OFF-PUMP CORONARY ARTERY BYPASS SURGERY

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Coronary revascularisation plays an important role in the management of patients with ischaemic heart disease. Its principle builds on restoring antegrade flow thereby relieving angina. As a result, the need for medication is reduced which, in turn, may improve quality of life and socioeconomic independency. Also the prognosis is beneficially affected. This is not only true for patients with severe coronary atherosclerosis such as patients with left main or three vessel disease, but also for patients with less advanced disease.[w1–3]

WHY OFF-PUMP BYPASS SURGERY?

The first milestones in coronary revascularisation were surgical. It all started after the second world war with the implantation of the internal mammary artery indirectly into the cardiac muscle (the Vineberg procedure). A few years later, procedures for direct coronary artery revascularisation were designed, initially including endarterectomy, followed by the construction of an anastomosis between a donor artery or vein and the coronary artery. Interestingly, these first operations were performed on the beating heart without the use of extracorporeal circulation and cardiac arrest.[w4] The results of these early initiatives were generally unpredictable, preventing general acceptance and widespread use. It became clear that the safety and efficacy of surgical coronary revascularisation in terms of in-hospital complications and immediate and long term clinical outcome greatly depends, among other factors, on the quality of the anastomosis between the donor graft and recipient coronary artery. To predictably create these delicate and very precise hand sewn anastomoses, the surgeon needs a still and bloodless field with full exposure of the target area, enabling the required complex and coordinated manipulation of the microsurgical instruments.

In this respect, the introduction of cardiopulmonary bypass (CPB) and cardiac arrest by Favaloro in 1967 proved to be a tremendous step forward. Because basic surgical requirements could now be properly addressed, consistent high quality anastomoses could be produced by the broad majority of cardiac surgeons. Indeed, the reported excellent clinical outcome and long term results initiated a tremendous increase in the number of bypass operations reaching the clinical status of "gold standard". Earlier efforts using different techniques were completely overwhelmed and almost forgotten for nearly 30 years. Excellent long term clinical results have been reported in a wide variety of patients, especially when using the internal mammary artery.[w5 w6] The superiority of coronary artery bypass grafting (CABG) with the use of CPB and cardiac arrest—the so-called conventional CABG—with respect to angina reduction and the need for repeat revascularisation, in comparison with medical treatment and percutaneous transluminal coronary angioplasty (PTCA), is subject to little discussion.[w6–8] As a result, conventional bypass surgery has been quoted as "safe, effective, durable, reproducible, complete, versatile and teachable".[w9]

The question, however, is whether bypass surgery with CPB and cardiac arrest is indeed safe. Data from the National Cardiac Surgery Database of the Society of Thoracic Surgery encompassing 170 895 patients are summarised in table 1.[w10] Overall, the proportion of patients suffering no complications was only 64.3%.[1] In addition, health insurance data and data from clinical studies disclose that 10.2% do not leave the hospital within 14 days after the operation and 3.6% of the patients are discharged to a non-acute care facility.[2 w11] The scope of the problem becomes clear when one considers that bypass surgery is performed in approximately 800 000 patients/year worldwide. Conventional bypass surgery is increasingly being questioned and this has stimulated the quest for novel surgical techniques guaranteeing the good results of precise direct coronary revascularisation, but avoiding factors believed to adversely affect the outcome and, thus, leading to less perioperative morbidity, faster recovery, shorter hospital stay, and reduced costs. One of these factors may be the use of cardiopulmonary bypass.

In this paper, the clinical experience and the reasons why isolated, off-pump surgery may lead to improved outcome are addressed. Off-pump surgery is defined as CABG surgery on the beating heart without the use of CPB and cardiac arrest, irrespective of the surgical access to the heart. Isolated bypass surgery implies coronary bypass surgery without concomitant cardiac or vascular procedures at the time of bypass grafting.

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Table 1 Perioperative complications during isolated CABG (%)

	First operation	Reoperation
Number of patients	157159	13736
Mortality	2.6	7.3
Myocardial infarction	1.1	3.4
Reoperation	4.6	7.4
For bleeding	2.2	3.1
Stroke	2.4	3.1
Permanent	1.7	2.2
Transient	0.7	0.8
Pulmonary		
Prolonged ventilation (>24 hours)	5.3	10.2
Oedema	1.9	3.4
Pneumonia	2.2	3.8
Acute distress syndrome	1.4	1.8
Renal failure	2.9	5.2
Dialysis required	0.8	1.7
Gastrointestinal complications	2.3	3.0
Multiorgan failure	0.6	1.4
Infection	4.9	6.0
Sternal	1.3	1.5
Leg	1.3	1.5
Urinary tract	1.4	1.4
Sepsis	0.9	1.6

Modified from Borst and Gründeman.[w10]
CABG, coronary artery bypass graft surgery.

