



Massimo Lemma

On-Off 1-year results

Patients undergoing coronary artery bypass grafting who are at high risk of complications have traditionally been managed with cardiopulmonary bypass. However, in recent years there has been a growing number of centres carrying out coronary artery bypass grafting without the use of 'the pump'. *Confluence* spoke to Dr Massimo Lemma, Cardiovascular Surgeon at Luigi Sacco University General Hospital to discuss the benefits and challenges associated with off-pump surgery.

How are patients requiring coronary artery bypass grafting (CABG) currently treated with regards to the use of cardiopulmonary bypass, the so-called 'on-pump' or 'off-pump' techniques?

Dr Massimo Lemma (ML): The vast majority of patients are scheduled for CABG using cardiopulmonary bypass ('on-pump' surgery). Off-pump surgery (without the use of cardiopulmonary bypass) was a new procedure introduced at the beginning of the 1990s. There was a great enthusiasm at the time because, from a theoretical point of view, this technique is definitely safer in the sense that actually you can avoid the complications of a coronary artery bypass. You can also keep the heart beating so you do not have any ischaemic periods during the operation on the left ventricle.

The problem is that this technique is much more technically demanding, so currently in Europe, no more than 25–30% of all CABGs are performed off-pump. Overall, there are a few centres with enthusiastic surgeons who perform roughly 95% of their procedures off-pump, however, the rest of the centres perform few off-pump operations, primarily in patients at high risk (high risk in the sense that besides the coronary artery disease, they have many pathologies that can increase the perioperative risk of the patient). This can be problematic in that they are going to treat the patient at high risk with a procedure they consider much more technically demanding, and with which they are less familiar and less confident.

You mention that off-pump surgery is more technically challenging. Can you describe what is involved?

ML: Overall, the most important issue throughout the operation is the technical quality of the anastomosis at the end of the surgery.

Due to the differences with the on-pump technique, one key challenge is that those surgeons who have been trained for on-pump CABG must be re-trained for off-pump surgery because the surgical strategy has to be completely changed. The key point is to learn how to keep the patient haemodynamically stable throughout the operation. This means that the management of the left ventricle must be perfect. When we put a graft on the anterior wall of the left ventricle (for instance, left internal mammary artery to left anterior descending) this is not an issue, because the left ventricle is in its rest position in the pericardium. However, when we address the obtuse marginal branch or the posterior descending coronary artery, we need to change the position of the left ventricle – that is work in what I call the *ectopia cordis*, a displacement of the left ventricle in which it must be tilted with the apex outside the chest.

In order to keep the patient stable from the haemodynamic point of view, we have to use devices such as the Starfish NS Heart Positioner (figure 1; Medtronic, Inc., Minneapolis, USA) or ACROBAT-i Positioner System (MAQUET Holding B.V. & Co. KG, Rastatt, Germany), which are apical suction devices used in order to maintain the shape of the left ventricle elliptically. In order to rotate the left ventricle and expose the obtuse marginal branch of the posterior descending coronary artery, we put slings below the heart and a stitch at the level of the oblique sinus

fig. 1

The Octopus Tissue Stabiliser and Starfish Heart Positioner (Medtronic, Inc.)



of the pericardium. Manipulating these slings allows us to tilt and rotate the left ventricle upwards, but by doing this manipulation, we cause an enlargement of the left ventricle. However, by using the slings below the left ventricle, and using apical suction to pull up the apex of the left ventricle, we can keep it elliptical. Failure to correctly manipulate the heart can lead to acute heart failure.

However, if you are careful in manipulating the heart, you both keep the patient stable from the haemodynamic point of view and do not have to rush during the anastomosis; you do not have to hurry because the heart is beating and the patient is stable.

You recently released 1-year data from a study you conducted, the On-Off study, which assessed on-pump versus off-pump CABG in high-risk patients. Can you give us an overview of the original study?

ML: Early studies assessing off-pump CABG did not have favourable results. For example, the ROOBY trial assessed the results of on-pump and off-pump surgery in low-risk patients.¹ The results were not that good for off-pump surgery. Surgeons had to have performed >20 off-pump surgeries technique before participating in the study. On average surgeons had performed 120 cases (median, 50).¹ However, this represents surgeons without a great deal of experience in off-pump surgery, mainly residents or surgeons who were not devoted to off-pump surgery.

