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Chapter 11

Complex Coronary Artery Disease

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Additional information is available at the end of the chapter

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1. Introduction

With recent increase in percutaneous cardiac intervention (PCI) the patients undergoing coronary artery bypass (CABG) are getting more complex with other medical problem. [1] In some patients standard surgical or percutaneous intervention is no longer available due to its complexity.

We define complex coronary artery disease (CAD) as condition not amenable to percutaneous coronary intervention and standard surgical intervention. Conditions for complex CAD include necessity of reoperative CABG, coronary endarterectomy, calcified aorta and trans-myocardial laser revascularization (TMR).

We will discuss each topic with preoperative workup including history and physical, tests and images. Operative steps will be discussed as well as outcomes and evidence that support the treatment.

Complex CAD is a challenge for the cardiac surgeons and advanced technique and strategies are required to treat this difficult condition surgically. Reoperative CABG can be performed with proper preoperative assessment and surgical planning. Diffusely calcified CAD can be treated with coronary endarterectomy or TMR. In case of porcelain aorta, circulatory arrest, off-pump bypass or bilateral internal thoracic artery graft may be used.

A combination of these modalities is likely necessary for cardiac surgeons in the future to treat patients with complex CAD.

2. Reoperative CABG

Data suggests that fewer patients are undergoing reoperative CABG. [2] From 1990 through 1994, 7.2% of CABG was reoperations which decreased to 2.2% from 2005 through 2009. On

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the other hand, PCI before redo CABG increased from 14.5% (1990 through 1994) to 26.6% (2005 through 2009). The likely explanation for this is increased use of PCI for patients with previous CABG and more effective risk factor control. Also, use of internal thoracic artery (ITA) grafts to left anterior descending (LAD) coronary artery graft decreases the risk of reoperation and this had become standard graft choice for CABG. The patients who underwent reoperative CABG had more diabetes, dyslipidemia, hypertension, peripheral vascular disease and left main disease. In another words, we are seeing less reoperative CABG in a higher risk patients. Because ITA grafts rarely develop atherosclerosis, reoperation is primarily based on the patency of the saphenous venous grafts or other arterial grafts. Atherosclerosis occurs in majority of vein grafts explanted more than 10 years after surgery and this account for almost all the late graft stenosis. The friability of vein graft atherosclerosis is a substantial risk of distal coronary artery embolization during PCI and reoperation CABG.

Current recommendations for reoperation CABG include late stenotic vein grafts perfusing large area of myocardium mainly LAD or new distal CAD which is not perfused by the previous grafts. [3, 4, 5] Avoidance of graft injury during reentry is the key since perioperative myocardial infarction is the most significant predictor of mortality in patients undergoing reoperation. [6, 7]

2.1. Work up

Previous History Detailed specifics of the previous surgery must be obtained. Date of the surgery, operating surgeon, technical aspects of surgery including number of the grafts performed, which target was bypassed, presence of ITA grafts and what kind of grafts were harvested. Also presence of any complication during the last surgery can be obtained from medical record or directly from the patient. Information regarding aspirin, clopidogrel, warfarin and dabigatran is important that may dispose to intraoperative and postoperative bleeding.

Physical Examination Physical examination should include assessment of grafts such as Allen's test for radial arterial graft and previous scars to show saphenous vein harvest. Presence of peripheral artery disease should be assessed in case axillary or femoral cannulation is used for establishment of cardiopulmonary bypass. Venous Doppler study can be used for presence of greater and lesser saphenous vein and arterial Doppler studies can be used to assess the patency of radial and inferior epigastric arteries.

Cardiac Catheterization Cardiac Catheterization is the golden standard test to identify the new CAD. This will show native vessel anatomy, location of the lesion, patency of the previous graft including the LITA and size of the conduit. Non patency generally suggests presence of graft occlusion¸ but one must realize there is a chance that this may be incomplete study.

CT Angiography Another test that is being used in evaluation of the conduit is Computed tomography (CT) angiography. [8, 9] They are useful because they are able to precisely define the course of the previously placed conduits especially the LITA grafts. The condition of the Aorta, stenosis in the subclavian artery can also be assessed. Information gained from these methods will help guide the surgeons where the previous conduit will be during sternal entry.

