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REVIEW ARTICLE

Off-pump coronary artery bypass surgery: physiology and anaesthetic management†

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Increasing interest is being shown in beating heart (off-pump) coronary artery surgery (OPCAB) because, compared with operations performed with cardiopulmonary bypass, OPCAB surgery may be associated with decreased postoperative morbidity and reduced total costs. Its appears to produce better results than conventional surgery in high-risk patient populations, elderly patients, and those with compromised cardiac function or coagulation disorders. Recent improvements in the technique have resulted in the possibility of multiple-vessel grafting in all coronary territories, with a graft patency comparable with conventional surgery. During beating-heart surgery, anaesthetists face two problems: first, the maintenance of haemodynamic stability during heart enucleation necessary for accessing each coronary artery; and second, the management of intraoperative myocardial ischaemia when coronary flow must be interrupted during grafting. The anaesthetic technique is less important than adequate management of these two major constraints. However, experimental and recent clinical data suggest that volatile anaesthetics have a marked cardioprotective effect against ischaemia, and might be specifically indicated. OPCAB surgery requires team work between anaesthetists and surgeons, who must be aware of each other's constraints. Some surgical aspects of the operation are reviewed along with physiological and anaesthetic data.

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In the Western world, coronary artery bypass grafting (CABG) is one of the most commonly performed cardiac surgical procedures. In the last decade, there has been renewed interest in performing CABG without cardiopulmonary bypass (CPB). Avoiding CPB eliminates aortic cannulation and cross-clamping, and is expected to reduce systemic inflammatory response, coagulation disorders, and multiple organ dysfunction.

Off-pump coronary revascularization is an old technique, performed first in St Petersburg in 1964,[62] but was soon outshone by the rapid development of CPB and cardioplegia. A revival of the technique occurred during the 1980s in isolated series, and in centres where limited resources favoured off-pump techniques. Accordingly, large series have been undertaken in Buenos Aires (700 patients),[12] São Paulo (1274 patients),[20] Ankara (2052 patients),[114] and New Dehli (2800 patients).[116]

Off pump coronary artery surgery has been developed following two different approaches. Minimally invasive direct-access coronary artery bypass (MIDCAB) consists of anastomozing the left internal mammary artery to the left anterior descending coronary artery through a small anterior left thoracotomy. Nowadays, this technique has largely been abandoned, because it allows only single vessel surgery, is technically demanding, and may lead to suboptimal results. Moreover, postoperative pain is usually more severe after

†This article is accompanied by Editorial II.

Table 1 Claimed advantages of OPCAB compared with CABG and CPB

Endpoints	**References supporting**					**References disproving**			
Level of evidence	**I**	**II**	**III**	**IV**	**V**	**I**	**II**	**III**	**IV**
$\downarrow$ Global mortality	3		22 30 95 96 97	109		118	89	29 53 54 64 68 124	26
$\downarrow$ Global morbidity	3		22 30 95 96 97 109	109		118	89	21 29 53 64	
$\downarrow$ Mortality in high-risk patients			1 4 106					100	
$\downarrow$ Morbidity in high-risk patients			112 126		83 114			100	
$\downarrow$ Mortality in elderly patients			63 111	2					
$\downarrow$ Morbidity in elderly patients			17 99 111	2					
$\downarrow$ In ICU/hospital length of stay	8 97	58 119	17 63 94 111 126	2 68				21	
$\downarrow$ Global cost	7 8	58 65 89	17 67 96					21	
$\downarrow$ Transfusion rate	9 97	65 118	16 53 64 87 97	26	114				
$\downarrow$ Infarction rate	3 97		22	15				63	26
$\downarrow$ Stroke rate		38	16 36 93 94 99	116				4 29 54	
$\downarrow$ Neurological dysfunction		38 85	16			117		63 113	
$\downarrow$ Renal dysfunction		6 70	1				48	63	
$\downarrow$ Infections		8	96			33		1	
$\uparrow$ Pulmonary function		8 65				32			

thoracotomy than after sternotomy.[39] The second approach is multivessel grafting without CPB performed through a standard median sternotomy, which gives access to all coronary vessels, and allows standard techniques of mammary artery harvesting. The recent introduction of sophisticated stabilizing devices and exposure techniques[13] has resulted in an increased graft patency rate,[25] and in the widespread use of this technique for all coronary territories and for as many anastomoses as needed to treat the patient's coronary artery disease.[4 106] This review will focus exclusively on the latter procedure, called off-pump coronary artery bypass (OPCAB).

Rationale for avoiding CPB

For more than 30 yr, extracorporeal circulation has been the gold standard for CABG surgery. Despite the excellent results and the low mortality of the procedure, postoperative complications have continued to be a major concern. Eliminating CPB might theoretically reduce, if not prevent, some of these complications. Critical evaluation of the available literature comparing surgical coronary revascularization with or without bypass is hampered by two important factors. First, although there are 14 randomized and/or prospective controlled studies (level I or II of evidence), the majority of the clinical studies is of low level of evidence (level III to V) and include relatively small numbers of patients, usually compared with historical data. Moreover, they might be flawed by patient selection and surgical treatment bias. Second, the learning curve of this technically demanding novel approach and the usually small number of anastomoses initially performed on each patient in the early stages of its development, markedly affect the results of the different centres.[3] The impact of OPCAB surgery on patient outcome, as judged by the end-points of mortality and morbidity, is still debated. In an analysis of the National Adult Cardiac Surgery Database totalling 3396 OPCAB procedures, the risk-adjusted mortality decreased from 2.9% in conventional CABG to 2.3% in off-pump procedures, and the complication rate from 12% to 8%.[30] Some studies have shown similar results,[3 22 95 96 109] whereas others demonstrate no difference in mortality,[26 54 64 68 124] or morbidity.[21 29 53 89 118] Nevertheless, the need for transfusion is reduced in all centres.[9 26 53 87 97 118] Compared with on-pump revascularization, OPCAB surgery shows a slight trend towards fewer cardiac events for up to 3 yr of follow-up.[3] The results reported in the literature so far are summarized in Table 1, where the level of evidence of the studies is detailed.