DETERMINANTS OF PERIOPERATIVE MORBIDITY AND MORTALITY

Surgical risk is influenced by a number of patient related factors such as age, severity of coronary artery disease, left ventricular function, and the presence of comorbid conditions (for example, diabetes, renal insufficiency, pulmonary and peripheral vascular disease, obesity). On the basis of these demographic and clinical determinants, risk models have been developed which can be used to either calculate the surgical risk or to stratify patients into low, medium or high risk subgroups.[3 4]

In addition to these patient related factors—which unfortunately cannot be corrected but, at best, may be modified or optimised before surgery—a number of procedure related factors play a role (table 2). In case of conventional bypass surgery, access to the heart must be obtained via full sternotomy, the heart and ascending aorta are cannulated for CPB, cardiac arrest is induced, and the ascending aorta is manipulated for the construction of a proximal anastomosis in case of saphenous vein or free arterial grafts. All these steps contribute to patient trauma and are likely to be associated with potential complications or may provoke biological reactions. Given their technical nature, there is ample room for improvement or innovation.

Central to the discussion is the use of CPB and the classical midsternal split. CPB requires the cannulation of the heart and the ascending aorta which may induce atherosclerotic (micro)emboli. Intraoperative transcranial Doppler monitoring has disclosed that the highest embolic load of the brain occurs during the aortic manipulation in preparation of CPB.[5] During a later stage of the operation, these emboli may not consist of particulate matter but rather of air bubbles introduced into the circuit by retrieving spilled blood from the surgical field or imperfections in the connections despite the use of arterial line filters.[5] The magnitude of the embolic load correlates with the duration of CPB and is reflected by the severity of postoperative cerebral dysfunction. Given these findings, it is conceivable that avoidance of CPB will substantially decrease the risk of perioperative neurologic complications, especially in elderly and other high risk patients. Yet, to completely avoid aortic manipulation, bypass surgery on the beating heart should also entail the exclusive use of in situ mammary grafts. For extensive coronary artery disease, more complex techniques like graft interposition between an in situ mammary artery and a coronary artery may be needed to obviate the need for aortic side clamping. Recently, automated vessel coupling systems suitable for connecting saphenous vein grafts to the aorta have started to become available. While still unproven, these systems may enable safe anastomoses on the ascending aorta in the future, simplifying the surgical procedure. Elderly patients in particular may benefit from off-pump, no-aortic touch bypass surgery since the incidence of atherosclerosis of the ascending aorta—and thus the risk of emboli—increases with age.[3 w12]

In addition to the risk of microemboli, CPB induces a total body inflammatory response caused by the activation of the complement system due to contact of the blood with the artificial surface of the CPB circuit.[6 w13] All organs are affected to a varying degree, potentially leading to dysfunction and/or damage of the brain, lungs, heart itself, bowel, kidneys, and coagulation system. Although the role of CPB in this response has been established and a whole body of evidence indicates that avoidance of CPB reduces oxidative stress, inflammation, and perioperative morbidity, it must be stressed that other factors such as the trauma of the surgical incision and the use of anaesthesic drugs may contribute to this inflammatory response as well.[w14–17] Thus, changes in surgical access to the heart, anaesthesiology, and pharmacology during the off-pump bypass may lead to a reduction in inflammation and postoperative morbidity.

As opposed to the heart, CPB produces a non-pulsatile flow which is thought to have an adverse effect on the microcirculation, leading to arteriolar shunting. This may contribute to postoperative organ dysfunction or failure.[w18] Non-pulsatile flow is one of the mechanisms which, in combination with the inflammatory response and the release of free radicals, is thought to be responsible for postoperative renal failure.[7]

Irrespective of the exact pathophysiology of CPB induced postoperative morbidity and mortality, these side effects have revitalised the nearly forgotten art of off-pump bypass surgery. The increasing public awareness of these complications and of less invasive alternative techniques in coronary revascularisation (PTCA) and other fields of surgery contribute to this new impetus.