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Other images Chest X-ray will provide the information regarding the sternal wires and aortic calcification and lateral view will provide proximity of the heart to the sternum. If the patient does not have a sternal wire after previous CABG, it may indicate patient had sternal wound dehiscence with flap closure. Echocardiogram will provide any wall motion abnormality as well as any valve abnormality which may change operative strategy. Nuclear stress tests such as thallium scanning and positron emission tomography and/or stress (exercise or dobutamine) echocardiogram can be used to assess the viability of the myocardium. If there is no viability, surgical revascularization may not be indicated.

2.2. Operation

The reoperation CABG is more complex surgery compared to primary CABG. Technical challenges include sternal reentry, identification of old grafts, presence of graft stenosis and lack of bypass conduits.

Cardiopulmonary bypass strategy Typically, due to risk of graft injury, axillary or femoral artery cannulation is performed prior to sternotomy. Venous cannulation is obtained using femoral vein cannulation. For high risk cases, such as LITA lying underneath the sternum, Aorta underneath the sternum or right ventricle severly adhered to the sternum, CPB may be established prior to sternotomy. This allows lung deflation which retracts the heart away from the sternum.

Operating Room Setup External defibrillators must be attached to the patient prior to incision in case patient develops nonsustained ventricular arrhythmia during entry and dissection. For specific cases, thoracotomy can be performed for left sided graft to enable safe and efficient approach to the targets. [10]

Sternal Reentry Sternal wires are cut and midline of the sternum is marked for sternal reentry. Oscillating saw is used to divide the anterior table of the sternum. The sternal wires are left in place to protect the saw from cutting through the posterior table and possibly injuring the heart. When the anterior table has been divided, ventilation is stopped. And assistant elevate each side of sternum and posterior table is then sharply divided. Sternal wires are removed as posterior table is divided.

Dissection Once the sternum is divided, dissection of the mediastinum is performed. Traction superiorly not laterally is important, since lateral traction can tear the right ventricle and other important structures. Typically, dissection is performed from inferior to superior direction to minimize the chance of injuring critical structures. Identification of the diaphragm and pericardial edge is a marker for correct plane. Right pericardial edge is dissected from pericardiophrenic angle to the superior vena cava/right atrium junction and aorta is identified. Innominate vein is identified and dissected to avoid stretch injury. Anticipation of proximal anastomosis and graft is the key using the preoperative images and operative report. If there is an injury to the graft, CPB should be initiated and further dissection can be carried out. CPB can also be initiated on high risk patients to empty the heart and allow it to fall away from the sternum. Downside of this technique is the need to dissect while on heparin which results in more bleeding.

Cardiopulmonary Bypass Once Aorta and right atrium is dissected, the heart can be arrested. Effective myocardial protection is essential in previously revascularized heart. Both antegrade and retrograde coronary perfusion are critical. Antegrade cardioplegia may not be effective for areas supplied by ITA, and may dislodge emboli from the atherosclerotic debris from the disease vein grafts. On the other hand, retrograde cardioplegia protects from embolization and removes debris from the retrograde flow. 11 Epiaortic ultrasound is performed to prior to aortic crossclamp to identify any aortic plaques. [12] Mild hypothermia is induced after patient is placed on CPB. When there is patent LITA, it is standard practice to dissect and clamp. However, if the dissection is difficult, moderate hypothermia with either fibrillatory arrest or systemic hyperkalemia can be used to arrest the heart. Manipulation of the graft should be avoided until the heart is arrested since this can dislodge the debris.

Revascularization If LITA or RITA was not used, this will be the first choice for conduit. When ITA is used to replace a vein graft, the old vein graft should be left in place and arterial vessel should be anastomosed to the same coronary vessel. [13] If the vein graft is ligated this may induce ischemia to the target vessel. If saphenous vein is used for conduit, distal anastomosis can be performed directedly to the native coronary artery or to the cuff of 0.5mm of old vein graft if no distal stenosis is present. Proximal anastomosis is performed in similar fashion; however, if there are minimal aorta that can be used for anastomosis, graft can be connected to the previous proximal graft.

If there is associated procedure such as aortic procedure or valve procedure, distal anastomosis is performed prior to valve procedure to avoid manipulation of the heart after the prosthesis is in place. When adding ITA graft to stenotic LAD vein graft, it is advised to leave the stenotic vein graft to avoid hypoperfusion, although there is a risk of distal embolization from the old vein and competitive flow to the new graft.

