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Hybrid approach to multivessel coronary artery disease: is minimally invasive left internal mammary artery to left anterior descending artery and drug-eluting stents in other vessels a viable solution?

Despite more than 40 years of intense scientific and clinical research, controversy still exists regarding the most appropriate therapy for patients with multivessel coronary artery disease (MV CAD). Both cardiac surgeons and interventional cardiologists feel they possess the 'panacea' to treat the disease: coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) with drug-eluting stents (DES), respectively. Recently, the SYNTAX trial has provided evidence supporting the superiority of CABG for patients with severe MV disease; surgery is associated with lower rates of major cardiac or cerebrovascular events at 12 months post-treatment compared with PCI.¹ However, rates of death were similar for CABG and PCI over this time period.¹

While there appears to be a clinical benefit from CABG, surgical revascularization can impose a heavy burden in terms of invasiveness, bleeding, adverse neurological events, infection and pulmonary complications, especially in elderly or at-risk patients. Also, saphenous vein grafts (SVG) commonly used to treat non-left anterior descending (LAD) lesions during CABG are prone to occlusion. Routine post-operative angiography has revealed 6–12 month occlusion rates ranging from 13–21%.^{2,3} However, 95% of CABG procedures carried out in the US, recorded in the Society of Thoracic Surgeons (STS) registry, utilize an SVG.⁴ PCI, on the other hand, allows for the minimally invasive management of CAD, and as such can be associated with reduced costs and improved recovery periods. Compared with CABG, patients who undergo PCI are likely to require repeat revascularization.¹ However, recently released data from the Swedish Coronary Angiography and Angioplasty Register ([SCAAR] a very large, long-term observational study) have shown that new-generation DES (n-DES) are associated with improved patient outcomes, compared with

old-generation DES (o-DES) or bare metal stents (BMS).⁵ In the study, the rates of clinical restenosis at 1 and 2 years respectively, were 6.3% and 7.4% in the BMS group, 4.0% and 5.8% in the o-DES group, and 2.8% and 3.9% in the n-DES group.⁵

Following the BARI trial,⁶ it is widely accepted that the survival advantage offered by CABG is related to the presence of a patent left internal mammary artery (LIMA) to LAD artery. Data presented from the SYNTAX trial revealed that the presence of a proximal LAD lesion (and only that!) strongly advocates a surgical revascularization (evidence level I vs II).¹ Moreover, a minimally invasive direct CAB (MIDCAB; LIMA to LAD) technique has been performed, eliminating the need for sternal incision, aortic manipulation and cardiopulmonary bypass (CPB), while achieving the same patency rates as conventional surgery.^{7,8}

Hybrid coronary revascularization (HCR) intends to combine the advantages of both MIDCAB and PCI. Thus, HCR is a sternal-sparing, off-pump, minimally invasive, hand-sewn LIMA to LAD bypass graft though a 4–6 cm anterolateral minithoracotomy with PCI to non-LAD lesions, in order to achieve a functional complete revascularization. Uniting these two approaches could, in theory, provide the perfect revascularization: stents replace the need for the SVG, and MIDCAB provides a minimally invasive approach to reduce surgical morbidity.

Historically, HCR has been offered only to patients who have a high risk of complications during traditional CABG by median sternotomy.⁹ However, in the last few years, the use of HCR has increased in patients with MV CAD. This is primarily due to excellent clinical results from the latest generation of DES⁵ and to the desire of both patients and cardiologists for less invasive treatment options.

Despite the potential benefits of HCR, the technique has not been widely adopted. This can

be attributed to a number of factors including:

- A lack of co-operation between surgical and interventional groups
- The logistical difficulties surrounding the timing and sequencing of procedures
- The use of aggressive anticoagulation in surgical patients
- The resistance of the wider surgical community to adopt minimally invasive techniques

As a consequence of these issues, the status quo for the surgical treatment of MV CAD is to perform a sternotomy using a single LIMA and multiple SVG, under CPB. Despite recent guidelines, interventional cardiologists continue to treat MV CAD patients with multiple DES, with the aims of avoiding surgical risk and satisfying the patient's desire for a less invasive treatment. As previously discussed, both of these approaches have notable drawbacks. The time has come to convince surgeons that they should stop fully revascularizing patients themselves and, at the same time, to convince interventional cardiologists that they can rely on surgery for an excellent method for revascularization of LAD lesions.