Off-pump surgery on the beating heart also offers the opportunity to reduce the surgical incision and trauma to skin, soft tissue, and bone. Smaller access by means of various forms of minithoracotomy may reduce the risk of perioperative infection and enhance the speed of recovery. Sternotomy requires 6–12 weeks to heal and prevents early return to normal daily activities.[w19] Deep sternal wound infection occurs in 1–4% of the patients and is associated with a 25% mortality.[3] The determinants of deep sternal wound infections are obesity, the presence of diabetes, renal failure, redo surgery, and a number of operator related variables such as the use of more than one mammary artery and excessive use of electrocautery. Unfortunately, some of these risk factors such as obesity may not be compatible with reduced access

Table 2 Steps in conventional bypass surgery, consequences and potential solutions

Surgical trauma	Consequence(s)	Solution
Access to the heart Full sternotomy	Recovery time Infection (e.g.mediastinitis)	Minithoracotomy Port-access surgery Endoscopic robotic CABG
Cardiopulmonary bypass	Manipulation heart and aorta (microemboli) Inflammatory response	Off-pump CABG
Cardiac arrest Side clamping Aorta ascendens	Cell injury, necrosis Microemboli	Off-pump CABG No-touch aorta surgery (in situ arterial grafting) (graft interposition)

For details see text.

Clinical issues to be considered in CABG

- Effectively relieves angina (palliation)
- May positively affect event-free survival (prognosis)
- Non-negligible perioperative morbidity
- Cardiopulmonary bypass plays a major role in the pathophysiology of the perioperative morbidity
- Novel approaches such as off-pump beating bypass surgery are being proposed

type operations because of the prohibitive surgical difficulty of constructing a coronary anastomosis. The most benefit of a limited approach will probably be obtained in patients with diabetes, renal failure or redo heart surgery, provided that these patients do not have three vessel disease supplying viable myocardial tissue. In such a situation, full sternotomy may be more appropriate. A disadvantage of a minithoracotomy, however, is the increased amount of postoperative pain, especially when costal cartilages are traumatised as a result of substantial traction for surgical exposure or when multiple incisions are performed.[w20]

NOVEL APPROACH, NEW PROBLEMS

The potential advantages of a novel surgical approach, in this case off-pump bypass surgery, must be weighed against novel technical problems and limitations (table 3).

As stated before, the quality of the coronary anastomosis must be guaranteed. In the early days of off-pump bypass surgery, motion of the target area was controlled by pharmacologic reduction of global myocardial contractility and/or heart rate, with or without some primitive form of regional stabilisation by means of traction sutures. The breakthrough, however, came with the introduction of advanced regional mechanical stabilisers such as the CardioThoracic Systems Ultima device and the Utrecht Octopus in the mid 1990s.[8 w14] These devices consistently reduced the motion of the target area sufficiently to offer workable conditions for the majority of the surgical community. These stabilisers are, respectively, compressive and suction type devices that are fixed to one side of the operating table or chest wall retractor, with the other end apposed to the epicardial surface. As a result the coronary artery anastomosis can be constructed with enough surgical comfort and allow graft patency rates comparable to conventional CABG.[w10] Not surprisingly this has augmented the number of off-pump bypass operations from a negligible number in 1995 to 10% in 1999, and is expected to be 50% by 2005.[w21]

Yet, to construct a coronary anastomosis safely, the surgeon also needs a bloodless field. Therefore, the flow of the recipient coronary artery must be temporarily interrupted. For this purpose, vessel snares (suture or silicone elastomer tape) or atraumatic vascular clips are used proximally and often also distally to the coronary arteriotomy. This is invariably associated with myocardial ischaemia. Although generally well tolerated, it may occasionally provoke arrhythmia and haemodynamic instability, eventually necessitating conversion to on-pump bypass surgery and cardiac arrest. The interruption of the flow of the right coronary artery is known to provoke these complications. This can be addressed by placing an intracoronary shunt or seal when performing the anastomosis.[w22 w23] Although unproven, these mechanical solutions, as well as the coronary sutures or clips, all add to endothelial damage which may contribute to the development of late luminal narrowing.[1 w24] In addition, the clinical value of shunts is questioned since they may be cumbersome to use and, with respect to the shunt, blood flow through the shunt is only 30–50% of the native coronary flow.[1]

Ensuring a dry, bloodless field may also be hindered by back bleeding from perforating septal branches in the vicinity of the arteriotomy. This can be addressed by frequent blotting, intermittent saline infusion, or the use of high flow carbon dioxide moisturised insufflation.[9] It will be clear that, as opposed to conventional CABG, the off-pump surgeon needs an innovative and more flexible attitude to create optimal conditions consistently during surgery.