The course of patients in the early postoperative period is usually improved with OPCAB surgery compared with on-pump surgery. The duration of ventilatory support, ICU length of stay, and hospital length of stay are significantly diminished in almost every study.[2 8 17 58 63 94] The overall short-term cost is therefore decreased by 14% to 30%.[7 8 65 67 89 96] Early outcomes and one-month graft patency rates (94–99%) appear to be comparable with those seen with conventional on-pump surgery, at least when the surgical team has overcome the difficulties of the learning period.[24] The long-term patency rate is still unknown. The incidence of postoperative infarction, depending on many intraoperative factors, does not show striking differences between on-pump and off-pump techniques, although myocardial enzymes and troponin I release are reduced after off-pump surgery.[5 15 97 118] The incidence of atrial fibrillation is probably unchanged.[84 110]

The results are not clear-cut concerning neurological outcome. Cross-clamping and cannulation of the ascending aorta, as well as the flow jet from the arterial cannula of CPB, are eliminated in OPCAB surgery; this should reduce the incidence of embolic events from the atheromatous aorta.[94] Although the total number of embolic events on transcranial Doppler is effectively decreased,[16 38 122] the occurrence of strokes was only found to be significantly

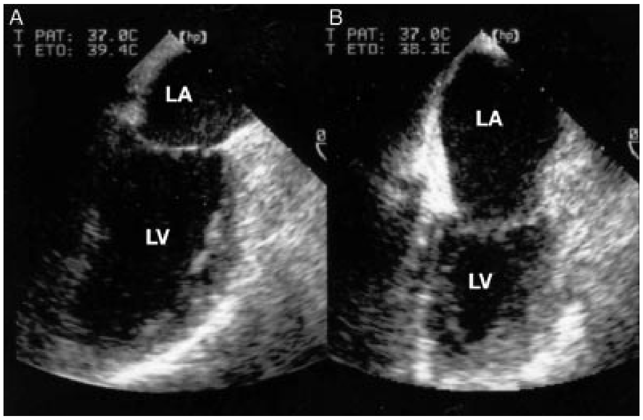


Fig 1 Changes in volume of the left atrium and the left ventricle during heart verticalization. (A) TOE two-chamber view at 90° of the patient's heart in its supine position. The left atrial (LA) volume is about one-third of the left ventricular (LV) volume. (B) Without modifying the position of the TOE probe, the heart has been lifted up in a vertical position in order to operate on its postero-inferior wall. The relative dimensions of LA and LV in this new 90° two-chamber view are reversed: the atrium, being now under the ventricle, is larger than the ventricle in which the end-diastolic volume is reduced by 50%. Both pictures are taken in protosystole.

lower in isolated studies,[93 94 116] or in octogenarians.[36 99] The incidence of postoperative strokes may depend on the manipulation of the ascending aorta for proximal anastomoses, and reduced stroke rates may be achieved by surgical techniques avoiding aortic clamping completely, such as branching bypass grafts on peripheral arteries emerging from the aortic arch.[23 24] The effect on cognition is also debatable, because the few published studies show conflicting results.[38 63 85 113 117]

There is increasing evidence that off-pump procedures are associated with reduced postoperative rise in markers of systemic inflammatory response (SIRS), such as C3a, C5a, TNF-α, or interleukin (IL)-6 and IL-8.[8 33 37 77] However, the clinical significance of these data is still uncertain, because IL-8 and C3a are linked to the amount of surgical tissue injury, IL-10 has anti-inflammatory properties, and heparin inhibits complement activation.[79] The effects of CPB on SIRS depend largely on the balance between pro-inflammatory and anti-inflammatory mediator release. As some population subgoups might show a greater pro-inflammatory cytokine response, such as elderly patients or patients with left ventricular (LV) dysfunction, they should benefit particularly from off-pump procedures.[8 115]

In a low-risk population, surgical coronary revascularization, with or without CPB, has low morbidity and mortality rates.[89] Possible advantages of OPCAB surgery are therefore more likely to be found in high-risk patients with significant comorbidities and an expected mortality of 6–10%.[106] Mortality appears to be lower in some series,[1 4 106] but not all[89 100] (Table 1). In elderly patients, results are improved with OPCAB surgery: mortality and postoperative complication rates are significantly lower;[17 63 99 111] the incidence of a low postoperative cardiac output is reduced from 32% to 10%; and strokes are reduced from 9% to 1%.[2 17 36 99] Similarly, emergency coronary surgery or surgery performed on patients with impaired ventricular function (ejection fraction <0.35) have shown encouraging results.[83 112 126] Available reports show only some trend toward possible renal protection, but there is probably no difference for patients on dialysis.[1 6 48 70] The results concerning insulin-dependent diabetics show no improvement in comparison with conventional surgery.[4 83]

OPCAB has been shown to be feasible in almost all patients requiring coronary bypass. The only contraindications are the presence of intracavitary thrombi, malignant ventricular arrhythmias, deep intramyocardial vessels, and procedures combined with valve replacement or ventricular aneurysmectomy. Despite difficulties because of pericardial adhesions, beating-heart reoperations for single- and multiple-vessel disease have been performed through thoracotomy or sternotomy incisions.[80]

Problems associated with OPCAB

During beating-heart surgery, the surgeon is faced with two main problems: first, to obtain an adequate exposure of the anastomosis site with restrained cardiac motion; and second, to protect the myocardium from ischaemia during coronary artery flow interruption. For these purposes, he must displace the heart, compress the ventricular wall, and if possible use a technique to allow coronary perfusion while performing the anastomoses. Thus, the anaesthetist must be prepared to handle severe haemodynamic alterations, transient deterioration of cardiac pump function, and acute intraoperative myocardial ischaemia. The team must be prepared for conversion to CPB in case of sustained ventricular fibrillation or cardiovascular collapse.

Haemodynamic alterations with cardiac manipulation

Surgical access to the left anterior descending coronary artery is relatively easy through a median sternotomy but, in order to work on the posterior or lateral walls, the heart must be lifted and tilted out of the pericardial cradle. This displacement of the heart has important haemodynamic consequences, resulting in a significant increase in atrial pressures, and a marked decrease in cardiac output (cardiac index <2 litre min^{-1} m^{-2}), leading to a reduced mixed-venous saturation (Sv_{O_2}), often <70%. Different parts of the procedure produce different haemodynamic disturbances.

