually.[1] According to recent projections, prevalence of IHD is expected to increase gradually in the world due to the rapidly increasing rates of metabolic syndromes such as diabetes and the aging population.[1] Additionally, IHD presents a cumbersome health burden (e.g., the cost of IHD is 1-1.5% of the total gross domestic product in USA), and it is estimated that more than 1 trillion dollars will be spent globally in 2030.[2]

The primary treatment option for ischemic heart disease (IHD) is myocardial revascularization, which can be achieved through either coronary artery bypass surgery (CABG) or percutaneous coronary intervention (PCI).[3] Both CABG and PCI have their own advantages and disadvantages. CABG is associated with better medium- and long-term survival rates, while PCI has a higher likelihood of requiring repeat revascularization procedure.[3] CABG still presents with the same procedural aggressiveness and invasiveness despite its history of more than half a century.[4] Since CABG is traditionally performed with sternotomy, it increases the risk of infection and delays healing. In addition, the cardiopulmonary bypass machine stimulates inflammatory processes, causes hemolysis and poses a significant risk for thromboembolism.[5,6] In an effort to reduce the risks and complications associated with traditional open-heart surgery, such as total sternotomy and the use of cardiopulmonary bypass, many minimally invasive techniques have been developed in recent years.[7] These techniques involve making smaller incisions and using specialized instruments and technology to perform the procedure, which can result in less pain, faster recovery times, and fewer complications. In this review, different minimally invasive CABG techniques are compared in terms of survival, durability, and feasibility.

MINIMALLY INVASIVE APPROACHES

Off-pump coronary artery bypass grafting surgery (OPCAB)

OPCAB, a variation of traditional CABG, involves performing surgery on a beating heart without using a cardiopulmonary bypass machine.[8] This technique is expected to reduce the risk of various complications related to the use of cardiopulmonary bypass, including hemolysis, inflammatory cascades, and thromboembolism, resulting in better outcomes and faster recovery.[8] It is major advantages are shorter in-hospital stays and enhanced recovery.[8]

Controversies surrounding OPCAB mainly relate to the durability and quality of the anastomosis, the learning curve for the procedure, and its effectiveness in reducing major adverse cardiac and cerebrovascular events (MACCE), and in-hospital mortality. Observational studies and single-center studies have reported promising results, showing a reduced length of hospital stay and lower risks of stroke and new-onset atrial fibrillation.[9-11] However, randomized controlled studies have not shown significant benefits in terms of MACCE or in-hospital mortality and have even shown increased rates of repeated revascularization and mortality *(Table 1)*.[12-14]

In the ROOBY trial, although there was no difference between OPCAB and conventional CABG in terms of preoperative complications and recovery, conventional CABG was found to be better in long-term survival.[12] The CORONARY trial found that OPCAB patients had a higher risk of pulmonary complications and higher rates of reoperation without any mortality benefit compared to traditional CABG patients.[13] In addition, the low number of distal anastomoses in the off-pump cohorts in the existing studies in the literature raises concerns about incomplete revascularization of heart teams.[9-14] In contrast, Diegeler et al. showed that patients who underwent OPCAB had lower incidence rates of atrial fibrillation, stroke, and ventilation time, as well as shorter hospital stays, than those who underwent conventional CABG.[14]

Despite concerns about the learning curve for this technique and the potential for fewer anastomoses, OPCAB may offer important advantages over traditional CABG for "subgroups of IHD patients".