Some considerations on surgical revascularization in MV CAD

The same surgical strategy (one mammary artery and multiple SVG under CPB) has been used in CABG operations since the 1980s. Although the surgical population has changed dramatically over this time (becoming older and sicker), very few centres have changed their techniques accordingly. This is despite the development of several strategies for surgical revascularization to eliminate CPB, sternal incision, or both.

The development of stabilizer technology led to off-pump CAB (OPCAB) being proposed as a surgical solution to achieve complete revascularization. Initially, given the increased need for re-intervention associated with PCI, it seemed that the emergence of OPCAB would limit the use of HCR.¹⁰ However, only a few centres have adopted OPCAB as a routine strategy: 20% of CABG are now performed in this manner in the US and Europe.¹¹ Expected advantages failed to be realized because of the need for a sternotomic approach, aortic manipulation and a troublesome approach to the posterolateral branches, causing suboptimal graft patency when compared with conventional on-pump CABG.¹² In practice, this

means that surgeons actually select patients for OPCAB based more on the coronary anatomy than with regard to risk factors. Moreover, occlusion rates of bypass grafts may be influenced by being placed on haemodynamically non-significant stenoses^{13,14} and surgeons are pushed to achieve complete anatomic revascularization, based only on angiographic evaluation (stenosis severity) without knowledge of the functional status of the lesion (fractional flow reserve evaluation).

The paradox of today's OPCAB is that it offers patients an invasive procedure to place suboptimal SVG grafts with suboptimal patency rates,^{3,15} which are very similar to DES.³ This is despite the fact that the demonstrated survival benefit of CABG is largely attributable to the LIMA-LAD bypass which provides excellent long-term durability.¹⁶ Patency rate is similar in the off-pump and on-pump groups,¹² and has the added advantage of being easily implanted and without requiring a sternal incision. Further, as OPCAB requires both a sternotomy and leg incisions, patients fail to recognize any reduction in invasiveness and continue to prefer repeated stenting procedures.

Large series of MIDCAB have been reported in the literature and the extensive data confirms excellent angiographic and clinical results.⁸ To further reduce chest wall manipulation associated with open MIDCAB, and to improve post-op pain control, thoracoscopic and robotic techniques have been employed for LIMA mobilization and LIMA-LAD anastomosis.¹⁷ However, to date, few surgeons have mastered such techniques, meaning their widespread adoption has not yet occurred.

Indeed, in endoscopic-robotic MIDCAB there are more technical errors than in standard beating heart surgery. Therefore we arrive at a new paradox whereby, in order to minimize an already minimally invasive operation, they complicated an easy approach jeopardizing the patency of LIMA-LAD anastomosis (lesions in LIMA-LAD system: OPCAB (1%) vs endoscopic MIDCAB (4.8%)).¹⁸

Today, patients and referring cardiologists are asking for surgeons to adopt the gold standard operation that is the mammary artery on LAD, performed in a safe, effective and minimally invasive fashion, with an excellent success rate. As a surgeon involved in minimally invasive techniques, I think we must make MIDCAB accessible to all centres that carry out cardiac

surgery, because, as previously discussed, one of the main reasons HCR has not been widely adopted is that the majority of cardiac surgeons are yet to master the required techniques.

Some considerations about DES in MV CAD

Improvements in DES design, the eluting drugs, and delivery platforms have resulted in significantly reduced restenosis rates compared with o-DES and BMS.⁵ Although restenosis rates are quite low in large vessels with short uncomplicated lesions, complicated lesions can have re-occlusion rates as high as 60% when treated with PCI.¹⁹ However, restenosis does not necessarily pose a significant challenge to either cardiologists or patients, since an in-stent restenosis is still relatively easy to treat with a non-invasive repeated revascularization.

Incomplete revascularization in patients for whom PCI is not suitable, notably those with chronically occluded, small, calcified or tortuous vessels, or long atherosclerotic lesions, is a limitation considered acceptable in the cardiology environment. For interventional cardiology, the feasibility of PCI is related to the technical skilfulness of the operator. However, the long-term outcomes are often related to multiple, uncontrollable factors related to the pathophysiology of the atherosclerotic disease. Nevertheless, the recent results of the SYNTAX trial clearly demonstrated that a patient with MVD, including proximal LAD, should be treated with surgical revascularization, rather than multiple PCI.¹ However, in clinical practice, proximal LAD lesions continue to be treated with PCI, even if most interventional cardiologists today show a more prudent attitude towards complex lesions, due to possible legal implications.