First, the heart is tilted in a vertical position with the apex at its zenith; the atria are then situated below the corresponding ventricles, and the blood must flow up into the ventricular cavities. Therefore, the filling pressures, as measured in the right and left atria, are increased much more than the corresponding ventricular end-diastolic pressures,[78] and must be maintained at a higher than normal level to

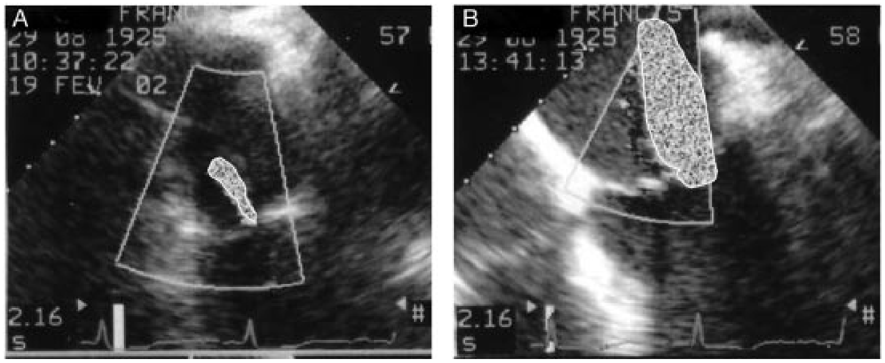


Fig 2 Modification of a mitral regurgitation with heart manipulation. (A) When the heart is in its normal position, a trivial regurgitation is present. (B) When the heart has been lifted up in a vertical position, the regurgitation has increased to a grade II.

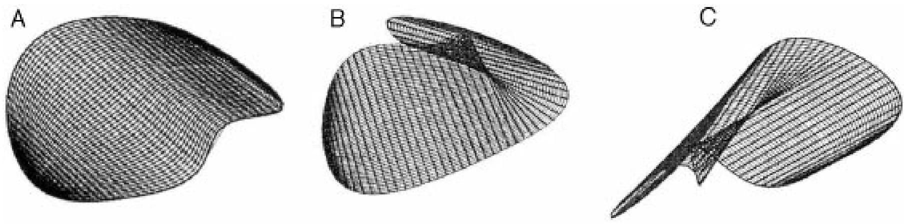


Fig 3 Modification of mitral shape with heart manipulation reconstructed in its three-dimensional aspect, as viewed from above (from reference 49, with permission). (A) Normal saddle shape of the mitral ring when the heart is in its normal position. (B) When the heart is moved to the vertical position, the mitral ring is severely distorted. (C) When the lifted heart is rotated to gain access to the lateral wall, the ring is further folded and twisted.

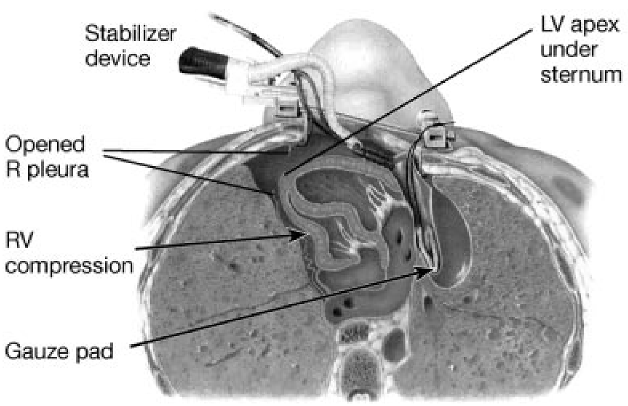
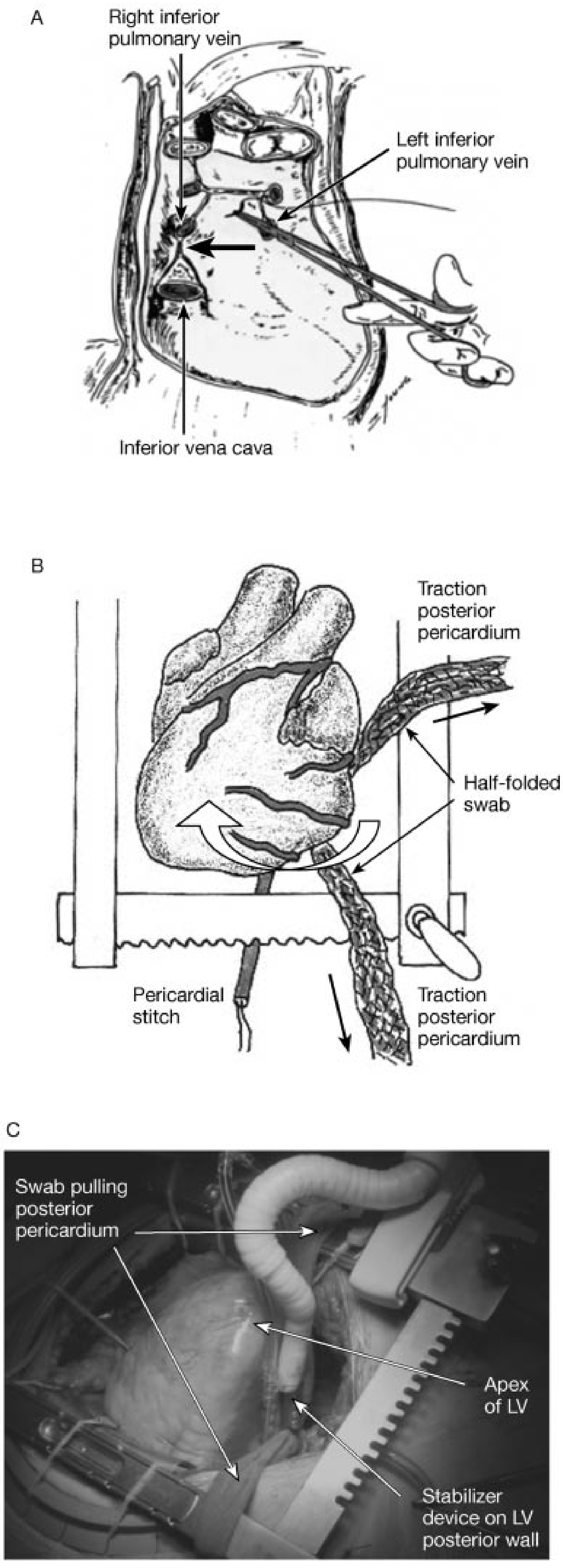