Minimally invasive direct coronary artery bypass surgery (MIDCAB)

The survival of patients with IHD depends, at a large extent, on the treatment and patency of the left anterior descending (LAD) and left main coronary arteries (LMCA). One of the oldest techniques for restoring arterial flow to the heart is bypass surgery, which involves anastomosis of the left intrathoracic artery (LITA) to the LAD.[15] Stenting is useful in single-vessel coronary artery disease, and has been

shown to fail in the long term while surgery is successful in the long term. However, it might have severe complications due to invasiveness. To overcome these problems, a minimally invasive direct CABG (MIDCAB) technique was developed in US, as an alternative to conventional heart surgery or stent placement.[16]

MIDCAB is an off-pump technique that has been discussed in terms of anastomosis quality, graft patency, and success rate compared to elective PCI in single-vessel disease.[16] The patency of the LITA after MIDCAB is reportedly 100% in the first six months, with a 10-year patency rate above 90%.[17] In terms of long-term survival, Mastroiacovo et al. found a 15-year and 20-year survival of 83% and 70%, respectively. It is considered as a high rate for patients with IHD. Thence, MIDCAB is considered a powerful option for the treatment of single-vessel coronary disease.[18]

Recently published American guideline on ischemic heart disease recommended 2a PCI for the treatment of LAD or left main (LM) coronary artery disease, at which point MIDCAB may be beneficial for long-term survival and repeated revascularization.[19] The meta-analysis from Gianoli et al. comparing MIDCAB and PCI revealed that PCI had a lower in-hospital mortality rate, whereas MIDCAB demonstrated superiority in terms of long-term survival and repeated revascularization.[20] In another meta-analysis, MIDCAB was found to be superior in major cardiac events from 6-months to 1-year, and repeated revascularization.[21] Additionally, MIDCAB was found to be superior in the relief of angina symptoms compared to PCI.[22] Piperata et al. showed the less invasive version of MIDCAB, they safely performed robotic-assisted MIDCAB for 17 patients without postoperatively 30-day mortality.[23]

In the management of single vessel coronary artery disease, MIDCAB should be given serious consideration as a strong option for coronary surgery. To better understand its effectiveness, further subgroup studies are needed. Additionally, it is important to invest more in the development of surgical instruments and techniques in this direction.

Minimally invasive cardiac surgery-coronary artery bypass grafting (MICS-CABG)

In an effort to minimize the invasiveness of treating IHD via open median sternotomy, several off-pump techniques were developed such as off-pump median sternotomy (OPCAB) and off-pump thoracotomy (MIDCAB) for single vessel disease.[24] However, recent advances in cannulation techniques, endoscopic surgical instruments, and surgical experience have led to the introduction of Minimally Invasive Cardiac Surgery-Coronary Artery Bypass Grafting (MICS-CABG) as a viable alternative for multi-arterial coronary disease.[24]

In a study with 450 patients who underwent MICS-CABG conducted by McGinn et al., MICS-CABG using an average of 3 grafts was found to have no major cardiac adverse events (MACCE) in the first six months, with 100% LITA patency and an overall graft patency of 92%.[25] Rajput et al. reported positive results with MICS-CABG for multivessel IHD, performing the procedure on 100 patients with an average of 2.33 grafts.[26] One of the benefits of minimally invasive heart surgery is the potential to reduce the risk of intraoperative and in-hospital mortality, thus allowing for surgery in patients with surgical gray zone. In a study by Barsoum et al., MICS-CABG was found to be associated with better recovery and overall survival rate than conventional CABG in upper 75 years old multivessel IHD patients.[27] Despite these favorable studies, Teman et al. found no significant difference in mortality and MACCE between 139 MICS-CABG and 278 ON CABG patients.[28]

Based on the available evidence, it appears that MICS-CABG is a feasible surgical option for patients with IHD who fall into the "gray zones". However, further research is needed to fully understand its efficacy and identify which patient groups may benefit most from this procedure.

