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A new approach to multivessel disease: simultaneous hybrid revascularization. An interview with the Heart Team

As Heart Teams strengthen their working relationships over time, they can begin to implement ever more complex hybrid procedures. *Confluence* spoke to cardiac surgeon Dr Ivy Modrau and cardiologist Dr Anne Kaltoft about their recent experience with simultaneous hybrid revascularization, an experimental procedure combining LIMA to LAD coronary bypass via a minimal invasive off-pump procedure and stenting of other diseased vessels in one session in the hybrid room.

Can you tell us why you started looking at a simultaneous hybrid approach?

Ivy Modrau (IM): Earlier this year, our team published results from a pilot study in multivessel disease. That study assessed the feasibility and early safety of off-pump coronary artery bypass (OPCAB) grafting of the left internal mammary artery (LIMA) to the left anterior descending (LAD) artery through an inferior J-hemisternotomy (JOPCAB), combined with percutaneous coronary intervention (PCI) of non-LAD lesions.[1] In this pilot study, the hybrid revascularization was carried out in a 'staged' manner (interventions carried out on separate days) in 100 patients with multivessel coronary artery disease (CAD).

This staged hybrid approach proved to be safe and feasible. The procedure was carried out successfully according to the preoperative strategy in 97% of patients, but one patient had a procedure-related AMI within 24 hours. Therefore, including peri-operative (24 hours) major adverse cardiac or cerebral events, the procedural success rate was 96%. Of the four failures, two of the failures were successfully treated with coronary artery bypass grafting (CABG) as revascularization of a chronic occlusion by PCI failed. One patient, who had LIMA graft thrombosis and procedure-related myocardial infarction, was re-operated by conventional CABG as the LAD had shown diffuse atherosclerotic disease at JOPCAB. One PCI-related myocardial infarction was observed. We had zero mortality and one stroke on the fourth day in the 30-day data. The complete results will be published in a forthcoming issue of *EuroIntervention*.[2] One point to note is that the population included in this study was relatively low-risk: patients had an average SYNTAX score of 13 and a logistic EuroSCORE I of 2.1. This was due to the study protocol excluding those with complex disease, referring them for conventional surgery.

This study was the forerunner to our current pilot trial investigating simultaneous hybrid revascularization. Following the successful results of the original trial, we wanted to see whether it would be possible and meaningful to carry out the whole procedure in one session: this new protocol calls for the JOPCAB procedure and stenting of other diseased vessels in one session in the hybrid room. Such procedures are not yet routine. All of the operations carried out to date have formed part of this second pilot study, which we hope will be the precursor to a planned randomized trial.

How does the simultaneous hybrid approach work?

IM: The major concern with the simultaneous hybrid approach is, of course, bleeding. This is because you need double antiplatelet treatment for stent implantation and we are concerned about that from the surgical point of view. We put a lot of thought into the anticoagulation and antithrombotic regimen when writing the protocol. Our protocol dictates that we treat all patients with low-dose aspirin up until the start of surgery which is performed first. Then, while we are closing the chest, we call our colleagues from cardiology to come to the hybrid suite. They will have prepared their access already before we start surgery, not by the sheath, but all the washing and

draping is done. After surgery, all heparin is neutralized by protamine to ensure haemostasis.

When the cardiologists arrive in the hybrid room, the first thing they check is the patency of our graft. Once that is done, clopidogrel is administered to the patient through a nasogastric tube and we start unfractionated heparin once again with a target activated clotting time of 250 seconds.

Dr Anne Kaltoft (AK): Once the patient is prepared, PCI is carried out using predominantly second-generation drug-eluting stents, similar to what we would use in other patients.

Can you tell us about your ongoing study?

IM: As this is a relatively new approach there are few protocols available, so we had to develop one. We intend to enrol 50 patients, which is not as many as were included in the first pilot, as the primary focus of this study is bleeding risk associated with the new procedure. This number of patients will be sufficient to investigate this. The trial started in February 2013 and to date we have enrolled nine patients.