What we have done was to try to change the perspective. We have selected centres with

surgeons expert in off-pump surgery, so this trial was expertly staged, and we also decided to treat only high-risk patients.^{2,3} We only looked at these patients because, in general, on-pump surgery is associated with an average mortality of approximately 2% depending on the risk of the patient. However, if you want to achieve a statistically significant result versus a procedure with low mortality, you need to enrol in a prospective randomized trial of thousands of patients. Therefore, by selecting only high-risk patients and deciding to use a composite endpoint, we could reduce the number of patients required in order to achieve a powered study.

The composite endpoint was based on operative mortality at 30 days due to a myocardial infarction, the incidence of stroke, the incidence of renal failure, reoperation for bleeding and acute respiratory distress syndrome.² At 30 days, there was a significant benefit seen in patients treated off-pump compared with those treated on-pump ($p=0.0092$). The result was vastly in favour of off-pump surgery; the operative mortality was 1.9 for off-pump and 3.4 for on-pump surgery. If you consider that these patients were patients at high risk, with a preoperative EuroSCORE greater or equal to eight, it appears that off-pump surgery can really reduce the incidence of operative mortality and the other complications comprised in the primary endpoint.²

At the 2014 European Association for Cardio-Thoracic Surgery (EACTS) meeting in Milan we presented on the secondary endpoints.³ The secondary endpoints were split into two groups. Firstly, we had acute secondary endpoints at 30 days, which comprised incidence of post-operative atrial fibrillation, the insertion of intra-aortic balloon pump, the length of the ventilation (if the ventilation was longer than 24 hours), the incidence of lung infection and the length of intensive unit stay, and the length of hospital stay. Secondly, we considered secondary endpoints at 1 year: overall mortality, the incidence of major adverse cardiac events (MACE), the incidence of angina and the presence of a positive stress test.³

At 30 days we could not see any significant difference in the incidence of acute secondary endpoints. Regarding the secondary endpoints at 1 year, there was no difference between patients treated on-pump and off-pump in terms of overall

mortality, the incidence of angina or the presence of a positive stress test. However, there was a difference in the incidence of MACE in favour of off-pump surgery ($p=0.005$). Furthermore, if you split the three MACE that we have considered (cardiac death, myocardial infarction and repeat revascularization), we have seen that cardiac death was significantly lower in off-pump surgery ($p=0.0043$). At 1 year, three patients died after off-pump surgery while 10 patients died in the on-pump group.³

We have also checked with both a univariate and multivariate analysis in this group of patients, and what we have seen is that if there is an ejection fraction below 50%, off-pump surgery is protective in the sense that this variable is associated with a better survival.

Overall, it appears that off-pump surgery is not only protective in high-risk patients at 30 days, but there is also an extension of this protection to one year in these patients.

Are there any other data that support the use of off-pump in high risk patients?

ML: A paper published by John Puskas in *The Journal of Thoracic and Cardiovascular Surgery* reported a retrospective propensity-matched analysis in which the authors show that high-risk patients definitely benefit from off-pump surgery compared with on-pump surgery ($p=0.005$).⁴ They compared the results of their patients on- and off-pump with a predicted risk of mortality based on the STS Risk Score. What they found was that when you have a risk score greater than 5 and you schedule the patient for an off-pump procedure, you see that there is a divergence between the predicted risk of mortality and the observed mortality, in the sense that the observed mortality is lower than the predicted risk of mortality.

Given that the On-Off study was an expertise-based trial, how do you feel these data will translate into everyday clinical practice?

ML: To me, generally speaking, the future of cardiac surgery will be towards minimally invasive approaches. We have to reduce the stress of the operation and, in my opinion, the ideal strategy is to avoid using the pump for CABGs and to avoid the need to clamp the ascending aorta. By doing these two things we can really reduce the invasiveness of our procedure. Indeed, we have

operated on many of these patients off-pump through a small incision in the chest without clamping the aorta. This technique is even more technically demanding, but it is the best possible, least invasive surgical procedure for the patients.