2.3. Outcomes

From Society of Thoracic Surgeon database, surgical coronary revascularization has evolved over the last decade, with reoperative CABG now uncommonly performed in contemporary practice. reoperative CABG dropped from 6.0% in 2000 to 3.4% in 2009. [14] Reoperative mortality is high in reoperative group, operative mortality declined from 6.1% in 2000 to 4.6% in 2009 despite the fact that patients now more frequently present with left main disease, myocardial infarction, and heart failure. In centers with large operative experience, reports have demonstrated consistently lower mortality. There is increasing evidence that the preemptive strategies discussed here may minimize technical and postoperative complication. [15] Patients also now present more frequently for urgent or emergent surgery and following previous PCI. They also now have a higher incidence of other comorbidities such as increased weight, diabetes, hypertension, hypercholesterolemia, renal failure, and cerebrovascular disease.

Despite operating in patients with more complex coronary artery disease and greater medical comorbidities, there have been significant improvements in operative morbidity and mortality in this challenging population. The primary reason for increased mortality appears to be related to perioperative myocardial infarction (MI), due to graft injury, graft failure, inade-

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quate myocardial protection and postoperative graft failure. Other significant predictors of mortality after reoperative coronary revascularization include age, female gender and emergency operations. [16] Long-term outcome is successful after a high risk surgery. 10-year survival is reported to be 55-69% and negative predictors of long term survival is preoperative left ventricular dysfunction, increasing age and diabetes mellitus. [17]

3. Coronary endarterectomy

Coronary endarterectomy is performed when the target has severe atherosclerosis and is not a suitable target. This procedure removes the atherosclerotic plaques with the intima and allows the conduit be anastomosed to the target. Often, decision of coronary endarterectomy is made intraoperatively and conduit is anastomosed to the endarterectomized vessel. This requires precise technique and experience since inadequate procedure leads to occlusion of the native artery and the bypass conduit. Main perioperative challenge is maintainance of patency because removal of the endothelial surface of the coronary artery disposed to platelet aggregation and subsequent thrombus formation. Therefore, anticoagulation method including usage of postoperative heparin and clopidogrel is encouraged.

3.1. Operation

Right coronary artery (RCA) is the most common vessel which coronary endarterectomy is performed. LAD endarterectomy is a technically complex procedure when compared to RCA endarterectomy due to the location and configuration of the septal and diagonal branches. LAD atherosclerotic core is narrow and delicate which increases the risk of disruption under tension. Unidirectional traction on the plaque can cause shearing off the branches. It is quite common that an extended arteriotomy or multiple arteriotomies are performed to achieve adequate plaque extraction. In cases where an extended arteriotomy is performed, the proximal third is used as the site of LITA anastomosis while the distal aspect of the vessel is reconstructed with a vein patch. In cases where 2 or more distinct arteriotomies are created, the LITA may be used for both sites as a separate graft; however, it is common practice that the LITA be used for 1 arteriotomy site and vein graft(s) used for the remainder. [18]

Endarterectomy Endarterectomy for a diffusely diseased coronary artery is used when 1-mm probe is not passed. It is often necessary to create long arteriotomy. After the coronary arteriotomy, an endarterectomy spatula was used to identify the plane of dissection and then to mobilize the plaque proximally and distally. A 1-mm probe was advanced gently through the plane of dissection to break away resistant adhesions. A combination of gentle traction on the plaque and countertraction on the adventitia is useful to extract the plaque. When proper distal tapering of the specimen was not achieved, the arteriotomy was extended distally for complete extraction of the plaque. The proximal end of the endarterectomy should be distal to the most proximal lesion, to avoid competitive flow through the native coronary artery, to the level of the first diagonal branch at most. The atherosclerotic plaque varies from soft to extremely calcified and adherent. This characteristic dictates the length of the arteriotomy

inasmuch as adherent plaques cannot be removed easily through a limited arteriotomy to at least the distal two thirds of the length of the target. If this was the case, the arteriotomy was extended to allow for complete extraction of the atherosclerotic core.

Cardioplegia Flush After complete extraction, retrograde cardioplegic solution was given to flush out any debris that may have embolized distally. A visible flow of retrograde cardioplegic solution through the diagonal and septal branches is indicative of successful endarterectomy.