Fig 4 The heart position using the technique of 'rocking' with a tissue stabilizer device. The right ventricle is squeezed between the left ventricle and the right hemi-sternum; the right ventricular outflow tract is compressed (courtesy of Medtronics™).

maintain ventricular filling.[90] The atrial size can increase by 50% and become larger than the ventricle (Fig. 1).[49 78] Mitral and pulmonary venous flows show patterns of impaired diastolic filling and moderate diastolic dysfunction.[49]

Second, the stabilizer device used to immobilize the area of the anastomosis pushes on the ventricular wall, restricts local motion and decreases ventricular dimensions. The location of the stabilizer device, combined with the degree of heart dislocation, determine the overall effect on global cardiac output. As the anterior and lateral walls have wider displacement in systole and diastole than the septal and posteroinferior walls, their contribution to stroke volume is predominant. Compression on the anterior and lateral walls has therefore more serious haemodynamic consequences than compression on the posterior wall. The most profound disturbances are observed during lateral wall exposure for anastomosis on the circumflex artery because the heart is then lifted more extensively than for surgery on the left anterior descending artery.[49 78 84]

Third, a vertical position of the heart induces distortions of the mitral and tricuspid annuli, as the intracardiac structures are folded primarily at the atrioventricular groove. The annular plane of the valves is modified, and significant regurgitation may occur. The mitral annulus, reconstructed in three dimensions with transoesophageal echocardiographic (TOE) monitoring, is bent over, folded and twisted.[49] This may result in significant mitral and tricuspid regurgitation (Figs 2 and 3). The sudden appearance of large 'v' waves (>30 mm Hg) on the pulmonary artery catheter readings, without signs of LV failure, illustrates the same mechanism. The distortion of the atrioventricular annulus can also result in a functional stenosis. The most profound effect seems to occur on abnormal valves, which become more distorted. The same phenomenon may be observed on the aortic valve; a trivial aortic regurgitation may become severe when the heart is 'enucleated' from the pericardium.



Surgical techniques

Strategies used by the surgeon to manipulate the heart markedly influence the haemodynamic response of the patient. The numerous techniques described can be roughly classified into two categories: (i) heart 'rocking' by a tissue stabilizer device; and (ii) 'enucleation' by pericardial stitches.

The first technique consists of displacing the heart with gauze pads and/or rocking it with suction stabilizer devices. In these conditions, the thin right ventricle (RV) is squeezed between the pericardium and the bulky left ventricle, and compressed under the right hemi-sternum, resulting in severe haemodynamic compromise (Fig. 4).[90] Transoesophageal echocardiography reveals a bulging of the interatrial septum to the left, no dilatation of the LV, and part of the cramped small RV with right outflow tract obstruction.[90] In an animal model, Gründeman[51] reported a 165% increase in RV end-diastolic pressure and a 62% decrease in RV end-diastolic area; LV pressures did not change although LV diastolic cross-sectional area decreased by 20%. Opening of the right pleura may reduce haemodynamic compromise.[90] The Trendelenburg manoeuvre re-establishes the circulatory status and the coronary blood flow at the expense of a further rise in RV preload, an increased LV preload, and an increased heart rate.[50]

The second technique consists of enucleating the heart by aspirating the apex with a suction device, or by pulling the posterior pericardium with multiple[12] or single[13] stitches. The latter approach appears more attractive because of its simplicity and efficiency. The stitch acts as a lever placed in the oblique sinus of the pericardium, and the heart is exposed by traction on the arms of a half-folded swab snared down on the pericardium (Fig. 5). The arms are never pulled across the heart in order to avoid any compression, which may lead to functional compromise.[13 99] The cardiac output transiently collapses only when the heart is tipped over for inserting the pericardial stitch. The stabilizing device is used only to immobilize the local area of the anastomosis; it is not used for positioning the heart nor for exposing the cardiac wall.[84] Even if the RV end-diastolic pressure is elevated, the predominant haemodynamic effect is on the

Fig 5 Exposure of the heart with the posterior pericardial stitch of the 'no-touch' technique. (A) Location of the stitch in the oblique sinus of the posterior pericardium on the right side of the spine, halfway between the level of the right inferior pulmonary vein and the inferior vena cava.[13] Ideally, the stitch should be placed slightly to the right of the spine (arrow); this allows TOE imaging from the oesophagus. (B) The suture is passed through a half-folded swab and snared down, bringing the folded end of the swab in close contact with the posterior pericardium. For exposing a specific wall of the heart, both limbs of the swab are pulled (arrows) in a direction opposite to the target wall with the target artery located between both limbs, in order to avoid any compression of the heart. This represents 'no-touch' handling of the heart.[84] (C). In the final position, the heart is enucleated from the pericardium in a vertical position, the apex at the zenith; each cardiac wall is accessible to surgery. On the picture, the tissue stabilizer is applied on the posterior wall with minimal compression.

left ventricle, with a 12–23% decline in LV stroke volume and a 10–50% increase in left atrial filling pressure.[78 121] The severity of the haemodynamic changes is linked to the site of the anastomosis: it is more pronounced during circumflex artery grafting, because lateral wall contraction contributes more to stroke volume than does the posterior wall, and because the tilting is more accentuated than for left anterior descending artery grafting.[78 84 121]

Usually, the speed of heart positioning has more dramatic effects than the displacement itself. Surgeon and anaesthetist must therefore work in close collaboration to ensure progressive positioning and rigorous pressure adjustment.[90] To improve surgical access to the lateral and posterior walls of the heart, the operating table is tilted to the right or positioned in the Trendelenburg position, respectively. Leg elevation appears the most efficient technique to improve preload. Indeed, this manoeuvre increases the right atrial transmural pressure, whereas the head-down position increases intrathoracic pressure and right atrial pressure similarly. Cardiac output is therefore increased with leg elevation, but not in the head-down position.[88 98]