MINIMALLY INVASIVE CORONARY ARTERY BYPASS GRAFTING POTENTIAL

Off-pump financial benefits and no inferiority to on-pump CABG

Studies comparing the financial costs of OPCABG and ONCABG have shown that OPCABG has either significantly lower initial hospitalization costs or no significant difference compared to ONCABG. The total length of postoperative stay, total blood products used, and type of surgical device used is identified as the main causes of the financial gap between the two procedures. However, this financial gap is closing as follow-up is longer, possibly because hospital readmissions are more frequent in OPCAB.[29-31] The overall cost of the procedures evaluated with their outcomes by the means of cost per quality-adjusted life-year (QALY) gained showed a higher cost-effectivity for the OPCAB. QALY for both of the procedures was found similar.[32,33] Patients who underwent OPCAB have a more rapid recovery and fewer postoperative complications (postoperative stroke, new-onset renal insufficiency, respiratory failure) with lower in-hospital mortality rates.[34,35] For the first month after the surgery, OPCAB's resolutions are more favorable than ONCAB's. However, long-term outcomes are not accordant with short-term outcomes. OPCAB over the time of one year lost its superiority over ONCAB. The long-term outcomes of OPCAB are still controversial, debating whether OPCAB has worse long-term survival and a higher rate of incomplete

myocardial revascularization after one year.[29-36] However, it is worth mentioning the results of some previous studies could be influenced by the lack of modern equipment and inadequate experience.[36] Lamy et al. demonstrated no significant difference in the first 30-days, 1-year, and 5-year composite outcomes with a similar rate of repeat revascularization.[13] Additionally, OPCAB was found to be beneficial for high-risk patients, without any specified reasons.[37] As mentioned earlier, it can be due to reduced risk of massive hemolysis, over-induced inflammatory cascades, and thromboembolisms. Overall OPCAB showed similar outcomes with similar or less resource utilization compared to ONCAB with minor superior outcomes in the first month after the procedure. OPCAB is financially beneficial with no inferiorities in the short term. Still, more studies must be done on long-term outcomes.

PCI-stent versus MIDCAB-CABG for single-vessel disease

MIDCAB and PCI are both revascularization techniques used for patients with single-vessel disease, especially left anterior descending artery revascularization or left main stem revascularization, however, their clinical outcomes and superiority have been subject to debate. The comparison between the two procedures has been evaluated in the literature in terms of several outcomes, including MACCE, target vessel revascularization (TVR), QALY, and length of stay (LOS). Deppe et al. conducted a meta-analysis with 2,885 single-vessel disease patients; they found that PCI had an increased incidence of MACCE after six months of follow-up. Additionally, PCI was associated with an increased rate of repeat TVR.[38] TVR rate might be from 3.8 to 5 times higher for PCI compared to MIDCAB shown meta-analysis.[38,39] PCI has higher recurring angina rates in six months of follow-up but it loses its significance over 1-year of follow-up and has similar rates of angina recurrence as MIDCAB.[21] Rao et al. have demonstrated that even with higher costs compared to PCI, the QALY gained over the long term favors MIDCAB. Therefore, MIDCAB is considered more cost-effective with favorable outcomes in the long-term.[40] In a meta-analysis by Gianoli et al. MIDCAB has a higher mortality rate, which is associated with cardiac mortality in short-term follow-up; however, MIDCAB showed better survival rates in the long-term.[20] Further studies are required for comparison of PCI with second-gen DES and MIDCAB. Overall, when considering MACCE, TVR, and cost-effectiveness, MIDCAB is considered superior to PCI in the long-term.

MICS-CAB versus conventional CABG for multivessel disease

The benefits of minimal invasiveness over various forms of sternotomy have been theorized and demonstrated in numerous studies, i.e., Lapierre et al.[41] state a shorter hospital stay, significantly fewer wound infections, and a faster return to physical activity in the MICS-CABG group compared to the OPCAB group, although with a larger proportion of MICS-CABG group receiving single-vessel vascularization. Ziankou et al. compared conventional CABG, OPCAB, and no-touch aorta MICS-CABG (MVST-CABG). They demonstrated less intraoperative blood loss and fewer blood transfusions in the MVST-CABG group. Being predominantly an off-pump procedure, MICS-CABG offers the advantage of avoiding or minimizing aortic clamping and manipulation, which are known to correlate with peri-operative neurological complications.[42] Nevertheless, Liang et al.[43] showed no significant differences in rates of stroke between conventional and MICS-CABG; therefore, further investigation might be needed.