Vein Patch The saphenous vein patch was applied to the endarterectomized vessel with a long arteriotomy and the LITA was then applied to either the middle of the vein patch or the proximal end of the arteriotomy or LITA onlay patch grafting was used for a relatively short arteriotomy after confirming that there was no tension on the graft.

Myocardial Protection Myocardial protection is achieved with combination of antegrade and retrograde blood cardioplegia. Retrograde cardioplegia is essential during endarterectomy as it allows for flushing of debris proximally, thereby minimizing the risk of myocardial infarction secondary to plaque emboli. Furthermore, retrograde cardioplegia serves a diagnostic purpose; brisk flow through the entire artery indicates complete plaque extraction.

Postoperative Drug Regimen Prevention of platelet aggregation and thrombus formation is crucial to prevent graft and native vessel occlusion. An aggressive protocol is generally required and includes intravenous heparin in the immediate postoperative phase as well as lifetime treatment with clopidogrel (with loading dose) and aspirin.

3.2. Outcome

The risk of endarterectomy patients are higher compared to CABG alone. In some reports, long term patency is inferior to CABG, but in experienced hands operative mortality of 3.0% and 5-year survival of 87% can be achieved. [19] The most significant complication is perioperative MI after endarterectomy. It is significant higher compared to CABG alone including MI occurrence which occurs in 5-10%. [20] Multiterritory endarterectomy is associated with worse long term survival (64% 5-year survival and 36% 10-year survival), but this could be due to higher risk patient population. [21]

LAD endarterectomy was intially reported with increased incidence of morbidity and mortality. [22 23] With technical modifications including LITA grafting with saphenous vein patch and LITA onlay patch grafting, the outcomes in this high risk group has significantly improved. [24] Endarterectomy provides good results and mainstay of the treatments for patients with severe diffuse coronary artery disease not amenable to PCI and traditional surgical intervention.

4. Calcified aorta

The atherosclerotic involvement of the ascending aorta presents technical challenge in patients undergoing CABG. The degree of calcification ranges from isolated plaques to total calcifica-

tion which is known as porcelain aorta. The danger of applying cross clamp is associated with markedly increased incidence of cerebral or systemic embolism. The avoidance of multiple aortic manipulations is the key and strategy must be designed based on this principle.

Atherosclerotic disease of the ascending aorta is becoming an increasing problem and is important to understand the prevalence of this disease entity. Mills and Everson reported 2.0% of unclampable aorta in their CABG population of 1735 patients. [25] Other reports have indicated its occurrence between 2-5% [26, 27]. Goto et al reported in their 463 patients undergoing CABG reported stroke rate of 10.5% in patients with severe atherosclerosis compared with 1.8% in normal or near-normal control patients. [28] The challenges in such situation are to make the accurate diagnosis and operative strategy.

4.1. Work up

Due to its potential to modify surgical strategy, preoperative or intraoperative diagnosis of unclampable aorta is the key. Accurate diagnosis of aortic atherosclerotic disease is of paramount importance. No diagnostic criteria have been established to date, and often unclampable aorta is diagnosed intraoperatively by manual palpation or epiaortic ultrasonography. Disease of the carotid artery and abdominal aorta, stenosis of LAD and age has been reported to be associated with unclampable aorta. [29] Given the predictors of atheromatous aortic disease are age, hypertension, diabetes, dyslipidemia, peripheral vasculopathy and diabetes [30], screening for calcified aorta is recommended in these patient groups.

Images- CXR, Cath, CT scan, TEE Chest X-ray and cardiac catheterization images may demonstrate the presence of atherosclerosis but is not always sensitive. Routine use of screening CT scan in this high risk group is useful to prevent incidence of stroke. [31] CT scan without contrast will delineate the white calcium in clear contrast to the non-calcified aorta which will appear dark. Intraoperatively, epiaortic ultrasound is superior to manual palpation of the ascending aorta and to Transthoracic echocardiography (TEE) for detection of atherosclerosis. [32]

Epiaortic Ultrasound Epiaortic ultrasound may reduce the frequency of neurological injury after surgery due to cerebral embolism by allowing for the identification and avoid atheroma at the site of cannulation and further manipulation. Introduction of epiaortic ultrasound was associated with reduction in prevalence of stroke from 1.2% to 0.7% in retrospective review of 8547 patients undergoing CABG surgery. [33] With this, epiaortic scanning now appears to be the gold standard in diagnosis of atherosclerosis in ascending aorta.