In my experience, close co-operation between an interventional cardiologist and a cardiac surgeon capable of performing safe and effective MIDCAB for LAD revascularization, can reduce the need for complex LAD PCI. The cardiologist can then treat the double vessel disease by PCI. In addition, the combined use of PCI and MIDCAB takes advantage of fractional flow reserve-guided evaluation of haemodynamically non-significant stenosis whose revascularization is not indicated.¹⁶ The invasiveness of a full sternotomy should be considered only if there are no other options available that will produce acceptable results.

Therefore, as noted by Delhaye et al.,²⁰ the benefits of choosing to perform a sternotomy for LAD revascularization alone are debatable.

Interestingly, PCI has recently emerged as an alternative for selected patients with left main (LM) disease. The procedure has been recently upgraded to a class IIb recommendation in guidelines²¹ and several observational analyses have demonstrated comparable short- and mid-term survival between CABG and PCI for LM stenosis, despite a higher incidence of repeat revascularization in patients treated with PCI.^{22,23} The relatively large size of the LM coronary artery makes this vessel an attractive lesion to treat percutaneously in patients with focal disease. Of note, LM PCI (LM-circumflex [CFX] stenting) is performed more safely after recording a patent LIMA-LAD anastomosis, following MIDCAB surgery, and results for this procedure compare favourably with OPCAB outcomes.²⁴ In isolated LM ostial stenting there should not be any residual stenosis and any graft (including LIMA-LAD) previously implanted is going to occlude due to competitive flow in the native arteries. Due to concerns about competitive flow to the LIMA after isolated ostial LM stenting, traditional OPCAB is currently my preferred approach for these patients.

In conclusion, the traditional surgical scepticism about increased repeat revascularization in any strategy involving PCI should be evaluated carefully. Indeed, this is critical when examining HCR. It is interesting to note that in the real world most candidates for a hybrid approach are not those patients who would otherwise get CABG, but who would instead be treated with MV PCI. These patients would, therefore, have a higher need for repeated revascularization without the opportunity to have received the proven long-term durability of a LIMA-LAD bypass. Hybrid candidates potentially have better short- and long-term survival and reduced incidence of adverse in-hospital events compared with OPCAB. This is combined with a lower requirement for repeat revascularization compared with multivessel PCI, since LIMA-LAD is the most suitable and effective treatment for proximal LAD disease. Thus, by successfully combining these positive features we provide the survival advantage of LIMA-LAD bypass with minimally invasive nature of PCI: a 'best of both worlds' strategy.

Considerations about patient selection and strategies for HCR

Selecting patients for HCR requires close co-operation between the cardiac surgeon and interventional cardiologist. It is essential to evaluate the suitability of the coronary anatomy for PCI, as well as specific characteristics for minimally invasive LIMA-LAD revascularization in prospective patients. Very small or long intra-myocardial LAD segments are technically challenging for the minimally invasive surgeon. It is also important to evaluate how aggressive PCI (non-LAD occluded vessels) should be, as the presence of a patent LIMA-LAD graft may change the safety for the interventional cardiologist. In general, the ideal candidate for HCR has a suitable LAD for MIDCAB with proximal lesions in the right coronary artery (RCA) and CFX artery. Exclusion criteria for patient selection are those with severe chronic obstructive pulmonary disease (forced vital capacity <60% of predicted value), severe pulmonary hypertension, severe obesity (relative) and actively ischaemic patients. In this last patient group (unstable patients with ST-segment-elevation myocardial infarction, or acute myocardial infarction), if the culprit lesion is on LAD an urgent MIDCAB can be very challenging or too risky to carry out.