What are the potential benefits and limitations of the simultaneous hybrid approach?

IM: If you can achieve the same quality of treatment in terms of outcomes, then the next step is to look at which treatment is the most tolerable for patients; which procedure gives the best quality of life afterwards. It is very important for a young patient to be able to carry on with their life and for an old patient not to spend too long in recovery and rehabilitation.

AK: Ultimately, in the long term, we will hopefully see that these patients keep their vessels open after eight or nine years, whereas we would usually see that the vein grafts would close after that time.

IM: Those patients treated to date have been very positive about the procedure. They can go home on the fourth or fifth day following the operation. They tell us: "I can do my daily swimming", "I can go for a walk with my dog", "I can do everything". In order to assess this objectively, we are measuring quality of life, and also cost of treatment up to a year so that we can assess objective measures of this. Indeed, we will measure cost-effectiveness vs conventional CABG in patients who are age-, sex- and EuroSCORE-matched.

The biggest challenges in this approach are logistical. This is because both the surgical and cardiology teams, as well as the hybrid room, need to be available at the same time. As a result of this, we have only been able to enrol nine patients since the trial started in February 2013. In contrast, the staged approach can be done anywhere without any pre-conditions. We will have to be patient when waiting for the results of our study in order to give a recommendation as to whether we think that it is worth further exploration.

AK: I do not see many clinical contraindications for the simultaneous approach, but the logistical issues can be quite challenging. As interventional cardiologists we have to be ready when the surgeons have finished and we do not exactly know when that will be, which means it is difficult to manage our work in the catheterization laboratory. To be both places at the same time is a logistical challenge.

What preliminary results have you obtained using the simultaneous hybrid approach?

IM: Shortly after we started, there was a publication from China in which a large cohort underwent simultaneous hybrid revascularization according to a protocol that was very similar to ours, so we felt like we were on the right track.

At present, it is too early to have a concrete idea of the outcomes, as we have only enrolled nine patients. However, the most important concern was bleeding risk and the data here look very promising; patients do not appear to bleed a lot. This is likely because of the carefully designed protocol, with heparinization, protaminization and proven graft patency, followed by further heparinization for the PCI. We have had one patient for re-operation, due to bleeding of the LIMA. However, this problem was not induced by clopidogrel (though this may have enhanced it) but overall it was a surgical problem that could have occurred after any cardiac surgery.

Why have you chosen to use JOPCAB rather than minimally invasive direct coronary artery bypass (MIDCAB)?

IM: We practised the MIDCAB through a mini-thoracotomy a few years ago and we found that the feasibility of this procedure was not as good as hoped. There are some technical

challenges; for example, patients with adhesions, lung dysfunction and patients where the heart displaced. So now we offer JOPCAB, the mini-sternotomy, to all these patients. There are very few contraindications to this procedure.

Which patients have been included in your pilot studies?

AK: At the moment, the guidelines identify a group that may benefit from a traditional hybrid approach. These are patients with special considerations: for example, those in whom a full sternotomy would be contraindicated and those for whom on-pump-bypass is not an option.

To date, the patients who have been included in our study are those with a proximal stenosis of the LAD and non-LAD lesions that can be managed with a maximum of three stents. We do not include patients with chronic occlusions into the ongoing trial as we were not fully satisfied with the results of the staged approach in that sub-group. Patients with very long and calcified lesions of the LAD are considered, but only where there still is a good peripheral vessel for implanting a LIMA.

IM: We have also excluded patients in whom clopidogrel is contraindicated. Indeed, we frequently sit in conference with our colleagues from cardiology, who can tell us whether it is a complicated or a non-complicated stenting that we await, so we listen to each other and choose the patients where we think this is the best option.

