Special Article

Current Trends in Surgical Reperfusion of the Myocardium

Sotirios N. Prapas

Department of Cardiac Surgery, "Henry Dynant" Hospital, Athens, Greece

Key words:
Myocardial reperfusion, surgical techniques, arterial "pi circuit".

Manuscript received:
September 8, 2004;
Accepted:
November 11, 2004.

Address:
Sotirios N. Prapas

Department of Cardiac Surgery
"Henry Dynant" Hospital
107 Mesoghion Ave.
11526 Athens, Greece
e-mail:
sprapas@dunanthospi.gr

The classical coronary bypass with extracorporeal circulation and the exclusive use of venous grafts has not lived up to expectations for an uncomplicated perioperative outcome and good functioning of the grafts in the long term. Four decades of coronary artery surgery have featured a long quest for a safer method and for more appropriate grafts. This article describes the surgical landscape as well as the current trends in the era of surgical myocardial reperfusion.

A retrospective

In 1967, the Argentinean Favaloro, working at the Cleveland Clinic, carried out an historic surgical procedure, bypassing the right coronary artery with a saphenous vein graft under extracorporeal circulation and thus opening the way to the classical coronary bypass operation.[1] Adopting this technique, Johnson in Milwaukee introduced multiple coronary artery reperfusion with venous grafts.[2] Around the same time, a Russian, Kolessov, had already introduced the philosophy of coronary bypass on a beating heart in 1966 by achieving the anastomosis of the left internal mammary artery (IMA) to the anterior descending branch.[3] The developments that followed those breakthroughs and continued until the present day had to do with the use of an arterial graft, the spread of the beating heart technique, the discovery of less invasive approaches or methods, and finally, the utilisation of the technology of the robotics era and anastomotic devices. As regards the grafts, the first clinical implantation of a left IMA to the anterior descending branch in the western world was performed in New York, in February 1968, by Green.[4] In 1974, Barner reported the reperfusion of 100 patients using bilateral IMA.[5] The good results very soon led surgeons to seek methods for the further utilisation of the IMA, which was in regular use at the start of the 1980s, and to carry out compound grafts such as the T-graft,[6] the Y-graft,[7] the pi-graft[8] and others.

At the same time, the quest for other arterial grafts led to the use of the radial artery since 1971, the right gastroepiploic artery since 1987,[9-11] and the inferior epigastric artery since 1990. It is noteworthy that the initial evaluation of the patency of the radial artery was poor, with the result that the graft was abandoned until 1991, when a Frenchman, Acar, revived its use with a similar vascular preparation protocol and the perioperative use of diltiazem.[12] The avoidance of extracorporeal circulation was introduced, mainly for financial reasons, in Latin America by Benetti[13] and Buffolo[14] during the 1980s. However, widespread acceptance of the off-pump coronary artery bypass (OPCAB) technique came later, towards the end of the 1990s, via the experience acquired a few years earlier from minimally invasive techniques and through the

adoption of commercial stabilisers to facilitate anastomoses. In 1995 Benetti introduced the minimally invasive direct coronary artery bypass (MIDCAB) technique, implanting the endoscopically prepared left IMA to the anterior descending branch with an inferior "mini" sternotomy.[15] However, the method was made popular in 1996 by Calafiore in Italy, who was able to perform not only the anastomosis but also the preparation of the IMA through a small anterior thoracotomy with direct monitoring: the LAST operation.[16] Even though the use of the method is limited to reperfusion procedures involving the anterior wall only, it provided the spark for the manufacture of commercial products that really opened the way to the wider acceptance of the OPCAB technique, 35 years after Kolessov's efforts and 15 years after Benetti's and Buffolo's original operations.

Rapid technological developments and the widespread adoption of percutaneous angioplasty at the end of the 1990s led surgeons to seek out progressively less invasive methods. One such researcher was Loulmet, who introduced robotic reperfusion in December 1998.[17] The ground had been prepared earlier and the concept of "port access" surgery had been introduced as a means of carrying out multiple vessel reperfusion via small incisions. This technique was based on the triple-lumen catheter built and tested experimentally by Peters in 1993. This catheter, when introduced via the femoral artery, was able to achieve intraluminal occlusion of the aorta with a balloon, the administration of cardioplegia and degassing of the left ventricle.[18] The clinical study of the system for coronary bypass procedures was carried out during 1995-96 in the universities of Stanford and New York. Its connection with extracorporeal circulation was achieved via a cruro-femoral approach and the surgery was performed using endoscopes and small incisions that facilitated access to the target vessel.[19]

The introduction of robotic technology allowed the possibility of surgery with an entirely closed chest cavity: total endoscopic coronary artery bypass (TECAB). At the same time, increasing experience with off-pump surgery led in early 2000 to the first beating heart procedures using a robotic system.[20,21] Finally, it is worth mentioning the first clinical applications, at the dawn of the new century, of automatic anastomotic devices in the ascending aorta for carrying out central anastomosis, or of systems for peripheral anastomosis, mainly represented by the MVP-system, which is comprised of 2 magnetic elliptical rings that are fixed to the graft and the coronary vessel and held together by magnetic attraction.

