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LINC : Leipzig Interventional Course

FAKKEL
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Interventional Cardiology is a fascinating world if you care about patients and like technology! Patient treatment and using top technology goes hand-in-hand and many hundreds of different medical devices are used in daily practice. LINC on top offers the opportunity to experience live-cases: very instructive for colleague interventionalists and extremely educational for e.g. clinical trial people involved in the evaluation of the medical devices used without having the possibility to have their foot into the OR or cath-lab.

Over the past years I have been confronted with many different medical devices and still, I learned a lot. Please have a look in this report, maybe you discover also something new.

My take home messages and learnings:

GENERAL

- Vascular surgery and endovascular therapies complement each other, but the endovascular therapies can be applied more easily and with less trauma; as a result, these less-invasive technologies allow to treat the patient earlier and to limit the progression of the diseases. This in turn reduces the total number of severe cases. This might be a disadvantage for vascular surgeons as “they should all learn to use endovascular techniques to avoid that they get out of a job” as Dr M Bosiers – a vascular surgeon himself – mentioned during the panel discussion. Similarly, also Dr E Blessing showed a cartoon with a surgeon dressed up and standing on the sidewalk with a panel saying “Will Operate For Food”. It illustrates the current thinking and the trend; yet one can also consider the role of the surgeon moving into a “rescuing position” where the surgeon is absolutely necessary to offer a bail out option in case the percutaneous transvascular angiography (PTA) fails and where the surgeon is offered to treat the most difficult cases.
- We can hear two approaches: in some hospitals this type of CLI (Critical Limb Ischemia) patient get treated from a multidisciplinary approach and every approach is discussed within the team of radiologists, angiologists, vascular surgeon, interventionalist before and after the treatment; in other hospitals this is not at all the case and the impression is left that the first one (surgeon or interventionalist) who sees the patient, will also treat him without cross-check with the other colleague. In this case no criteria are used to decide how the patient can best be treated, unfortunately. The BASIL trial demonstrated (see below), however, equal outcome at one/two years with respect to limb salvage and mortality.
- Venous stenting requires different stents with different technical properties than arterial stents. However, most of the time the product that is available and that is believed it can help solve the problem is also used, irrespective of its indication. So, many coronary artery stents/balloons (<3 mm) are used in the pedal approaches, but also for venous applications to solve IVC or SVC blood cloths. Of course, this usage is off-label, but it can help some patients.
- A typical interventional approach is

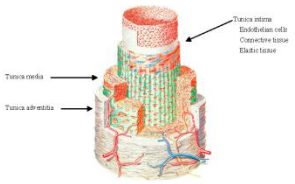
  - First remove blood thrombus/plaque
  - Then position a stent
  - Then inflate the balloon to distend the stent
  - Then check for distal embolization (even when filter downstream is used)
  - If embolization is present, give bolus of (r)t-PA
  - If thrombus/plaque cannot not be penetrated, crossing techniques is applied + balloon dilation to open up the sub-intimal space and to create a new pass-through
- Currently, first choice of treatment is drug-eluting balloon (DEB), then – with failed PTA – bypass surgery.
- The FDA requires to have demonstration of uniformity of coating onto devices (both radially as axially) and demands to have a variability (between different products, but also along the different places within 1 device) of less than 10 %.
- IN Germany the DRG system will reimburse for a given procedure, irrespective of the different types/number of devices are used. In talking with Eurocor people, a new system is implemented such that novel therapies (eg DEB – where multiple balloons need to be used for 1 procedure) also get reimbursed on a per unit use basis. The new system is called NUB (?).

CROSSING TECHNIQUES

- Passing a completely occluded part of eg the Superficial Femoral Artery (SFA), occurs more and more via a "sub-intimal" rather than via an "intraluminal" approach. Using different types of guidewires one can enter this space and advance – with or without a loop formation – downwards to bridge the area of the thrombus. Re-entry into the vascular lumen is often a problem and different special products were developed:
  - Medtronic: *Pioneer*, applying a bended needle that can be protruded through the wall;
  - Boston Scientific: *Offroad*, which inflates distally a tri-angular balloon to deflect the tip away from the vascular wall towards the lumen, allowing a straight needle to protrude the inner layer of the vascular wall and create the re-entry.
- These special re-entry devices are not used so often, in about 5% of the cases, yet they can also cause some extra trauma (outward vessel perforation, creating hematoma and ruining the vessel for future bypass surgery) and are costly.