Haemodynamic instability and a drop in systemic blood pressure may occur when compressing or luxating the heart. Little displacement is required when reaching the left anterior and diagonal arteries. This is not the case when the circumflex or right coronary artery needs to be grafted. A nearly vertical displacement may be needed for the posterior wall, which is obtained by either deep pericardial traction stitches or a sling or a supporting device.[w25] Such a notable displacement is surprisingly well tolerated in most patients, but can provoke a significant drop in blood pressure and myocardial flow.[10 w26] Patients with left ventricular hypertrophy or poor ventricular function may not tolerate such a manoeuvre.[w25] Yet these patients are potentially ideal candidates for off-pump bypass surgery since a slight depression of myocardial contractility, induced by global ischaemic cardiac arrest during bypass surgery with CPB, may prohibit weaning from CPB or may lead to a low output syndrome which is the most common cause of operative mortality.[3 w27] Generally, all regions of the heart can be reached in the great majority of patients by perfect placement of the traction stitches and by improving venous

Table 3 Disadvantages and technical limitations of off-pump coronary artery bypass surgery

Technical issues	Proposed solutions
Motion of the heart	Pharmacologic or mechanical stabilisation
Tempory interruption of coronary flow	Luminal shunt during construction of anastomosis Arteriotomy seal Distal perfusion cannula
Blood flow in arteriotomy	Temporary luminal shunt Saline infusion Carbon dioxide gas blower
Pressure drop	Trendelenburg, inotropic support, fluid
Limited space for: preparation of mammary artery identification of coronary artery construction of anastomosis	Miniaturisation of instruments Endoscopic video assisted surgery

Determinants of perioperative morbidity

- Age
- Extent of coronary artery disease
- Ventricular function
- Comorbid conditions
- Extent of the surgical trauma
- Use of cardiopulmonary bypass
- Global ischaemic cardiac arrest
- Manipulation and instrumentation of the ascending aorta

return by utilising the Trendelenburg position with or without additional fluid load and inotropic support.[w25]

Conventional bypass surgery via full sternotomy and CPB with a decompressed and arrested heart provides sufficient visibility and space to construct safely and adequately an anastomosis on all coronary arteries. This may be more difficult in limited access approaches and off-pump bypass surgery. Moreover, limited visibility may also interfere with identification of the target coronary artery. Therefore, training and patient selection are crucial in off-pump bypass surgery to optimise the learning curve. The left anterior descending, distal right, and proximal posterior descending arteries are relatively easy to approach with a limited anterior thoracotomy or subxyphoidal incision. Full sternotomy may be the most optimal approach for patients with three vessel disease.

Still experimental are the advanced robotic instruments capable of increasing surgical dexterity sufficiently to enable thorascopic bypass surgery, preferably with the aid of three dimensional visualisation.[w28] These systems have not yet provided the breakthrough of total endoscopic CABG (TECAB) mainly because of the still substantial technical difficulty in creating a robot-sewn anastomosis. Currently, interest seems to be shifting towards alternative, automated ways of performing the distal coronary anastomoses. While glued anastomoses certainly hold promise, most advancement has been in the area of mechanical connecting systems such as small, intraluminal stent-like structures, intraluminal magnets, and extraluminal devices with small hooks. While these connectors are already available for the larger, proximal anastomosis on the aorta, the relatively small size of the coronary arteries and their delicate, friable walls impose large obstacles for the development of reliable systems that may ultimately enable TECAB in large groups of patients.

CLINICAL EXPERIENCE

The clinical experience with off-pump bypass surgery is summarised in table 4. These data should be interpreted with caution since all but one originate from non-randomised observations made by pioneers in the field. Therefore selection bias, time bias, observation bias, and publication bias cannot be ruled out. Also, there is quite some variation in the definition of the outcome measures and in the consistency and methods of the acquisition of the clinical events between the studies. Taking into account these limitations, these data suggest that perioperative mortality and morbidity following off-pump bypass surgery compares favourably with those of the National Cardiac Surgery Database summarised in table 1. Only one study conducted at the University Medical Center Utrecht, using the Octopus Tissue Stabilizer, directly compared off- and on-pump bypass surgery by means of a randomised clinical trial.[11 12] This study revealed, however, no superiority in 30 day clinical outcome and only a modest superior cognitive outcome at three months which became negligible at 12 months after off-pump bypass surgery.[12]

Taking into account the expectations of off-pump bypass surgery, these findings were somewhat disappointing. The study, however, was conducted in patients of whom 50% had two vessel disease with a normal ventricular function and little comorbidity. This is also reflected by the low incidence of complications in patients who underwent on-pump bypass surgery. Two findings, however, favour off-pump CABG: there was a reduced need for blood products in the off-pump group, and there was a 41% reduction in postoperative creatine kinase MB release. The former is a consistent finding in most of the observational studies summarised in table 4. The latter suggests that avoiding CPB reduces the degree of myocardial necrosis which is in accordance with a significant reduction in troponin I release in off-pump patients reported previously.[13 14] Apparently local ischaemia during clamping of the coronary arteries is less harmful than global cardiac ischaemia. The clinical importance of this finding is that postoperative elevation of cardiac markers of necrosis has been identified as an independent correlate with one year clinical outcome.[w29]