Long-term results from the use of grafts

As shown in an historic study by Loop in 1986, the use of at least one mammary artery graft significantly improves the expected 10-year survival.[22] Equally important is a second study, 13 years later, by Lytle et al in 1999, who showed that the use of both IMA is associated with better long-term results than is the use of just one, while also improving survival and reducing cardiac events.[23] This finding was confirmed in large series of patients by Schmidt et al,[24] Buxton et al,[25] Pick et al,[26] as well as in a systematic overall evaluation of the bibliographic data by Taggart et al.[27] Dozens of techniques have been described for maximising the use of the IMA, such as bilateral direct use, sequential use, use as a free graft, creation of compound grafts based on the IMA, and other variations. All these were aimed at total arterial reperfusion with exclusive use of the two IMA or the supplementary use of another arterial graft.[28-30] At the same time, the need for a greater length of IMA led to the technique of "skeletonized and pedicled" IMA, which proved to lead to an increase in automatic flow[31] and a reduction in sternal wound complications,[32] while in no case did it disturb the anatomy and physiology of the graft.[33,34] Incidentally, in other arterial grafts, such as the radial artery, "skeletonization" is associated with damage to the endothelium or an increase in perioperative complications from vessel spasm.[35,36] The absolute contraindications for the use of the IMA do not exceed 1% and are related with subclavian artery stenosis, chest injury or skeletal anomalies. Relative contraindications for bilateral use, which in most centres have been refuted, are diabetes mellitus, chronic respiratory problems, advanced age, obesity, severely reduced left ventricular function and acute myocardial infarction.

As is well known, diabetic patients make up a large proportion of the total of patients with coronary artery disease (around 30-35%). Apart from the higher risk of perioperative infections, they have a greater likelihood of bypass dysfunction and higher long-term mortality.[37] Coronary bypass is the treatment of choice for the coronary patient with diabetes mellitus.[38] The BARI study and others recommend the use of the mammary artery in diabetic patients, since the 5-year mortality is lower than in patients who receive venous grafts or who undergo percutaneous angioplasty.[39] In the case of bilateral use of the mammary artery a higher risk (from four- to tenfold) of sternal wound complications has been described.[40] However, the use of skeletonized mammary arteries, even in insulin-dependent patients, gives results similar to the use of a single IMA: 4% versus

2.7%, respectively. At the same time, the diabetic reaps the benefit from the use of both IMA over the passage of time, since a high proportion of the deaths from cardiac cause disappear.[41] Skeletonizing the mammary arteries also seems to be particularly beneficial to the other high-risk groups, such as the aged,[42,43] and patients with chronic respiratory problems,[44] while it is associated with less blood loss during the preparation of the graft.[45]

Concerning the phenomenon of hypoperfusion in the case of compound grafts, it must be said that the flow reserve of a pedicled IMA is similar to the peripheral outflow and approaches three times the flow necessary for complete myocardial reperfusion. The hypoperfusion phenomenon may occur in cases of significant myocardial hypertrophy,[46] or a small-lumen IMA in the proximal sections of the compound graft before the anastomoses.[47] A series of studies has demonstrated the good long-term patency of the T-graft using a free mammary artery end-laterally in the pedicled,[48] or the radial artery, especially in the case of multiple anastomoses or remote branches.[49] Finally, the long-term results from the use of the mammary artery continue to be exceptionally good.[50]

Pym, Suma and Carter were the first to report the use of the right gastroepiploic artery (RGEA) in coronary artery surgery. At the beginning of the 1990s the RGEA was the third most used arterial graft after the two IMA,[51,52] but it later fell into disuse because of the wide acceptance of the radial artery and the analysis of its long-term results. Suma showed angiographic graft patency 85% at 5 years and 62% at 10 years.[53] Personally, I would include among the disadvantages of the graft its tendency to spasm because of the overrich muscular sheath compared with the IMA, the technical difficulties during anastomosis because of the relatively small lumen, the mismatch with wide-diameter target vessels and dysfunction of the graft during its use in a persistently moderately stenotic right coronary artery. Its advantages include the fact that it is a pedicled graft with the capability of adapting its flow and that it is suitable for reperfusion of the posterior descending branch, which is difficult to approach with the pedicled right IMA. Finally, together with simultaneous bilateral use of the IMA it allows complete arterial myocardial perfusion. This model was studied clinically in large series of patients, by researchers such as Tavilla (207 patients),[54] Nishida (239 patients),[55] and Bergsma (256 patients).[56] They describe 7-year survival 88-91%, absence of angina 85-92% and absence of cardiac events 78%. However, the findings from series where both IMA and other grafts such as venous or radial artery grafts were used are similar.[57] Finally, the aorta non-touch technique could potentially serve as a model of reperfusion without the use of extracorporeal circulation.[58]

The radial artery is used for coronary artery surgery as a free graft and these days has largely replaced the venous grafts that are used in a similar fashion. It is a wide-diameter graft, prepared at the same time as the mammary arteries, it can easily be anastomosed to the aorta, it is of satisfactory length and it is "user friendly" because of its thick wall. Good long-term results were reported from the revival of its use by Acar.[59,60] Today, about a decade after the time it was widely used, it is possible to judge its long-term results regarding patency. Possati et al reported 92% patency from 90 radial artery grafts at 8 years.[61] Tatoulis et al, in 177 grafts, found 94% patency after the first year and 89% at 4 years.[62] In the same series, the patency of 1345 left IMA, 605 right IMA and 3714 venous grafts was at 5 years 98%, 96% and 95%, respectively, at 10 years 95%, 81% and 71% and at 15 years 88%, 65% and 32%, respectively. At the same time, in the conclusions of this excellent study, apart from the type of graft the patency was also associated with the target vessel (superiority of the anterior descending for all grafts), as well as with the degree of stenosis of the vessel. In the latter case, the 4-year patency of the radial artery when the vessel stenosis was >80% was 92%, otherwise it was 83%. The poorest patency was seen in anastomosis of a moderately stenotic right coronary artery with a pedicled or free right IMA or with a radial artery. This observation could provide justification for the recommendation of Suma et al to use a venous graft in such cases.[53] In these days of drug-eluting stents, it might be preferable to carry out supplementary angioplasty after reperfusion of the left system in cases with a moderately diseased right coronary artery.