I believe that off-pump surgery is the future of myocardial revascularization and, therefore, surgeons should be retrained to carry out off-pump surgery. It is not an issue to train surgeons in centres that are expert in off-pump surgery, since performing this technique is the daily routine in these centres. For example, when new surgeons come and visit us to understand how we manage the patient during an operation, they may have the feeling that the procedure is extremely simple, because for us off-pump surgery is routine. We treat the vast majority, 95.5%, of our patients off-pump. The exception is the patients with an acute coronary syndrome and a low cardiac output. This patient usually is performed on-pump but without clamping the ascending aorta, i.e. we keep the heart beating.

You have outlined the potential benefits of this technique but what are the possible limitations associated with it?

ML: The limitation of the technique is that the patient must be stable from a haemodynamic point of view. We see few such patients as the vast majority of them are treated with primary percutaneous coronary intervention (PCI). However, there are a few patients that can't be treated with a primary PCI and so they are scheduled for an emergency surgery. In these cases, if the patient remains haemodynamically unstable it is definitely better to put the patient on-pump.

Sometimes you can have patients with very diffuse coronary artery disease, so when you have to perform, and this happens very rarely, a complex procedure like an open endarterectomy, it is again better to put the patient on-pump. Alternatively, but again in very few patients, you have intramural vessels – vessels that you can't see on the surface of the left ventricle because they are deep within the myocardium – and sometimes you can't achieve a revascularization off-pump, so you have to put the patient on-pump. Finally, all those patients who require myocardial revascularization associated with a mitral valve repair due to mitral valve regurgitation must be treated on-pump.

How likely is it that this technique will be taught in academic centres to trainee surgeons?

ML: To me it depends on who is running the centre – if the head of the centre believes in off-pump surgery, then the future of that centre will be to have lots of experts in off-pump surgery. However, if you do not have a centre in which the whole team, surgeons and anaesthetists believe in off-pump surgery, it is definitely harder to start such a programme.

Furthermore, it is difficult to try to convince people that off-pump surgery can be done easily because, in general, it requires what is called the ‘deliberate practice’. Deliberate practice is something that pushes you out of your comfort zone on a daily basis. You need to re-train yourself and there is a price that you have to pay. We say ‘no pain, no gain’, so if you are not willing to pay a price in terms of your confidence, in terms of stress that you can have at the very beginning of your experience, you will find it more challenging to succeed.

Even if you believe in off-pump surgery, you must follow precisely a programme of implementation of technique in your centre, and this means that it is not only the surgeons who must be happy with the technique but the whole multi-disciplinary team. However, when the whole team believes that the technique is worthwhile, the results are definitely astonishing in the sense that you can treat patients on dual antiplatelet therapy with a

lower risk of bleeding complications, and you can see that you can treat patients with a high degree of renal failure without any further worsening of their function post-operatively. The patients are also weaned from the mechanical ventilation faster, so there are lots of benefits as the whole operation is less invasive.

However, it is critical to remember that the quality of the myocardial revascularization must be perfect; it must be what the same surgeon can achieve on-pump. If you compromise on the quality of the myocardial revascularization just because you want to go off-pump, and so you reduce the number of distal anastomoses or you do not use two mammaries because they are more technically demanding, well, this is not a good approach. What you have to do is to maintain the same quality using off-pump surgery.

Are more data required to help people feel more confident in this technique?

ML: It can be challenging to publish papers which report good results in off-pump surgery because I feel that many journal reviewers, unfortunately, do not believe in off-pump surgery. This can mean that you feel that the quality of your paper must be two-times better than usual in order to be assessed and to be published. Ultimately, even if you have good results and publish the results in good journals such the *European Journal of Cardiothoracic Surgery*, it is not easy to be cited by other surgeons.

Address for correspondence
Dr Massimo Lemma
Luigi Sacco University Hospital
Via GB Grassi 74
20157 Milan
Italy

REFERENCES:

1. Shroyer AL, et al. *N Engl J Med* 2009;361(19):1827-37.
2. Lemma MG, et al. *J Thorac Cardiovasc Surg* 2012;143(3):625-31.
3. Lemma M, et al. 2014; Abstract 261. Presentation at the 28th EACTS Congress.
4. Puskas JD, et al. *Ann Thorac Surg* 2009;88(4):1142-7

DISCLOSURES: LM is a consultant for Medtronic, Europe.