Information on long term results of off-pump CABG is derived from the cases studies cited above (table 4) and the randomised clinical trial we directed at the University Medical Center Utrecht. Again, taking into account the limitations of

Table 4 In-hospital and 30 day clinical events after off-pump bypass surgery

Author (ref)	Year	Number of patients	Death	CVA	AMI	RF	Inf	Redo	AF
Subramanian[w26]	1997	182	3.8	0.5	3.8	nr	2.7	3.2	8.0
Sternik[w27]	1997	64	3.1	1.6	3.1	nr	nr	nr	nr
Diegeler[w30]	1998	209	0.5	nr	1.9	nr	nr	2.4	nr
Jansen[w31]	1998	100	0.0	2.0	4.0	nr	1.0	1.0	12.0
Magovern[w19]	1998	60	0.0	0.0	nr	nr	nr	1.7	nr
Tasdemir[w32]	1998	2052	1.9	0.8	2.9	0.2	0.5	0.9	17.0
Calafiore[w33]	1999	122	0.0	0.0	0.0	nr	nr	0.8	9.8
Arom[4]	2000	350	3.4	1.4	0.6	5.0	nr	2.8	14.0
Cartier[w34]	2000	300	1.3	1.6	4.0	nr	4.6	5.0	30.0
Koutlas[w12]	2000	53	0.0	2.2	0.0	0.0	0.0	0.0	26.0
Hart1[17]	2000	1582	1.0	0.6	1.3	0.9	0.3	1.2	15.0
Varghese[w35]	2001	35	2.9	nr	2.9	5.7	nr	nr	23.0
Yeatman[w36]	2001	75	1.3	0.0	2.7	6.7	0.0	2.7	12.0
Hernandez[18]	2001	1754	2.5	1.3	nr	nr	nr	4.5	21.0
Puskas[19]	2001	200	1.0	1.5	1.0	nr	0.0	1.5	nr
Van Dijk (39)	2002	142 off-p	0.0	0.7	4.9	0.0	5.0	4.0	20.0
		139 on-p	0.0	1.4	4.3	1.0	5.0	2.0	21.0

All events are expressed as percentage.
AF, atrial fibrillation; AMI, acute myocardial infarction; CVA, cerebrovascular accident; Inf; infection; nr, not reported; off-p, off-pump coronary artery bypass surgery, on-p, on-pump coronary artery bypass surgery; Redo, postoperative rethoracotomy for bleeding, infection or graft revision; RF, postoperative new renal failure.

Expectations and potential limitations of off-pump bypass surgery

- No need for cardiopulmonary bypass
- Reduction of surgical trauma
- Reduction of perioperative morbidity, recovery time, hospital stay, and costs
- Limited access, motion of the heart
- Quality of the anastomosis
- Haemodynamic changes, inducing organ dysfunction and reducing applicability
- Completeness of revascularisation

the observational studies, survival free from myocardial infarction after off-pump bypass surgery compares favourably with off-pump surgery. A striking feature is a higher occurrence of angina pectoris after off-pump bypass surgery and a higher frequency of percutaneous revascularisation during the follow up period.[4] This may be explained by less complete revascularisation and, thus, the learning curve of this surgically more demanding operation. This was not observed in the randomised clinical trial we conducted (Natho H, *et al*, unpublished data).

With respect to graft patency, data from observational studies in comparison with historical controls suggest similar early graft patency between off-pump (91–99 %) and on-pump (94–99%) bypass surgery.[15 16]

THE FUTURE

Doctors together with their patients now have a therapeutic spectrum of myocardial revascularisation procedures. At one end there is plain balloon PTCA which is the least invasive modality, followed by stents and other more advanced novel catheter technologies, and adjunctive pharmacologic and genetic intervention. The other end of the spectrum consists of bypass surgery. The most invasive approach, conventional CABG via full sternotomy, is now being challenged by full and limited access off-pump CABG. The slightly disappointing absence of notably better early clinical outcome after off-pump CABG draws our attention to the gap in the spectrum. This place could be filled by TECAB, the perfect intermediate between percutaneous techniques and current surgery. While not possible for mainstream clinical use yet, this could change within a time frame of as little as five years. In the meantime, the trend towards better clinical outcome, however slight, should urge surgeons to expand carefully the use of off-pump techniques and limited size incisions whenever possible.

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