The patency of venous grafts at 10 years is unsatisfactory, since 40% of grafts are occluded, 30% are stenotic and only 30% function well. Dion et al increased the percentage of good patency to 76% at 8 years only for cases with sequential use of a venous graft.[63] The inferior epigastric artery did not live up to expectations, since it was a short graft with a tendency to atheromatosis in the initial segment, and in practice it has been mostly abandoned.

In view of the above, I consider that the choice of third graft after the two mammary arteries should be based mainly on the long-term patency, but also on other factors. In comparison with the RGEA the radial artery is superior, mainly in terms of ease of use and

secondly because of its slightly better long-term results. A free graft can be anastomosed to the aorta with access to all targets, while as part of a compound graft it can facilitate complete myocardial reperfusion,[64] even without manipulation of the aorta.[65,66] Limiting the blood supply of the upper limb to a single vessel, the tendency to spasm and the few complications from the use of the radial artery are counterbalanced by the communication between the chest and the peritoneal cavities and the similar drawbacks associated with the use of the RGEA. The superiority of the radial artery over venous grafts seems clear; however, there are no studies of radial artery patency beyond the 10-year period in which we see the rapid deterioration of function in venous grafts. It is a fact that the radial artery does not show medium-term atheromatous lesions[67] and has been associated with a better clinical outcome in a number of studies. Zacharias et al found 6-year survival to be 92.1% in patients with an IMA graft in the left anterior descending branch and 1 or 2 radial arteries, compared with 86.8% when venous grafts were used instead of radial arteries. Over that interval the patency was 71% for the radial arteries and 59% for the venous grafts.[68]

The radial artery is also the graft of choice for occluded venous grafts on reoperation.[69] The opposite applies, of course, in cases with a pathological Allen test (around 5%) or in patients with renal disease where the radial arteries have been used or must be preserved for use in shunts. Also, the use of venous grafts in cases of moderate obstruction of the target vessel seems to be associated with a lower probability of graft occlusion than when arterial grafts are used, as was demonstrated by Shimizu et al in a recent study.[70] Finally, venous grafts are a goldmine in patients with an urgent need for reperfusion, because of their rapid preparation, in aged patients with expected survival less than a decade, in cases of acute perioperative dysfunction of an arterial graft, or in cases where the surgeon prefers them based on greater experience in their use, especially for the right coronary artery.

Evaluation of surgical techniques

The use of extracorporeal circulation is of technical convenience to the surgeon but leads to a general inflammatory reaction, called systemic inflammatory response syndrome (SIRS), which has been studied extensively and is mainly related with contact between the blood and the biological surfaces, its dilution and the absence of pulsatile flow. The negative pathophysiological consequences of the phenomenon are associated with postoperative dysfunction of many organs as well as the blood.[71,72] Various drug protocols, methods and clinical approaches, such as the use of a leukocyte filter,[73] extracorporeal circulation with pulsatile flow,[74] the use of heparinised surfaces,[75] and others that have been suggested from time to time have been able to mitigate the phenomenon but never to eliminate it. Fortunately, in clinical practice—especially in a patient who is well-monitored preoperatively—it is not related with clinical morbidity. However, high risk patients often pay a price for using extracorporeal circulation in the perioperative period. In a series of studies of low or medium risk patients the early outcome from the use of extracorporeal circulation was the same as for the OPCAB technique.[76,77] Nathoe et al[78] found similar long-term results as regards survival, incidence of cardiac events, need for reoperation and one-year graft patency (93% for on-pump versus 91% for OPCAB).

OPCAB has proved superior in high risk patients. In acute coronary syndromes with progressing infarction and myocardial deterioration the use of extracorporeal circulation is disadvantageous, since it imposes an additional burden on the myocardium and myocardial protection is compromised.[79] OPCAB is also associated with a better outcome in patients who undergo operation soon after a myocardial infarction,[80,81] as well as in those with a low ejection fraction.[82] The same applies to aged patients, where OPCAB is associated with significantly lower mortality, incidence of stroke, duration of mechanical ventilation and hospitalisation in general.[83-86] In low and medium risk patients with chronic respiratory problems the outcome is independent of the use of extracorporeal circulation.[87] If other risk factors are present, however, the outcome of OPCAB surgery is clearly better.[88] It is significant that in specific patients keeping the pleural space closed leads to fewer respiratory complications.[44,89] OPCAB also offers better protection of renal function in comparison with classical surgery[90,91] and the recommendation to treat renal patients with OPCAB is generally accepted. OPCAB is associated with better results and fewer strokes in patients with carotid artery disease or peripheral vascular disease.[92] Off-pump reoperation is feasible in a large proportion of cases and has excellent results.[93-95]

The less invasive techniques, such as MIDCAB, LAST, endoscopic atraumatic coronary artery bypass (Endo-ACAB), also have their place nowadays, but are performed by a small number of qualified surgeons. The Endo-ACAB technique, as described by Vassiliades[96] with the use of endoscopic cardiac posi-

tioners, has overcome the limitations of the other two techniques and is applied for multiple vessel myocardial reperfusion. The philosophy behind the less invasive incisions introduced by the above techniques also finds application in reoperations through the use of the subxiphoid incision for the inferior wall (use of RGEA), or small lateral thoracotomy for the lateral wall (central anastomosis to the descending aorta), profiting from the limited endopericardial detachment of the heart. The most important thing of all is that it is possible to perform less invasive reperfusion of the anterior descending branch combined with percutaneous angioplasty of other vessels. The above view is supported by a comparative study of outcomes in patients with disease of the anterior descending branch, where MIDCAB access and surgical reperfusion was associated with a better outcome in comparison with angioplasty and stent implantation in the same vessel.[97]