Intraoperative myocardial ischaemia

During OPCAB surgery, coronary artery cross-clamping to ensure bloodless anastomotic conditions results in brief periods of myocardial ischaemia, usually manifested by ST-segment elevation and new regional wall motion abnormalities (RWMA) on echocardiographic imaging.[81] A 16 min mean occlusion time of the left anterior descending artery necessary to perform an anastomosis is associated with a decrease in peak systolic shortening from 5.8% to 1.8%,[18] and results in myocardial lactate production. The significance of the ischaemia depends on the percentage stenosis of the target vessel and of the degree of collateralization; occlusion of highly collateralized vessels produces less ischaemia than occlusion of 'terminal' vessels.[61] The most intense ischaemic events occur when flow is interrupted in a discretely stenotic vessel, usually between 50 and 80% stenosis, with poor collateralization.[26] Severe ischaemia during clamping of a non-occlusive right coronary artery (RCA) can result in dangerous arrhythmias such as complete atrioventricular (AV) block attributable to interruption of the blood flow in the AV node artery. Some surgeons therefore favour revascularization of the RCA through distal anastomoses placed beyond its bifurcation.[41 84] Usually, it is recommended to start the sequential anastomoses with the most severely stenotic or occluded vessel.[26 84]

Different techniques are available in order to reduce the consequences of coronary blood flow interruption during OPCAB surgery: improvement in myocardial oxygen balance, ischaemic and pharmacological preconditioning, pharmacological prophylaxis, and surgical shunting.

Improvement of myocardial oxygen balance

Improvement of myocardial oxygen balance can be achieved by decreasing myocardial oxygen consumption and/or increasing myocardial oxygen supply. A reduction in oxygen consumption can be achieved through a decrease in heart rate and contractility. This is usually realized by β-blockers and calcium antagonists. With the verticalization of the heart, LV wall tension remains low despite increasing atrial filling pressures, as these pressures do not reflect the actual end-diastolic pressure of the ventricle. Therefore, it should not contribute to an increase in oxygen demand.

An adequate coronary perfusion pressure is crucial for myocardial oxygen supply. Physiologically, aortic diastolic pressure is the driving force for coronary perfusion. Clinically, its closest measurement is the mean arterial pressure (MAP) measured in the radial or femoral artery.[92 101] During anaesthesia with halogenated agents, a MAP <65 mm Hg, or a coronary perfusion pressure <50 mm Hg, are associated with intraoperative ischaemia,[69] which is in agreement with OPCAB literature, where the accepted minimal MAP ranges from 60 mm Hg[5 70 90 113] to 80 mm Hg.[41] It seems advisable to keep a MAP ⩾70 mm Hg allowing a safety margin above the critical coronary perfusion pressure. This may be achieved by administration of a vasopressor like phenylephrine or norepinephrine. A lower value is acceptable as long as signs of ischaemia are absent.

The aim is an overall equilibrium, where a low cardiac output is tolerated in so far as it meets the demands of the organism, as shown by an Sv_{O_2} >60%; the MAP is maintained at or above 70 mm Hg without LV dilatation as monitored by TOE. In order to prevent increased myocardial oxygen demand when ischaemia is threatening, β-stimulants are best avoided until complete revascularization.

Preconditioning

Ischaemic preconditioning, or improvement of tolerance to ischaemia by brief ischaemic bouts followed by reperfusion, is an attractive technique for protecting the myocardium during the obligatory period of myocardial ischaemia required by OPCAB surgery.[66 67] Preconditioning may also be induced pharmacologically, which appears more desirable in high-risk patients in whom an ischaemic type of preconditioning may further jeopardize diseased myocardium. Experimental studies have shown that volatile anaesthetics such as isoflurane or sevoflurane protect the myocardium against ischaemia by activation of a preconditioning-like mechanism when administered at 2 minimum alveolar concentration (MAC) at least 30 min before the ischaemic insult.[27 57 127 128] So far, preconditioning by halogenated anaesthetics has been favourably evaluated only in patients undergoing on-pump CABG surgery.[11 35 52 55] Propofol and etomidate, if used at clinically relevant concentrations, should not affect the preconditioning mechanism.[35] Collectively, these observations tend to indicate that administration of halogenated anaesthetics may limit the adverse effects of ischaemic myocardial damage.

Pharmacological prophylaxis

In patients suffering from coronary artery disease (CAD), perioperative use of β-blocking agents has been shown to be the most effective preventive measure.[45] Possible benefit has been obtained with α_2-agonists such as clonidine.[86] Preoperative treatment of patients scheduled for coronary revascularization is maintained and included in the premedication. During the operation, a short-acting selective β_1-blocker like esmolol, given as repeated bolus or continuous infusion, is very efficient in lowering excessive heart rate.[5 28] However, it might seriously reduce LV function, as measured by a 42% decrease in mean arterial pressure and a 35% drop in cardiac output, resulting in a decrease in Sv_{O_2} from 81 to 65%.[28] This LV depression leads to an increase in the pulmonary arterial pressure (PAP), whereas right intraventricular pressure might already be elevated because of right outflow tract compression or sudden mitral regurgitation.

A calcium antagonist such as diltiazem may has some theoretical advantages over β-blockers in the intraoperative period. It has been shown that, for the same decrease in heart rate, diltiazem lowers PAP, whereas esmolol tends to increase it.[28] In addition to reducing AV conduction and heart rate as β-blockers do, calcium antagonists offer the advantage of inducing vasodilation in arterial conduits.[105] Moreover, as an increase in intracellular free calcium is one of the primary causes of reperfusion injury and post-ischaemic myocardial dysfunction, calcium antagonists might prevent some post-ischaemic lesions.[105] Some centres administer a continuous infusion of diltiazem (0.1 mg kg^{-1} h^{-1}) from incision to chest closure.[28 84 91] However, there is no objective evidence that calcium antagonists may improve outcome in OPCAB surgery.