AK: We really benefit from having the conference; sitting together and looking at the angiogram, and deciding for each patient which treatment would be the best, because if, for example, you have large bifurcations involved in the circumflex or in the right coronary artery, it might not be optimal to do a PCI on these vessels, perhaps the patient would be better off with conventional CABG. We try to individualize.

It sounds like the Heart Team plays a really crucial role in deciding what is best for patients. Were there any challenges in setting up that system? How easy would it be to implement the strategy you are using in other hospitals?

IM: We are aware that setting up the recommended Heart Team is a major challenge in many places. I think having been a part of this pilot study, we have had the opportunity to work together closely and that facilitates co-operation. We started to understand each other, our limits, but also the potential we have to treat our patients. By knowing each other better we are better able to tailor our treatment for our patients.

AK: Working closely together you realize that there are very big benefits, not only for the patients but also for both the surgeons and the cardiologists. We have to realize that this has been possible at our centre mainly due to key people: Ivy Modrau is definitely one of them and another is her colleague Per Hostrup from the Surgical Department. You really need dedicated stakeholders who take on this challenge and take it to the next level.

IM: I think it is very important for surgeons and cardiologists to put personal interests aside and not withhold patients. Together, we must assess the patient's comorbidities, looking at the possible peri-operative risks and deciding on the optimal treatment based on that. We must also rely on clinical experience as we all know that not every patient that we see in clinical practice would have been included in a randomized trial; often the most ill patients are not included in the trials and so not all patients are represented.

AK: For cardiologists, it has been very nice to realize that JOPCAB may have fewer complications than traditional CABG, so we have more confidence referring our patients. It would definitely be positive if other departments in other hospitals would start considering doing hybrid procedures – whether they are simultaneous or staged – if people could start talking together, the surgeons and the cardiologists, and looking at the individual patients to decide which treatment would be the very best for this patient.

How much long-term follow-up do you think you will need to provide sufficient evidence to encourage a wider uptake of this approach? Will we see this included in guidelines soon?

AK: For the patients included in this pilot study, there is a five-year follow-up. A European multi-centre hybrid study is now planned and we hope to participate in this, which will hopefully get started at the beginning of next year. That is the only way to get to sufficient evidence I think. It must be a randomized trial, but we are trying to get ready and to know as much as we need to set up everything in the right way so that we get the

IM: Well, I think before you have it in a guideline you will have to have more proof. We are working on that but at the moment it would be very useful to apply this technique in a protocol until we have more results.

What have you learnt as a consequence of these pilot studies?

IM: The hybrid approach has changed the kind of patients who get referred to surgeons, due to the discussion in the Heart Team. Before we started this project, patients with single LAD disease hardly ever got to surgical attention, whereas now, while many still are managed with PCI, a substantial number of these patients are now managed with a JOPCAB procedure.

AK: That's exactly right. Two or three years ago if I did an angiography and saw what might even be a long or calcified LAD lesion, if there was only this single lesion, I would continue doing PCI and would not even consider surgery. Today, however, I always consider surgery when I see complex LAD lesions because I know that JOPCAB is available just around the corner – it is a very good technique and is good for the patient. Unfortunately, some of my colleagues still think that PCI is always the best, but I am not sure they are right, not on the LAD. On the other hand, if my only option was to refer the patient for a conventional open chest CABG just to have a LIMA, I would not do it.

IM: I think it has become much more enjoyable to work when you have a sparring partner. You can just go over and talk things through. For example, when you see patients prior to conventional surgery and anticipate a lot of complications because of some facts we were not aware of at the point of referral. We would just arrange for the patients to be treated by hybrid or PCI on the same day because we are becoming more flexible. That is my hope regarding the simultaneous approach. When we did start the staged hybrid procedure, it took about half a year before we had the infrastructure and understanding, to be able to say 'This is easy, it is routine'. It always takes a little while to get everyone involved and to get people relaxed with a new treatment to the point where everyone knows what to do. That always takes a little while and I think that will be the same with this simultaneous hybrid; it's just a matter of time.

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