The use of the Da Vinci robotic system has so far either found similar applications to those of Endo-ACAB, replacing the endoscope for the preparation of the IMA, or has achieved reperfusion of one or two targets on the anterior wall or perhaps also the right coronary artery.[98-99] The future will show the capabilities of a robotic system for multiple vessel myocardial reperfusion, an expectation that may be feasible with the use of absolutely safe automatic anastomotic devices and other technological achievements. These have already begun to be used in coronary artery surgery, but with equivocal results.[100]

Manipulation of the ascending aorta

Atheromatous lesions of the ascending aorta in patients who are undergoing coronary bypass surgery are seen in about 13% of cases.[101] Detachment and embolism of atheromatous material as a result of surgical manipulations is the main cause of perioperative stroke.[102,103] In practice, this means that the incidence of such episodes is a function of the degree of atheromatosis of the ascending aorta and of the manipulations that are carried out during surgery. Additionally, given that the existence of atheromatosis in the aorta increases linearly with age and that one third of patients who undergo coronary bypass nowadays are aged over 70 years (a fraction that is tending to increase[104]), the problem of an atheromatous ascending aorta is likely to become even greater than at present. In the past various series of techniques were proposed for the reduction of the risk involved in manipulations of the ascending aorta, such as placement of an aortic cannula in the aortic arch, the anonymous, subclavian or femoral artery,[105,106] the use of deep hypothermia to avoid aortic occlusion,[107] or even combined with replacement of the ascending aorta and execution of central anastomoses on the cannulated graft.[108]

However, none of the above techniques eliminated the possibility of perioperative stroke. Indeed some of them were associated with greater morbidity and mortality than usual. Carrying out coronary artery bypass on a beating heart has the advantage of avoiding the placement of a cannula in the aorta, but manipulation of a pulsating aorta for the purpose of performing central anastomoses is associated with greater morbidity.[109] The avoidance of any manipulation of the ascending aorta leads to excellent results, minimising or eliminating the incidence of stroke or aortic dissection.[110,111]

Use of the arterial "pi-circuit"

Based on the points made by the studies mentioned above we have arranged in clinical practice to combine three principles: 1) complete arterial reperfusion; 2) the avoidance of extracorporeal circulation through the use of OPCAB; 3) the avoidance of manipulations of the ascending aorta (aorta non-touch). This aim was achieved through a natural route. Specifically, nature has provided for double perfusion circuits in most organs of the body (brain, stomach, bowel, etc.) as well as in the upper and lower limbs. The heart, despite its vital role, is supplied by a solitary coronary circuit and is thus unable to recruit a substitute when this circuit malfunctions. We were thus led to create the "arterial pi-circuit", which in combination with the diseased coronary net plays the role of an auxiliary circuit. It is based on the flow through two pedicled IMA that, as the basis of compound grafts (T or Y grafts, pi-graft, psi-graft), via anastomoses or lengthening with a radial artery (I graft) acquire the ability of multiple connections with the coronary net via peripheral anastomoses with the diseased vessels.

The theoretical advantages of the "pi-circuit" are that it combines the benefits of the use of purely arterial grafts with the avoidance of any manipulations of the ascending aorta during off-pump surgery. At the same time, it is an absolutely self-regulating circuit, since it is connected via two IMA with the systemic circulation and is subject to all laws of regulation of vascular flow. Peripherally, as a closed circuit, it supplies each vessel based on its efflux. Furthermore, we believe that because of the time delay of the pulsatile phase of circulation from the aortic root, from which

the coronary net originates, to the subclavian arteries, the region of origin of the two IMA, we are led to a "phasic irrigation" of the coronary vessels with all the beneficial consequences for the better perfusion of the coronary net. The latter belief is currently the subject of laboratory investigation seeking confirmation of the theoretical approach.

During the last three years (2001-3) we have implemented the "pi-circuit" in combination with OPCAB in 992 coronary patients with excellent early results, namely 0.9% mortality and no cases of stroke.[112] The medium-term results show a survival rate of 96%. Nine of the 41 deaths were related with a coronary event or end-stage heart failure. Another 8 patients (0.8%) underwent supplementary angioplasty and 2 patients (0.2%) were reoperated. Finally, the early and medium-term mortality of patients with a Euroscore under 3 was zero (unpublished results).

Conclusions

A study of data in the literature in combination with personal experience leads to the following conclusions. The use of extracorporeal circulation is well tolerated by patients of low or medium weight and facilitates surgical procedures. In experienced hands OPCAB is the method of choice in high-risk patients, such as the aged, those with renal disease or chronic respiratory problems, patients with carotid artery disease or peripheral vascular disease. It should also be used in reoperations and in patients with acute coronary syndrome or compromised left ventricular function.

The use of at least one mammary artery in the anterior descending branch—and even better, two pedicled IMA—is the cornerstone of coronary artery surgery nowadays, while the use of skeletonized grafts offers only advantages. In patients with three-vessel disease the choice of third graft should be based on age, target, degree of stenosis of the coronary vessel and the surgeon's experience. The main aim in younger patients should be complete arterial reperfusion; in the aged and in patients with an atheromatous ascending aorta it should be the avoidance of manipulations of that vessel, while in diabetics skeletonized IMA or other arterial grafts should be used. Reperfusion of the left coronary net with arterial grafts is associated with a better long-term outcome, while for the right coronary net the choice of graft has to do with the degree of stenosis of the vessel. The choice of minimally invasive access for reperfusion of the anterior descending branch, alone or in combination with percutaneous angioplasty for the remaining vessels, is a safe procedure and one that may well predominate in the future. Robotic surgery and the use of automatic anastomosers still have some way to go before they are proved to be safe, effective and widely applicable. The use of the arterial "pi-circuit" without extracorporeal circulation combines the advantages of the use of arterial grafts and the avoidance of manipulation of the aorta. In experienced surgical hands and in a team devoted to the method the early and medium-term results are excellent and seem to eliminate the occurrence of stroke.