Magnesium ions, up to 20 mmol in the form of chloride or sulphate, act similarly on myocardial cells; the only side-effect is a slight arterial vasodilatation.[44] Moreover, its use during cardiac surgery tends to decrease the incidence of atrial tachycardia.[43 76 123] Some centres recommend the use of $MgCl_2$ or $MgSO_4$ before pericardial opening.[76 84 106]

Even if nitroglycerin prevents arterial spasm on isolated human radial artery segments better than diltiazem, nitrates have never been proven to be efficient in preventing myocardial ischaemia during non-cardiac or conventional cardiac procedures.[47 107] In OPCAB studies, nitroglycerin has been used to reduce pulmonary arterial pressure,[15] to treat active ischaemia,[26 41] or as a hypothetical prophylactic measure. However, the nitroglycerin-induced decrease in preload is detrimental during heart verticalization when the filling pressures need to be increased to ensure optimal ventricular filling. Metabolic support with an intravenous glucose-insulin-potassium (GIK) solution does not offer significant clinical benefit for myocardial protection during OPCAB surgery.[108]

Surgical technique

In order to decrease the ischaemic time during anastomoses, the surgeon can insert a small shunt (1–3 mm size) into the coronary artery, which allows some blood flow, sufficient to prevent segmental wall motion abnormalities and to normalize or stabilize ST-segment elevation.[73] When coronary blood flow is maintained during the grafting procedure, only transient impairment of LV function is observed during the anastomoses.[125]

Monitoring technique

Conventional 5-lead surface ECG with automated ST-segment analysis is routine. However, heart manipulation modifies the positional relationships of the heart to the surface electrodes, and restricts its contact with surrounding tissues.[90] The shape of the tracing is altered, and the amplitude of the signal is reduced. For adequate monitoring of myocardial ischaemia, a new baseline must be established after each change in heart position in order to correctly interpret the observed ECG changes. Nevertheless, when the heart is completely enucleated, the diagnostic accuracy of ECG monitoring is reduced.

Invasive arterial blood pressure monitoring is mandatory to ensure adequate blood pressure. Of the studies reviewed, 74% consider a floated pulmonary arterial catheter (PAC) to be necessary. Right atrial and pulmonary wedge pressures must be interpreted within the framework of heart verticalization, as they should be significantly increased in order to push the blood up into the ventricle. Sv_{O_2} is a useful tool to evaluate global tissue oxygenation: an Sv_{O_2} decrease below 50% has been associated with the development of bowel ischaemia.[10] It is essential to maintain the tip of the PAC in the mainstream of a large pulmonary artery, as the handling of the heart might advance the tip of the catheter into the periphery, towards smaller pulmonary vessels that can be disrupted with balloon inflation.

During heart manipulation, RV and LV outflow might be momentarily asymmetrical. The continuous pulse contour cardiac output (PCCO), which provides a beat-to-beat measurement of cardiac output from the arterial pulse curve, might complete the data on cardiac pressures with information on LV output. However, both PAC and PCCO measurements have been found to be in close agreement.

The presence of air surrounding the heart, and the use of a posterior pericardial stitch and swab close to the oesophagus, restrict considerably the performance of TOE, particularly when the heart is in the vertical position. The images are usually of poor quality, although still interpretable. TOE is a useful device for evaluating ventricular function and effective ventricular end-diastolic volume, and for diagnosing new RWMA. During coronary flow interruption, new RWMA are found in 64% of patients, of which 50% recover

Table 2 Suggested protocol for anaesthetic management of OPCAB surgery

- Monitoring
  - ECG 5-lead plus continuous ST-segment analysis
  - Arterial catheter (femoral or radial)
  - Swan–Ganz pulmonary arterial catheter (through right internal jugular vein)
  - Two large-bore peripheral venous cannulae
  - TOE
  - Oesophageal and rectal temperatures, Foley catheter
- Anaesthesia maintenance
  - Fentanyl (total dose 15–20 μg kg^{-1})
  - Vecuronium
  - Isoflurane (1–1.5% throughout operation) or sevoflurane (1.5–2.5%)
  - Tracheal intubation with single-lumen tube (double-lumen only in case of thoracic approach)
- Preventive measures
  - Room temperature set at 24°C
  - Fluid warming
  - Forced-air heating device, heating mattress
  - Diltiazem (0.1 mg kg^{-1} h^{-1}) without loading dose, fixed rate from skin incision to sternum closure
  - Magnesium ($MgCl_2$) 2–3 g i.v. at pericardial opening
  - 500 ml of 6% hydroxyethyl starch 200/0.5 at pericardial opening
  - Auricular pacing wire connected to a pacemaker; ventricular lead added during surgery on right coronary artery
- Fluid management
  - Ringer's lactate and colloid perfusions as needed
  - Mannitol 0.5 gm kg^{-1} at the end of operation if fluid balance is excessively positive
  - Blood transfusion trigger: 8 gm dl^{-1} (higher threshold values if obvious ischaemia or central venous desaturation)
  - Blood loss processed by cell salvage
- Hypotension
  - Leg elevation
  - Norepinephrine perfusion
  - Increase i.v. fluid administration
  - Heart rate up to 50–60 beats min^{-1} through atrial pacemaker if persistent bradycardia
- Low cardiac output (Sv_{O_2} <60%)
  - Increase heart rate with atrial pacemaker wire
  - Increase preload
  - As far as possible, no β-stimulation before revascularization
  - Intra-aortic balloon pump if LV acute failure
- Indications for converting to CPB
  - Persistence of the followings for >15 min despite aggressive therapy:
    - Cardiac index <1.5 litre min^{-1} m^{-2}
    - Sv_{O_2} <60%
    - MAP <50 mm Hg
    - ST-segment elevation >2 mV
    - Large new wall motion abnormalities or collapse of LV function assessed by TOE
    - Sustained malignant arrhythmias

CPB=cardiopulmonary bypass; LV=left ventricular; MAP=mean arterial pressure; TOE=transoesophageal echocardiography.

completely and 33% only partially after anastomosis.[81] Mitral and pulmonary flow changes, typical of moderate diastolic impairment, can be observed during heart verticalization along with a reduced size of the LV and quantitative variation in mitral regurgitation.[49] TOE can also identify a patent foramen ovale, should an unexplained refractory hypoxaemia supervene. It is also useful for excluding intracavitary thrombus, which is a contraindication to beating heart surgery. As mortality and morbidity from TOE are extremely low (0 and 0.2%, respectively),[56] its risk–benefit ratio makes it a valuable tool for monitoring during OPCAB surgery.[81] It is used routinely in 52% of the reviewed series.