ARTERECTOMY DEVICES

- *TURBOHAWK* (Covidien –ev3): used for mild to moderate calcified arteries, while the "*SILVERHAWK"* is intended for softer tissue. This can be used to "shave away" the plaques from the inside wall of the blood vessel by high speed rotating blades inside the catheter. A sophisticated design allows simultaneous catching the debris in a tiny barrel (http://www.news-medical.net/news/20120124/Covidien-releases-results-of-TurboHawk-and-SpiderFX-combination-study-on-PAD.aspx - see picture at back). This technique is similar to the *ROTABLATOR* (Boston Scientific): http://www.bostonscientific.com/Device.bsci?page=HCP_Overview&navRelId=1000.1003&method=DevDetailHCP&id=10081831&pageDisclaimer=Disclaimer.ProductPage
- Boston Scientific has the *TRUEPATH* with a diamond head

- Avinger has the *Ocelot* that has an IVUS-like visualization on board that allows to help understand the level of plaque removal while inside the blood vessel.
- The Turbohawk can be applied in blood vessels from 7 down to 2 mm ! This makes it possible to use the device in very peripheral sites.
- Complications might be: down-stream embolization, perforation (one might hawk away to much intimal layer material) 

, flow limiting dissection.

COATING MATERIAL

- The majority of drugs used for anti-inflammatory tissue response are paclitaxel and serolimus. When used in DEB, nearly exclusively paclitaxel is used. These drugs need extra intermediate molecules to bind to the substances. As such, the paclitaxel used in the *COTAVANCE DEB* uses Iopromide as binding molecule (hydrophilic spacer).
- In the *FREEWAY* of Eurocor, the product Shellac is used as the binding molecule. Paclitaxel is sprayed onto the balloon in about 20 layers. Shellac seems to be a common product: it is a natural resin composed of shellolic and alleuritic acid. In the Cook DEB (*Advance*) Paclitaxel is applied without a carrier. Yet concentrations coated and delivered upon application are claimed to be equal to other competitive devices. Of course, it is uncertain how much exactly has been delivered to a given spot.
- All coating material must be hydrophilic, must exert a long term effect and must not be toxic.
- Different techniques of coating are applied, but this is not (often or intentionally) disclosed by companies. One can think of dip-coating or spraying the drug onto the device.

DRUG ELUTING BALLOONS (DEB)

- This is the revelation of the congress: the success of DEB is incredible.
- DEB's perform equally to stents when looking at the clinical outcome at 6 or 12 months, but they underperform when looking immediately post-treatment: the effect needs time to develop.
- Following DEB were mentioned:
  - Medrad: *COTAVANCE*
  - Biotronik: *PANTERA LUX*
  - Lutonix (now BARD): *MOXY*
  - Medtronic: *IN.PACT*
  - Eurocor: *FREEWAY* (smallest is 2 mm)
  - Cook: *ADVANCE* (smallest is 3 mm)
- If a lesion is of substantial length, then several DEBs might be needed to treat the whole lesion in contrast to a non-DEB as with each application the "drug amount" is delivered. This treatment is as such more expensive.
- During application of the DEB one has to be careful of not exposing the balloon unnecessary long to the blood stream prior deployment as otherwise the drug is already eluted away

before it can be applied to the vascular wall by compression of the balloon against the inner wall layer. Compression time is not standard and varies from 90 sec to 3 min.

- Also multiple applications of the balloon to the same area, might deposit too much drug onto the same spot.
- Eurocor people told the balloon is from PU, Cook people the balloon is from nylon.
- Diameters of DEBs are sufficiently small to allow for infrapopliteal/tibial/crural applications (2 mm).

STENTS

- Striking is the *REMEDY* from Kyoto Medical Planning which is biodegradable. No drug elutes from it. Biodegradation starts at 6 months and takes about 18 months. Material is poly-L-lactic acid (PLLA) and has 5-8 mm diameter and 4-8 cm length.

INFRAPOPLITEAL REVASCULARISATIONS

- Similar techniques Below The Knee (BTK) as Above (ATK) are applied for as down as possible. DEB come in small enough diameters to apply very distal.
- Cook has the *Shuttle Tibial* catheters and sheets in a 4F and 5F version.
- Bard has the *BANTAM* PTA dilatation catheter in 2-9 mm diameter as well as the BANTAM α for treatment of infrapopliteal lesions down to the foot with balloon sizes as small as 1.25 mm !
- The SAFARI technique is often applied (going in from a proximal AND from a distal, even pedal end; meet – or have *rendez-vous* – at the place of the obstruction. The interest for this technique is huge (the presentation room was packed with people and overloaded at least with 20 %)!
- There is also no consensus on how to approach this for best and – for claudication patients – if is good to try to re-open as many of the 3 arteries or if just 1 is enough. Subjective elements (operator) or the patient's life style, Rutherford class … might be taking into account. Yet in CLI patients, there is no question of Quality of Life, it is more a question of limb salvage or not! Mortality is very high in this last group (54% in 2 yrs).