References

1. Favaloro R: Saphenous vein autograft replacement of severe segmental coronary artery occlusion: operative technique. Ann Thorac Surg 1968; 5: 334-339.
2. Johnson D, Flemma R, Lepley D, Ellison E: Extended treatment of severe coronary artery disease: a total surgical approach. Ann Thorac Surg 1969; 170: 460-470.
3. Kolessov VL: Mammary artery coronary anastomosis as method of treatment for angina pectoris. J Thorac Cardiovasc Surg 1967; 54: 535-544.
4. Green GE, Stertzer SH, Reppert EH: Coronary arterial bypass grafts. Ann Thorac Surg 1968; 5:443.
5. Barner H: Double internal mammary-coronary artery bypass. Arch Surg 1974; 109: 627-630.
6. Tector A, Kress D, Downey F, Schmahl T: Complete revascularization with internal thoracic artery grafts. Semin Thorac Cardiovasc Surg 1996; 8: 29-41.
7. Calafiore AM, Giammarco GD, Luciani N, et al: Composite arterial conduits for a wider arterial myocardial revascularization. Ann Thorac Surg 1994; 58: 185-190.
8. Prapas SN, Anagnostopoulos CE, Kotsis VN, et al: A new pattern for using both thoracic arteries to revascularize the entire heart: the pi-graft. Ann Thorac Surg 2002; 73: 1990-1992.
9. Pym J, Brown PM, Charrette EJ, et al: Gastroepiploic-coronary anastomosis. A viable alternative bypass graft. J Thorac Cardiovasc Surg 1987; 94: 256-259.
10. Suma H, Fukumoto H, Takeuchi A: Coronary artery bypass grafting by utilizing in situ right gastroepiploic artery: basic study and clinical application. Ann Thorac Surg 1987; 44: 394-397.
11. Carter MJ: The use of the right gastro-epiploic artery in coronary artery bypass grafting. Aust N Z J Surg 1987; 57: 317-321.
12. Acar C, Jebara VA, Portoghese M, et al: Revival of the radial artery for coronary bypass grafting. Ann Thorac Surg 1992; 54: 652-660.
13. Benetti FJ: Direct coronary surgery with saphenous vein bypass without CPB or cardiac arrest. J Cardiovasc Surg 1985; 26: 217-222.
14. Buffolo E, Andrade JC, Succi J, Leao LE, Gallucci C: Direct myocardial revascularization without CPB. Thorac Cardiovasc Surg 1985; 33: 26-29.
15. Benetti FJ: Video assister coronary bypass surgery. J Card Surg 1995; 10: 620-625.
16. Calafiore AM, Gianmarco GD, Teodori G, et al: Left anterior descending coronary artery grafting via left anterior small thoracotomy without CPB Ann Thorac Surg 1996; 61: 1658-1665.