Possible reservations regarding a more widespread implementation of MICS-CABG include the risk of incomplete vascularization and problems with patency in the long run. However, McGinn et al.[25] demonstrated complete revascularization in 95% of patients that received MICS-CABG. Lapierre et al.[41] achieved complete revascularization in all patients regardless of MICS-CABG or OPCAB, and Liang et al.[43] demonstrates no significant differences in repeat revascularization in conventional CABG vs MICS-CABG. Despite the excellent short-term results, data regarding long-term follow-up is relatively scarce.

The steep learning curve remains an issue but can possibly be overcome by prepping for cannulation for CPB, and it is advisable to acquire a large experience in performing conventional off-pump CABGs through a sternotomy approach and MIDCAB procedures before beginning with MICS-CABG surgery.[5] As a result, MICS-CABG is

Table 1: Randomized controlled trials about On pump versus Off pump.

Endpoints	GOPCABE[14]	CORONARY[13]	ROOBY[12]
Short term mortality	No significant difference	No significant difference	No significant difference
MACCE (major cardiac adverse events)	No significant difference	No significant difference	No significant difference
Long term outcome	No significant difference	No significant difference	Favors on on-pump CABG

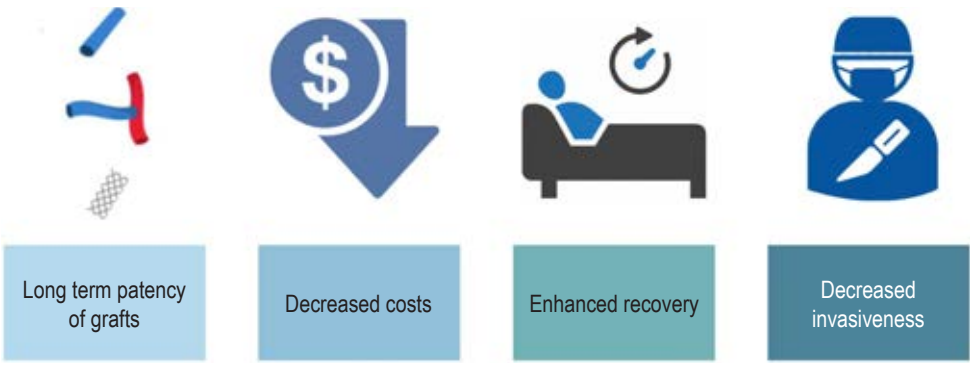

Figure 1:

Potential of minimally invasive surgical revascularization.

demonstrated to be comparably excellent to conventional CABG in terms of short and mid-term outcomes. Nevertheless, most studies point to the possibility of selection bias and the highly limiting inclusion criteria for MICS-CABG procedures. Longer follow-up durations and the results of the ongoing MIST trial (The Minimally Invasive Coronary Surgery Compared to Sternotomy Coronary Artery Bypass Grafting Trial, NCT03447938) might encourage more widespread implementation of MICS-CABG programs.[44]

CONCLUSIONS

IHD is the leading cause of cardiovascular mortality worldwide. Current interventions such as CABG and PCI are curative, yet they present nontrivial complications such as an increased risk for mortality (e.g. CABG) or increased need for revascularization (e.g. PCI). Recent guidelines have shifted to favor PCI due to its lack of invasiveness and risk for mortality. However, novel surgical interventions such as OPCAB, MIDCAB and MICS-CABG may allow for a less invasive procedure with a decreased risk of mortality and need for revascularization. Advantages of MIDCAB and MICS-CABG allow for a minimally invasive approach, while OPCAB allows for a more visible surgical area. However, disadvantages include the need for a quality anastomosis and the lack of evidence surrounding the procedures. More studies should be done on the mid- to long-term effectiveness of OPCAB, MIDCAB and MICS-CABG. Additionally, further comparison should be done between the three compared to the standard of care, either CABG or PCI.

In conclusion, novel minimally invasive CABG techniques may provide patients and surgeons with a more optimal way to reduce cost, mortality, and the need for revascularization regarding IHD *(Figure 1)*.

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