4.2. Operation

Management of this complex disease remains a major dilemma. Several techniques including aortic graft replacement, aortic endarterectomy, no touch technique and off-pump bypass has been described to cope with this difficult problem.

Techniques Using Hypothermic Circulatory Arrest Both Aortic graft replacement and endarterectomy are performed using period of hypothermic circulatory arrest.

- Deep Hypothermia Deep hypothermia (18-20°C) should be attained on CPB. Following fibrillation of the heart, a left ventricular vent is placed.
- Distal Anastomosis During the cooling phase of CPB, the distal anastomoses are performed in the following order: LAD, RCA/posterior descending artery, and marginal branches. Of note, when the heart is lifted during construction of distal anastomoses, bypass flow should be reduced to allow for decompression, thereby optimizing exposure and minimizing damage to the heart. Frequently, at least 1 proximal anastomosis is performed under a brief period of circulatory arrest.
- Endarterectomy When calcification is localized, endarterectomy can be performed under circulatory arrest to created portion of aorta which is decalcified to place a crossclamp.
- Ascending Aorta Replacement In extreme case, the ascending aorta should be replaced under deep hypothermic circulatory arrest. Proximal anastomosis is performed directly to the graft.

No touch Technique No touch technique described by Suma et al can be used [34]. In this instance, CPB is established between right atrium and aortic arch or femoral artery. Left ventricular vent is placed. Aortic cross clamping and cardioplegia delivery was avoided. Ventricular fibrillation was induced while target was occluded using elastic stitches. Pedicled artery graft is used for anastomosis. In case the saphenous vein is used, it is anastomosed to the artery graft or to the ascending aorta where calcification is spared.

Off-pump bypass Off-pump bypass can be used in case arch and femoral artery is calcified as well. In this case, all arterial revascularization is performed using in situ internal thoracic and radial artery. Y grafts are created to internal thoracic artery if radial artery is used.

4.3. Outcome

Aortic endarterectomy and aortic graft replacement provides opportunity to revascularize the coronary artery and eliminate danger of systemic emboli. It is reported to be performed safely, [35, 36] but these procedures do add complexity and risk due to the circulatory arrest.

No touch technique and off pump technique provides theoretical benefit to the procedure, but has not been able to provide definite superiority. Off pump technique offers inferior possibility of complete revascularization especially to the lateral branches of circumflex artery. On the other hand, no touch technique still requires insertion of the arterial cannula which can predispose to systemic and cerebral emboli. Gaudino et al compared these two techniques in 211 unclampable aorta cases and reported no touch technique had greater incidence of neurological complications, renal insufficiency, and stay in the intensive care unit and hospital. However, at midterm follow-up, more patients of the off pump group had ischemia recurrence. [37] Stroke rate was 2.3% and in-hospital mortality was 2.8% in this study.

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5. Transmyocardial laser revascularization

Transmyocardial laser revascularization (TMR) is one of the first described surgical procedures intended to treat severe diffuse CAD not amenable to CABG or PTCA in patients who have had previous percutaneous coronary interventions and/or CABG procedures. This severe coronary artery disease can lead to incomplete revascularization following CABG and is powerful independent perioperative adverse events. Indications for TMR include NYHA class III/IV symptoms refractory to medical treatment with coronary disease that is not amenable to revascularization. [38, 39, 40]TMR is generally contraindicated in patients who are candidates for revascularization or those who are not candidates but have an ejection fraction below 20%.

By inducing angiogenesis with a laser (carbon dioxide, holminumyttrium– aluminum-garnett), TMR has been shown to decrease the severity of angina symptoms compared to medical therapy. [41, 42] As such, the primary indication for TMR is persistent and disabling angina refractory to medical therapy. Owing to its success as sole therapy, TMR is used in conjunction with CABG. The safety and efficacy of TMR in this subset of patients has been well described; operative mortality and morbidity may be significantly less than CABG alone. [43]

Since Food and Drug Administration (FDA) approval in 1998, over 20,000 TMR procedures have been performed in the United States. [44]

5.1. Operation

Left thoracotomy and Heart Exposure A left anterolateral thoracotomy is the incision of choice in patients undergoing TMR as the sole surgical procedure. The heart is exposed, allowing for the access to the anterior, apical, and posterolateral planes of the left ventricle. Careful attention must be paid to not injure the previous bypass grafts. LAD is identified and used as a landmark for the location of the septum. TMR is provided through a hand piece that delivers energy through hollow tubes to the epicardium.