17. Loulmet D, Carpentier A, d' Attelis N, et al: First endoscopic coronary artery bypass grafting using computer assisted instruments. J Thorac Cardiovasc Surg 1999; 118: 4-10.
18. Peters WS, Siegel LC, Stevens JH, et al: Closed chest cardiopulmonary bypass and cardioplegia: Basis for less invasive cardiac surgery. Ann Thorac Surg 1997; 63: 1748-1751.
19. Stevens JH, Burdon TA, Peters WS, et al: Port-access coronary artery bypass grafting: a proposed surgical method. J Thorac Cardiovasc Surg 1996; 111: 567-573.
20. Falk V, Grunenfelder J, Daunt D, Burdon TA: Total endoscopic computer enhanced beating heart coronary artery bypass grafting. Ann Thorac Surg 2000; 70: 2029-2033.
21. Kappert U, Cichon R, Schneider J, et al: Closed chest coronary artery bypass surgery on the beating heart with the use of a robotic system. J Thorac Cardiovasc Surg 2000; 120: 809-811.
22. Loop FD, Lytle BW, Cosgrove DM, et al: Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. N Engl J Med 1986; 314: 1-6.
23. Lytle BW, Blackstone EH, Loop FD, et al: Two internal thoracic artery grafts are better than one. J Thorac Cardiovasc Surg 1999; 117: 855-872.
24. Schmidt SE, Jones JW, Thornby JL, Miller CC III, Beall AC Jr: Improved survival with multiple left sided internal thoracic artery grafts. Ann Thorac Surg 1997; 64: 9-15.
25. Buxton BF, Komeda M, Fuller JA, Gordon I: Bilateral internal thoracic artery grafting may improve outcome of coronary artery surgery. Risk-adjusted survival. Circulation 1998; 98 (suppl ii): ii1-6.
26. Pick A, Orszulak T, Anderson B, Schaff H: Single versus bilateral internal mammary artery grafts: 10-year outcome analysis. Ann Thorac Surg 1997; 64: 599-605.
27. Taggart DP, D'Amico R, Altman DG: Effect of arterial revascularization on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. Lancet 2001; 358: 870-875.
28. Calafiore AM, Di Giammarco G: Complete revascularization with three or more arterial conduits. Semin Thorac Cardiovasc Surg 1996; 8: 15-23.
29. Dion R, Etienne PY, Verhelst R, et al: Bilateral mammary grafting. Eur J Cardiothorac Surg 1993; 7: 287-294.
30. Sundt T, Barner H, Camillo C, Gay W: Total arterial revascularization with an internal thoracic artery and radial artery T-graft. Ann Thorac Surg 1999; 68: 399-405.
31. Choi JB, Lee SY: Skeletonized and pedicled internal thoracic artery grafts: effect on free flow during bypass. Ann Thorac Surg 1996; 61: 909-913.
32. Kotsis V, Panagiotopoulos J, Sidiropoulos A, Protogeros D, Danou F, Prapas S: Use of bilateral skeletonized ITA's in OPCAB surgery is not associated with sternal wound complications: Heart Surg Forum 2003; Vol 6 (Suppl1): S32.
33. Ueda T, Taniguchi S, Kawata T, Mizuguchi K, Nakajima M, Yoshioka A: Does skeletonization compromise the integrity of internal thoracic artery grafts? Ann Thorac Surg 2003; 75: 1429-1433.
34. Athanasiou T, Crossman M, Asimakopoulos G, et al: Should the internal thoracic artery be skeletonized? Ann Thorac Surg 2004; 77: 2238-2246.
35. Rukosujew A, Reichelt R, Fabricius AM, et al: Skeletonization versus pedicle preparation of the radial artery with and without the ultrasonic scalpel. Ann Thorac Surg 2004; 77: 120-125.
36. Prapas S: The effect of skeletonization of the radial artery in the early clinical outcome using the "p-circuit". Heart Surg Forum 2004; Vol. 7 (Suppl. 1): S556.
37. Lawrie GM, Morris GC Jr, Glaeser DH: Influence of diabetes mellitus on the results of coronary bypass surgery. Follow-up of 212 diabetic patients 10 to 15 years after surgery. JAMA 1986; 256: 2967-2971.
38. Kurbaan AS, Bowker TJ, Ilsley CD, et al: Difference in mortality of the CABRI diabetic and nondiabetic population and its relation to coronary artery disease and revascularization mode. Am J Cardiol 2001; 87: 947-950.
39. The BARI Investigators: Seven-year outcome in the Bypass Angioplasty Revascularization Investigation (BARI) by treatment and diabetic status. J Am Coll Cardiol 2000; 35: 1122-1129.
40. Grossi EA, Espotito R, Harris LJ, et al: Sternal wound infection and use of internal mammary artery grafts. J Thorac Cardiovasc Surg 1991; 102: 342-346.
41. Lev-Ran O, Mohr R, Amir K, et al: Bilateral internal thoracic artery grafting in insulin-treated diabetics: should it be avoided? Ann Thoracic Surg 200; 120: 290-297.
42. Kramer A, Mastsa M, Paz Y, et al: Bilateral skeletonized internal thoracic artery grafting in 303 patients seventy years and older. J Thorac Cardiovasc Surg 2000; 120: 290-297.
43. Gurevitch J, Matsa M, Paz Y, et al: Effect of age on outcome of bilateral skeletonized internal thoracic artery grafting. Ann Thorac Surg 2001; 71: 549-554.
44. Bonacchi M, Prifti G, Salica A, et al: Respiratory dysfunction after coronary artery bypass grafting employing bilateral internal mammary arteries: the influence of intact pleura. Eur J Cardiothorac Surg 2001;19:827-833.
45. Calafiore AM, Vitolla G, Iaco Al, et al: Bilateral internal mammary artery grafting: midterm results of pedicled versus skeletonized conduits. Ann Thorac Surg 1999; 67: 1637-1642.
46. Jones EL, Lattouf OM, Weintraub WS: Catastrophic consequences of internal mammary artery hypoperfusion. J Thorac Cardiovasc Surg 1989; 98: 902-907.
47. Takami Y, Ina H: Effects of skeletonization on intraoperative flow and anastomosis diameter of internal thoracic arteries in coronary artery bypass grafting. Ann Thorac Surg 2002; 73: 1441-1445.
48. Tector A, McDonald M, Kress D, Downey F, Schmahl T: Purely internal thoracic artery grafts: outcomes. Ann Thorac Surg 2001; 72: 450-455.
49. Vicol C, Raab S, Beyer M, Reichart B: Myocardial revascularization using the arterial T graft: which conduit should be chosen for the free graft? Heart Surg Forum 2003; 6: 353-357.
50. Dion R, Glineur D, Derouk D, et al: Long-term clinical and angiographic follow-up of sequential internal thoracic artery grafting. Eur J of Cardiothoracic Surgery 2000; 17: 407-414.
51. Jegaden O, Eker A, Montagna P, et al: Technical aspects and late functional results of gastroepiploic bypass grafting (400 cases). Eur J Cardiothorac Surg 1995; 9: 575-580.
52. Hirose H, Amano A, Takanashi S, Takanashi A: Coronary artery bypass grafting using the gastroepiploic artery in 1,000 patients. Ann Thorac Surg 2002; 73: 1371-1379.
53. Suma H, Isomura T, Horii T, Sato T: Late angiographic result of using the right gastroepiploic artery as a graft. J Cardiothorac Surg 2000; 120: 496-498.
54. Tavilla G, Kappetein A, Braun J, et al: Long-term follow-up of coronary artery bypass grafting in three-vessel disease using exclusively pedicled bilateral internal thoracic and right gastroepiploic arteries. Ann Thorac Surg 2004; 77: 794-799.
55. Nishida H, Tomizawa Y, Endo M, et al: Coronary artery bypass with only in situ bilateral internal thoracic arteries and right gastroepiploic artery. Circulation 2001; 104: 761-780.