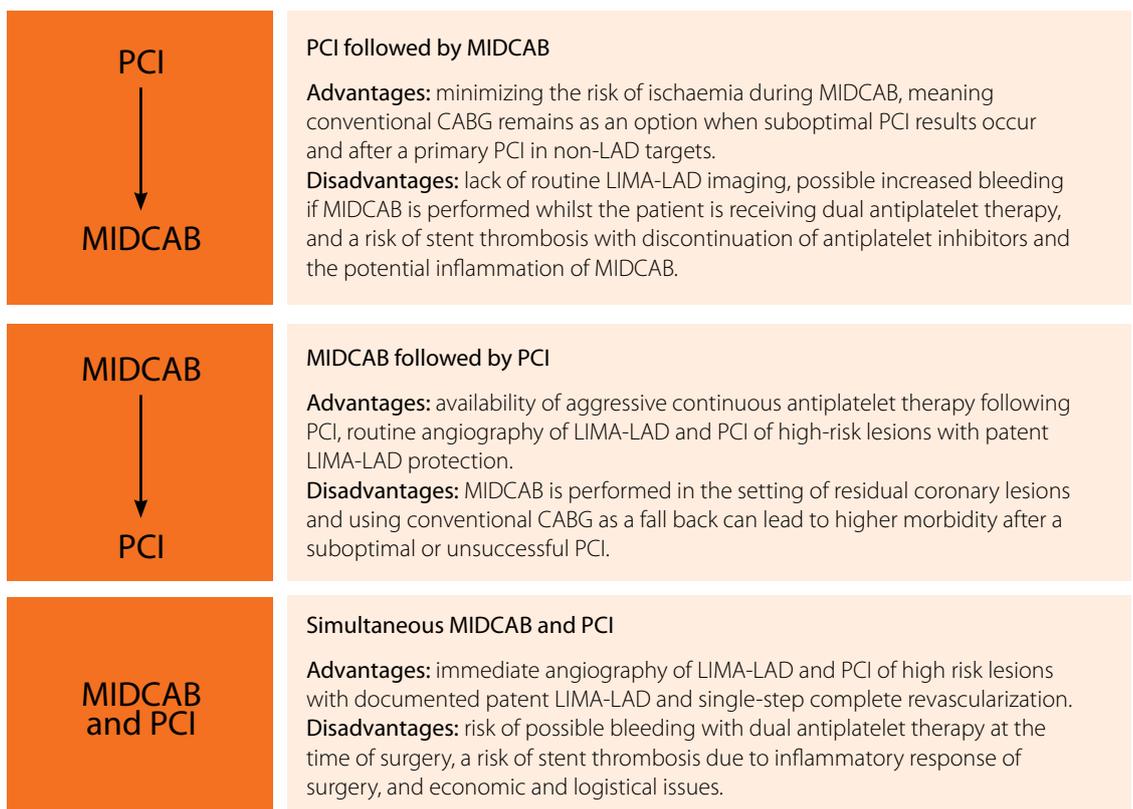
The significant planning required for HCR and the use of aggressive anticoagulation in these patients have been suggested as limiting factors to the wider acceptance of HCR. Again, close co-operation between the surgeon and interventional cardiologist can ensure that both parties can have confidence in patient selection and can allay any fears. Indeed, a case-by-case tailored strategy for each patient is mandatory: any attempt to codify the optimal approach is likely to prove misleading and will probably result in failure. There are, however, three basic approaches to HCR, all with their potential advantages and disadvantages (fig. 1).²⁵

Clearly, the order in which HCR is carried out is variable. However, in general, patients admitted with unstable angina attributable to a critical stenosis in the RCA or CFX are first treated with PCI, followed by MIDCAB. When LAD is considered the culprit this order is reversed (MIDCAB followed by PCI). Alternatively, some authors advocate a same-day combined surgical and PCI procedure performed in the operating theatre.^{4,26}

I think that simultaneous MIDCAB and PCI, though psychologically appealing to the patients, requires both facilities and a level of organization that

fig. 1

Alternative approaches to HCR: PCI followed by MIDCAB; MIDCAB followed by PCI; and simultaneous MIDCAB and PCI



are only available in selected centres. However, the concept that HCR requires a 'hybrid suite' is misleading and risks being a further obstacle to the uptake of this strategy. Instead, very close co-operation and communication between interventional cardiologists and cardiac surgeons is of paramount importance in order to achieve success, as previously discussed.

Finally, in today's economic climate, it is important to consider the costs of such procedures. At present, the total cost of the HCR probably exceeds the costs of CABG in most centres. Nevertheless, since HCR can reduce post-operative morbidity compared with results from conventional OPCAB,⁴ and patients return to work or normal activities quicker after hybrid procedures, such costs should be taken into consideration. Performing more

procedures, further integrating skill sets and co-ordinating protocols is likely to drive efficiency and reduce costs.

Conclusions

Over the last decade, the volume of data supporting MIDCAB means that it can now be considered one of the standard revascularization techniques available to patients with CAD. As patients with CAD are becoming older, with high risk scores, a tailored case-by-case approach to revascularization will need to be adopted for each patient, combining conventional CABG, CPB, OPCAB, MV stenting and HCR. After careful evaluation of coronary anatomy and clinical conditions of each individual patient, the heart team should decide the ideal approach to improve the quality of life and prolong life expectancy.

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