During the first 30 min after revascularization, the surface ECG frequently demonstrates significant T-wave inversion which might be linked to reperfusion injury.[31 120] Quantitative bypass blood flow measurement using an ultrasound transit time flowmeter is therefore convenient after the grafting procedure. The measured flow should be pulsatile and biphasic, with two forward components of short protosystolic and large diastolic flow, and one small component of retrograde telesystolic flow. The diastolic flow velocity should be >15 cm s^{-1}, and the mean graft flow at least 20 ml min^{-1}.[34] If the anastomosis is stenotic, the flow curve becomes spiky and mainly systolic. Absolute flow values are less significant than the pulsatility index (PI), which is obtained by dividing the difference between the maximal and the minimal flow by the mean flow; the optimal PI is between 1 and 5.[34] A low flow rate and an augmented PI have a high prognostic value for mid-term graft occlusion, and should lead to immediate graft reconstruction.[72] TOE is helpful in evaluating post-anastomosis regional contractility. Persistent RWMA have an accurate prognostic value for postoperative cardiac complications.[81]

Haemodynamic management

Knowing the haemodynamic patterns of the OPCAB procedure, it becomes possible to adopt a strategy that aims at maintaining an optimal myocardial oxygen balance. This is usually achieved by keeping myocardial oxygen consumption as low as possible, and by preserving a relatively high coronary artery perfusion pressure (MAP ⩾70 mm Hg) with an infusion of vasopressor and an increased preload.[41] A reduced cardiac output is accepted as long as the Sv_{O_2} remains >60% and metabolic acidosis does not develop. The 'Buffington ratio' is a useful index. It stipulates that patients suffering from coronary stenoses are at particular risk of myocardial ischaemia when their mean arterial pressure is less than the heart rate (MAP/heart rate <1).[19]

The patient frequently becomes hypotensive when the heart is tilted into a new position. Myocardial preload can be increased by leg elevation,[88] and by administration of fluids. Total fluid input is surprisingly similar to that during CABG performed on CPB. In our series, the mean amount of fluids infused during OPCAB surgery was 850 ± 230 ml of colloid and 2800 ± 800 ml of crystalloid.[84] Alternatively, α-adrenergic agents such as phenylephrine or norepinephrine are indicated when MAP remains low despite optimization of circulating blood volume, in order to prevent excessive fluid administration and a detrimental increase in lung water content. Many different regimens are used. Possible LV dilatation is monitored by TOE. Excessive heart rate is usually treated with a β-blocker, most frequently esmolol, after exclusion of hypovolaemia or inadequate anaesthesia. An α_2-adrenoreceptor agonist like dexmedetomidine might be useful in unresponsive cases.[102] If excessive bradycardia (heart rate <50 min^{-1}) develops, pacemaker wires connected to the right atrium can be used to increase the heart rate to 50–65 beats min^{-1}.[119] For main RCA anastomoses, a ventricular wire must be in place to avoid complete AV block. It seems advisable to avoid β-stimulation before revascularization as myocardial ischaemia might increase because of excessive oxygen demand. Although theoretically sound, this concept has not yet been proven clinically in OPCAB surgery.[90]

Anticoagulation is mandatory during OPCAB surgery. As there is no contact with foreign surfaces unlike CPB, the targeted activated coagulation time (ACT) is usually kept at 250–300 s as in major vascular surgery.[75 84] This is reached by the i.v. administration of heparin 1–2 mg kg^{-1} (100–200 IU kg^{-1}) before section of the internal mammary artery. The ACT is repeated every 30 min, and heparin added as required. This lesser degree of anticoagulation and the lower platelet activation in comparison with CPB significantly decreases the haemorrhagic risk and the transfusion rate.[9 114] Heparin reversal with protamine is optional. Mariani reported a hypercoagulable state after off-pump procedures,[75] which might put patients at risk of bypass thrombosis or thromboembolism. Some centres start aspirin and/or clopidogrel at the end of the procedure,[1] as aspirin reduces mortality and ischaemic complications after coronary bypass surgery.[74]

Indications for conversion to CPB remain difficult to define (Table 2). The limits are usually set at the following values, if they persist for >15 min despite aggressive therapy: cardiac index <1.5 litre min^{-1} m^{-2}, Sv_{O_2} <60%, MAP <50 mm Hg, malignant arrhythmias, ST modifications >2 mm, and/or complete cardiovascular collapse.[91] The rate of conversion to CPB varies between <1 and 4.9%.[22 67 119] Good communication with the surgeon is essential, and the repositioning of the heart is probably the first step to take before conversion.[41] The presence of a perfusionist with a 'dry ready' CPB machine in the operating suite is therefore current practice. The main factors associated with major haemodynamic instability leading to CPB assistance are cardiomegaly, lateral wall compression during anastomoses on the obtuse marginal or ramus intermedius, and ischaemia during main RCA grafting.[119] In cases of severe LV dysfunction (ejection fraction ≤20%), OPCAB can be performed under the assistance of intra-aortic balloon pumping in order to avoid CPB conversion.[59] Flow-controlled centrifugal or axial mini-pumps can offer a right-side as well as a left-side support of 1–3 litre min^{-1}.[71] With experience, however, OPCAB has become a procedure that can be performed without support, and these devices are mainly used for short-term circulatory support in cases of acute heart failure.