56. Bergsma TM, Grandjean JG, et al: Low recurrence of angina pectoris after coronary artery bypass grafts surgery with bilateral internal thoracic and right gastroepiploic arteries. Circulation 1998; 97: 2402-2405.
57. Farinas J-M, Carrier M, Hebert Y, et al: Comparison of long-term clinical results of double versus single internal mammary artery bypass grafting. Ann Thorac Surg 1999; 67: 466-470.
58. Hirose H, Amano A, Takahashi A: Aortic nontouch off-pump complete revascularization using 3 in situ arterial conduits: bilateral mammary arteries and gastroepiploic artery. Heart Surg Forum 2004; 7: 122-125.
59. Acar C, Ramsheyi A, Pagny JT, et al: The radial artery for coronary artery bypass grafting: clinical and angiographic results at 5 years. J Thorac Cardiovasc Surg 1998; 116; 981-989.
60. Tatoulis J, Buxton BF, Fuller JA, et al: The radial artery in coronary surgery: a 5 year experience - clinical and angiographic results. Ann Thorac Surg 2002; 73: 143-148.
61. Possati G, Gaudiro M, et al: Long-term results of the radial artery used for myocardial revascularization. Circ 2003; 108: 1350-1354.
62. Tatoulis J, Buxton B, Fuller J: Patencies of 2127 arterial to coronary conduits over 15 years. Ann Thorac Surg 2004; 77: 93-101.
63. Dion R: Book of proceedings, 16th meeting of EACTS, Monaco, Sept. 2002.
64. Muneretto C: Bisleri G, Negri A, et al. Left internal thoracic artery composite grafts as the technique of choice for myocardial revascularization in elderly patients: a prospective randomized evaluation. J Thorac Cardiovasc Surg 2004; 127: 179-184.
65. Pitsis A, Cullen H, Musumeci F, et al: A new strategy of total arterial revascularization. Ann Thorac Surg 1999; 67: 1186-1187.
66. Prapas S, Kotsis V, Zarbis N, et al: Off-pump coronary artery bypass with "deviation" of ITA's: the most natural revascularization. Heart Surg Forum 2001; 4 (Suppl. 2):S62.
67. Hagiwara H, Ito T, Kamiya H, et al: Mid-term structural change in the radial artery grafts after coronary artery bypass grafting. Ann Thorac Surg 2004; 77: 805-811.
68. Zacharias A, Habib RH, Schwann TA, et al: Improved survival with radial artery versus vein conduits in coronary by pass surgery with left internal thoracic artery to left anterior descending artery grafting. Circulation 2004; 109: 1489-1496.
69. Tatoulis J, Buxton BF, Fuller JA: The radial artery in reoperative coronary bypass surgery. J Card Surg 2004; 19: 296-302.
70. Shimizu T, Ito S, Kikuchi Y, et al: Arterial conduit shear stress following bypass grafting for intermediate coronary artery stenosis: a comparative study with saphenous vein grafts. Eur J Cardiothorac Surg 2004; 25: 578-584.
71. Picone AL, Lutz CJ, Finck C, et al: Multiple sequential insults cause post pump syndrome. Ann Thorac Surg 1996; 67: 978-985.
72. Paparella D, Yau TM, Young E: Cardiopulmonary bypass induced inflammation: pathophysiology and treatment. An update. Eur J Cardiothorac Surg 2002; 21: 232-244.
73. Morioka K, Muraoka R, China Y, et al: Leukocyte and platelet depletion with a blood cell separator: effects on lung injury after cardiac surgery with cardiopulmonary bypass. J Thorac Cardiovasc Surg 1996; 111: 45-54.
74. Dunn J, Kirsh MM, Harness J, Carroll M, Straker J, Sloan H: Hemodynamic, metabolic, and hematologic effects of pulsatile cardiopulmonary bypass. J Thorac Cardivasc Surg 1974; 68: 138-147.
75. Belboul A, Lofgren C, Storm C, Jungbeck M: Heparin-coated circuits reduce occult myocardial damage during CPB: a randomised, single blind clinical trial. Eur J Cardiothorac Surg 2000; 17: 580-586.
76. van Dijk D, Nierich AP, Jasnsen EW, et al: Early outcomes after off-pump coronary bypass surgery. Circulation 2001; 104: 1761-1766.
77. Gerola LR, Buffolo E, Jasbik W, et al: Off-pump versus on-pump myocardial revascularization in low-risk patients with one or two vessel disease: perioperative results in a multicenter randomized controlled trial. Ann Thorac Surg 2004; 77; 569-573.
78. Nathoe HM, van Dijk D, Jansen EWL, et al: A comparison of on-pump and off-pump coronary bypass surgery in low risk patients. N Engl J Med 2003; 348: 394-402.
79. Buckberg GD, Allen BS: Myocardial protection management during adult cardiac operations. In: Baue AE, Geha AS, Hammond GL, Laks H, Naunheim KS (eds.): Glenn's thoracic and cardiovascular surgery. Apple & Lange, Stamford, 1996, pp. 1653-1687.
80. D'Ancona G, Karamanoukian H, Ricci M, et al: Myocardial revascularization on the beating heart after recent onset of acute myocardial infarction. Heart Surg Forum 2001; 4: 74-79.
81. Mohr R, Moshkovitch Y, Shapira I, et al: Coronary artery bypass without cardiopulmonary bypass for patients with acute myocardial infarction. J Thorac Cardiovasc Surg 1999; 118: 50-56.
82. Shennib H, Endo M, Benhamed O, Morin JF: Surgical revascularization in patients with poor left ventricular function: on- or off-pump? Ann Thorac Surg 2002; 74: S1344-1347.
83. Hoff SJ, Ball SK, Coltharp WH, et al: Coronary artery bypass in patients 80 years and over: is off-pump the operation of choice? Ann Thorac Surg 2002; 74: S1340-1343.
84. Stamou SC, Dangas G, Dullum MK, et al: Beating heart surgery in octogenarians: perioperative outcome and comparison with younger age groups. Ann Thorac Surg 2000; 69: 1140-1150.
85. Al-Ruzzeh S, George S, Yacoub M, Amrani M: The clinical outcome of off-pump coronary artery bypass surgery in the elderly patients. Eur J Cardiothorac Surg 2001; 20: 1152-1156.
86. Prapas S, Panagiotopoulos J, Protogeros D, Sidiropoulos A, Linardakis J, Kotsis V: The OPCAB surgery with the use of Π-circuit: the procedure of choice for octogenarians. Inter Card Vasc Thorac Surg 2004; 3 (Suppl 1): S36-37.
87. Roosens C, Heerman J, De Somer F, et al: Effects of off-pump coronary surgery on the mechanics of the respiratory system, lung, and chest wall: comparison with extracorporeal circulation. Crit Care Med 2002; 30: 2430-2437.
88. Guler M, Kirali K, Toker ME, et al: Different CABG methods in patients with chronic obstructive pulmonary disease. Ann Thorac Surg 2001; 71: 152-157.
89. Palatianos G, Prapas S, Mastorakou I, et al: Preservation of a closed pleural space while harvesting the IMA reduces pulmonary morbidity. Poster Session, 81st Annual Congress of ACS, New Orleans, 22-27 Oct 1995.
90. Ascione R, Nason G, Al-Ruzzeh S, et al: Coronary revascularization with or without cardiopulmonary bypass in patients with preoperative non-dialysis-dependent renal insufficiency. Ann Thorac Surg 2001; 72: 2020-2025.
91. Prapas S, Protogeros D, Danou F, et al: Early and midterm outcome of patients with renal impairment undergoing OPCAB using the "Π-circuit". Abstract. The 14th World Congress, Beijing China, 2004 Oct 14-17.
92. Karthik S, Musleh G, Grayson A, et al: Coronary surgery in patients with peripheral vascular disease: Effect of avoiding cardiopulmonary bypass. Ann Thorac Surg 2004; 77: 1245-1249.