Choose type of laser Type of Laser Only CO2 and Holmium-chromium: YAG lasers (Ho:YAG) are clinically approved for TMR. The result of any laser-tissue interaction is dependent on both laser and tissue variables. CO2 laser has wavelength of 10,600nm, whereas Ho:YAG laser has wavelength of 2,120nm. The laser is synchronized to occur on the R-wave of the electrocardiogram to avoid induction of arrhythmias.

Application of laser Pulse energy of 20-30 J over 4 pulses per second creates 1-mm channels in the myocardium that can be visualized with a transesophageal echocardiogram. Using the CO2 laser, channels are first created at the base of the heart and are separated from each other by 1 cm to the apex of the heart starting inferiorly and working superiorly to the anterior surface of the heart. As there is some bleeding from the channels, gravity will keep the field clean by starting inferiorly.

It should be noted that TMR does not provide any added benefit to areas of myocardium that are scarred and have no viability. TMR on the transmural scar will not only be non-beneficial,

it will cause bleeding which may be problematic. Detection of transmural penetration is primarily by tactile and auditory feedback.

5.2. Outcome

Mortality following TMR ranges from 1% to 5%; however, this low rate of mortality is primarily generalized to patients who are electively taken to the operating room and are hemodynamically stable. When these patients are taken to the operating room emergently, mortality is reported to be 10-20%. One-year survival following TMR ranges from 79% to 96% and is not significantly different from patients who undergo medical therapy. The primary advantage of TMR over medical therapy and the principal indication for intervention is the reduction in symptomatology; studies have found that 25%-76% of patients will achieve a decrease of 2 or more angina classes following intervention, which is not the case of patients undergoing medical intervention. Review of the randomized controlled study suggests improvement in perfusion for CO2 TMR treated patients. [45 46] Long term results suggest improved angina symptoms and decreased hospitalization in five years. [47]

However, the benefit of TMR is controversial. Cochrane review published it data after reviewing seven studies (1137 participants of which 559 randomized to TMR). Overall, 43.8 % of patients in the treatment group decreased two angina classes as compared with 14.8 % in the control group. Mortality at both 30 days (4.0 % in the TMR group and 3.5 % in the control group) and 1 year (12.2 % in the TMR group and 11.9 % in the control group) was similar in both groups. The 30-days mortality as treated was 6.8% in TMLR group and 0.8% in the control group, showing a statistically significant difference. Their conclusion was there is insufficient evidence to conclude that the clinical benefits of TMLR outweigh the potential risks and the procedure is associated with a significant early mortality. [48]

TMR is used in conjunction with CABG as well. One randomized controlled study have found that TMR combined with CABG may confer excellent perioperative and survival rates, including decreased opeartive mortality, inotropic support, and intensive care unit stay, while prolonging 1-year survival compared to those patients undergoing CABG alone. [49] Furthermore, patients who undergo both procedures appear to be less symptomatic at follow-up.

In conclusion application of TMR in selected group for the treatment with severe angina due to diffuse disease can be used achieves a more complete revascularization.

6. Conclusion

Complex CAD remains a challenge for cardiac surgeons; however, evolving techniques and strategies can be used to overcome this challenge. Although reoperative CABG is a high-risk procedure, proper preoperative assessment and surgical planning has yielded excellent results. Patients who are not candidates for CABG or percutaneous coronary interventions due to diffusely diseased vessels can be offered coronary endarterectomy. Calcified aorta encountered during surgery can be managed by aortic replacement, endarterectomy, using no touch

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technique or off-pump CABG. TMR may be indicated for patients who have exhausted non surgical options. The outcomes in this complex coronary artery surgery are improving and the results have validated the safety, effectiveness and health outcomes. However, it is crucial to make good patient selection as well as intraoperative decision. Cardiac surgeons must familiarize themselves to these procedures as coronary artery disease patients will be more complex in the future.

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