Anaesthesia technique

Avoiding CPB does not shorten the length of the procedure. The duration depends largely on the number of anastomoses performed and the skill of the surgical team. OPCAB, however, accelerates immediate postoperative recovery. This trend towards shorter ICU and hospital length of stay has led anaesthetists to adapt their technique to a fast-track management with early extubation (i.e. between 1 and 4 h after the end of operation). This has been proven to be safe and cost-effective.[104] Hypothermia, as it constitutes an independent predictor of morbid cardiac events,[46] should be avoided by all possible means during the operation: fluid warming, a heat exchanger on the fresh gas flow, warming mattress etc. (Table 2). As much of the upper torso and lower limbs are exposed during surgery, forced-air heating devices are only marginally efficient; a room temperature up to 24°C is usually recommended.[26 40 68] Maintaining normothermia is extremely challenging, as the absence of CPB also removes the opportunity to warm up the patient on bypass.

Table 3 Main anaesthetic agents used for OPCAB surgery, as found in a survey of 46 studies. Data are presented as the number (%) of times each agent has been used

Propofol	25 (54)
Isoflurane	19 (41)
Midazolam	8 (17)
Fentanyl	31 (67)
Sufentanil	11 (24)
Remifentanil	7 (15)
Epidural	4 (9)
Intrathecal	2 (4)

From a survey of 46 recent studies where the technique is clearly described, the anaesthetic technique appears conventional (Table 3): fentanyl, propofol or isoflurane have been used in about two-thirds of the institutions. In some cases, general anaesthesia combined with intrathecal (sufentanil-morphine or bupivacaine),[14] or thoracic epidural (bupivacaine) analgesia is favoured.[2 40 68 91] Thoracic epidural anaesthesia has been shown to increase the diameter of epicardial arteries, increase collateral blood flow, decrease myocardial oxygen demand, decrease the incidence of arrhythmias and the rate of chest infection, and provide adequate postoperative analgesia.[60 104] Despite the advantages of cardiac sympatholysis for OPCAB surgery, randomized studies comparing general *vs* combined anaesthesia, did not show significant difference in patient outcome, except for a trend towards earlier extubation.[14 91 104] An ultra-fast technique with extubation in the operating room does not seem to be of any additional benefit to the patient or to be cost-effective.[40 82] As beating-heart surgery requires less heparinization than CABG on CPB, the risk of epidural haematoma is reduced compared with conventional cardiac surgery, and should be the same as in major vascular surgery. There is a trend to keep patients on aspirin and antiplatelet drugs until surgery. Therefore, the place of regional analgesia, although very attractive in OPCAB surgery, needs to be further defined. Table 2 suggests an anaesthetic protocol; many other options may be suitable or even better adapted to local practices.

Although anaesthetic technique has not been shown to influence postoperative mortality or morbidity in OPCAB surgery patients, there is increasing experimental evidence that some anaesthetic agents may be more suitable than others. Volatile anaesthetics such as isoflurane and sevoflurane have been shown to induce significant pharmacological preconditioning, which represents protection against ischaemia.[11 27 55 128] Although i.v. anaesthesia maintains haemodynamic stability in OPCAB surgery, propofol usually requires readjustment of the loading conditions because of its venodilating properties.[103] In addition, it does not seem to have significant cardioprotective effects.[35] When compared with fentanyl and sufentanil, remifentanil markedly reduces ventricular preload and heart rate.[42] Nevertheless, well conducted randomized studies are required to define the most appropriate anaesthetic protocol for OPCAB surgery. As haemodynamic stability can be achieved with many different agents, those mediating pharmacological preconditioning may be favoured.[55 128]

Whatever the anaesthetic technique used, the primary goals of the anaesthetist are to manage the haemodynamic disturbances associated with heart manipulation and to treat the ischaemic events caused by coronary occlusion. As the difference in outcome of OPCAB *vs* CABG on CPB appears mainly in high-risk cases, it is of the utmost importance for the anaesthetist to master the pathophysiological processes involved, because proper handling of compromised patients could make a significant difference to morbidity and mortality.

Conclusions

OPCAB is an attractive alternative to on-pump surgery, especially for patients with altered cardiac function and severe comorbidities, including old age and coagulation disorders. Anaesthetists involved in cardiac surgery must have knowledge of this specific procedure and its haemodynamic requirements. The primary goals of anaesthetic management are maintenance of adequate haemodynamics during heart enucleation and optimal myocardial protection during ischaemic events. The anaesthetic technique contributes to maintaining a stable equilibrium between myocardial oxygen consumption and the oxygen requirements of the body. Experimental and clinical studies suggest that halogenated agents have a protective effect against ischaemia in myocardial cells, making them the anaesthetic agent of choice. The place of thoracic epidural or intrathecal analgesia, although promising, is not yet defined. Anaesthetists play a proactive and integral part in the success of the operative course and outcome of OPCAB surgery, by their management of circulatory and ischaemic disturbances.

Longer version of this review

A longer version of this review can be seen in *British Journal of Anaesthesia* online. The figures also appear online in colour as supplementary data.

To help clarifying the comparison between different publications with dissimilar methodologies, the references are annotated into levels of evidence according to the guidelines of evidence-based medicine. Level I of evidence contains studies with prospective, randomized selection of patients, blinding and clear-cut results. Level II contains controlled non-randomized prospective studies. Level III comprises non-controlled non-randomized studies with contemporaneous controls. Level IV corresponds to retrospective studies with historical controls. Level V includes uncontrolled case series, observational studies and expert opinions. Technical descriptions, review articles and meta-analyses are not coded.

Addendum

Since acceptance of the manuscript, new prospective randomized studies have been published focusing on two crucial areas: clinical outcome after OPCAB surgery, and preconditioning with volatile anaesthetics.

The reduction in transfusion requirements, in myocardial injury as evidenced by troponin-I release, in length of ICU and hospital stay, and in global costs, have all been confirmed by three randomized prospective studies.[131–133] Morbidity and mortality are decreased in patients having OPCAB compared to conventional CABG surgery in two large comparative analyses of 7808 patients, the difference being greater in high-risk patients.[129–134] Neurological dysfunction and stroke were also reduced in OPCAB surgery compared with conventional CABG surgery in a prospective randomized study on 60 patients.[131]

The benefit of pharmacological preconditioning by volatile anaesthetics[55 128] has been confirmed in a prospective randomized controlled clinical trial in patients undergoing OPCAB surgery.[130] Patients receiving sevoflurane anaesthesia had less myocardial injury as evidenced by less postoperative troponin-I release compared with patients anaesthetized with propofol.[130]

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