93. Mohr R, Moshkovitz Y, Gurevitch J, Benetti FJ: Reoperative coronary artery bypass without cardiopulmonary bypass. Ann Thorac Surg 1997; 63: S40-43.
94. D'Ancona G, Karamanoukian H, Ricci M, et al: Reoperative coronary artery bypass grafting with and without cardiopulmonary bypass: determinants of perioperative morbidity and mortality. Heart Surg Forum 2001; 4: 152-158.
95. Prapas S, Sidiropoulos A, Panagiotopoulos J, et al: OPCAB, aorta non-touch, total arterial revascularization in REDO cases. Heart Surg Forum 2003; Vol 6 (Suppl 1):S42.
96. Vassiliades T: Atraumatic coronary artery bypass: technique and outcomes. Heart Surg Forum 2001; 4: 331-334.
97. Drenth DJ, Veeger JGM, et al: A prospective randomized trial comparing stenting with off-pump coronary surgery for high-grade stenosis in the proximal left anterior descending coronary artery: three-years follow-up. J Am Coll Cardiol 2002; 40: 1955-1960.
98. Aybek T, Dogan S, Andressen E, et al: Robotically enhanced totally endoscopic right internal thoracic coronary artery bypass to the right coronary artery. Heart Surg Forum 2000; 3: 322-324.
99. Kappert U, Cichon R, Schneider J, et al: Closed chest bilateral mammary artery grafting in double vessel coronary artery disease. Ann Thorac Surg 2000; 70: 1699-1701.
100. Watanabe G, Takemura H, Tomita S, et al: Skeletonized radial artery graft with the St. Jude medical symmetry bypass system (aortic connector system). Ann Thorac Surg 2004; 77: 1550-1552.
101. Wareing TH, Davila-Roman DJ, Barzilai B, et al: Management of the severely atherosclerotic ascending aorta during cardiac operations; a strategy for detection and treatment. J Thorac Cardiovasc Surg 1992; 103; 453-462.
102. Roach GW, Kanchuger M, Mangano CM, et al: Adverse cerebral outcomes after coronary bypass surgery. N Engl J Med 1996; 335: 1857-1863.
103. Murkin JM: Etiology and incidence of brain dysfunction after cardiac surgery. J Cardiothorac Vasc Anesth 1999; 13: 12-17.
104. Data Analysis of The Society of Thorac Surgeons National Cardiac Surgery Database, the Seventh Year. January 1998.
105. Leyh RG, Bartels C, Notzold A, Sievers HH: Management of porcelain aorta during coronary artery bypass grafting. Ann Thorac Surg 1999; 67: 986-988.
106. Sabik JF, Lytle BW, McCarthy PM, Cosgrove DM: Axillary artery: an alternative site of arterial cannulation for patients with extensive aortic and peripheral vascular disease. J Thorac Cardiovasc Surg 1995; 885-891.
107. Mills NL, Everson CT: Atherosclerosis of the ascending aorta and coronary artery bypass: pathology, clinical correlates and operative management. J Thorac Cardiovasc Surg 1991; 102; 546-553.
108. Stern A, Tunick PA, Culliford AT, et al: Protruding aortic arch atheromas: risk of stroke during heart surgery with and without aortic arch endarterectomy. Am Heart J 1999; 138: 746-752.
109. Chavanon O, Carrier M, Cartier R, et al: Increased incidence of acute ascending aortic dissection with off-pump aortocoronary bypass surgery? Ann Thorac Surg 2001; 71: 117-121.
110. Calafiore AM, Di Mauro M, Teodori G, et al: Impact of aortic manipulation on incidence of cerebrovascular accidents after surgical myocardial revascularization. Ann Thorac Surg 2002; 73: 1387-1393.
111. Prapas S: The OPCAB with aorta non touch technique abolishes the neurological complications. J Cardiovasc Surg 2003; Vol 44 (Suppl 1-5): S13-14.
112. Prapas S, Kotsis V, Sidiropoulos A, et al: Morbidity and mortality rates in patients undergoing off-pump coronary surgery without aortic manipulations. Heart Surg Forum 2003; Vol 6 (Suppl 1): S32.