MEDICATION

- During the procedure, especially for the infrapopliteal/crural artery/pedal artery treatments, a mixture of drugs is given to sedate (lidocaine) and to prevent spasm (?).
- No consensus exist about medication post-treatment but most often Aspirine + Clopidogrel is given at least for 4 weeks and up to 3 months as demanded mostly by the clinical trial protocols.

INTERESTING OTHER DEVICES.

- Implantable blood filters are frequently used, merely temporarily during vascular procedures such as arterectomy (plaque or blood thrombus removal) to catch debris flowing to the periphery or to the lungs. Some however are left in place, eg in the Inferior Vena Cava for up to 1-2 yrs! The *SPIDER FX* (Covidien) is such a filter that allows to be retracted into the shaft of an F6 sheat after being used and containing the debris of eg a dissolved blood cloth.
- V12 from Atrium: PTFE covered stent

- ClearWay from Atrium: "drip catheter" for resolution of thrombi by infusion of eg t-PA. the solution is eluded via a PTFE cover of very large pore size making drip perfusion over the length of the PTFE cover possible.
- Flixene IFG from Atrium. Is a PTFE AV graft with a special "T"-end shape to allow better insertion and outcome of the V-anastomosis to prevent hyperplasia.
- VIABAHN from GORE is a stented PTFA graft coated with heparin (Carmeda coating) and used for endovascular application. It comes in lengths up to 25 cm. They call the coating: Propaten Bioactive Surface. Viabahn is actually the longest covered stent: it comes in diameters from 5-8 mm and with 25 cm length. It also has a "contoured edge" at one end which may improve flow.
- Endologix showed 2 devices on display (no brochures available) for products not having CE mark yet, one of these (Linnex ?) is intended to allow filling up – after the intraluminal revascularization of the abdominal aorta is done - the aneurysm sack with a polymer that hardens out. No info on the type of polymer was given. A clinical trial is under its way, today they have 45 patients enrolled. CE mark is expected later this year. They also have the stent material *inside* the PTFE covering, all other companies have the stent at the outside wall.
- For pedal approaches, the physician needs to use his hands close to the foot and in the X-ray beam. The company "Upstream Peripheral" developed a 30 cm needle holder that help avoid this.
- Instead of using contrast media, which can be painful and damaging to the kidneys, the company Malek has a CO^2-angiography system developed. This system is already for 10 years on the market but has found little entrance into daily practice despite equal visualization. No studies are available however to proof this saying.
- LeMaitre brings a novel *Unballoon* Non-Occlusive Modeling Catheter onto the market to help shape the thoracic aorta stents better. They also have the *Valvulotome*, an over-the-wire venous valve cutter (valvulotomy). LeMaitre also has a hughe portfolio on ePTFE vascular grafts going from 4 up to 10 mm internal diameter. With or without enforcements, but uncoated; wall thickness 0.4 – 0.63 mm, intermodal distance : 20 $\pm$ 10 µm, suture retention strength min. 300 grams and average burst strength 218 $\pm$ 31 psi.
- Spectranetics has a laser-guide catheter (*Turbo Tandem)* to help dissolve plaques and thrombi. The debris size is so small that no blood filter is used or needed. Diameter is only 7-8 F (2 mm).
- Aptus Endosystems comes with an incredible fixation system: the *HeliFX aortic securement system*, which is in fact the application of sharp metal screw through the wall of EVAR-systems and aortic wall (even puncturing it completely and penetrating it with the sharp end outside the aortic wall!). The helical EndoAnchors might prevent dislocation of the vascular graft, but might cause also damage to the tissue surrounding the aortic wall.
- AGA Medical Corp, now a St Jude subsidiary, has "*Amplatzer vascular plug"* in different shapes and lengths to create an intentional obstruction, intended to be left in place permanently. The foldable plug is made from Nitinol. These plugs are used to occlude collaterals, AV-malformations, AV-fistulas…

CLINICAL TRIALS

END-POINTS

- Typical end-points in vascular surgery trials are different than in endovascular trials. In surgery, blood flow is most important and a vessel is called “patent” when some remaining blood flow can be detected. In endovascular trials, one looks primary to the absence of restenosis, which is more stringent endpoint: 100 % patent vessels (per the surgery definition) equals some 89% of “no restenosis” (Dixit Dr M Bosiers). In the end what is most important is “limb salvage” and prevention of amputation, especially in CLI patients.
- Late lumen loss (LLL)
- Target lesion revascularization
- Target lesion restenosis
- Absolute claudication distance (ACD)
- Pain free walking distance
- Core lab assessment is important, eg also for DUPLEX measurements
- Wound healing takes on average some 6 months, so this needs to be taken into account: there must be a wound healing specialist involved in trials to take appropriate care of the post-intervention care of the patients.

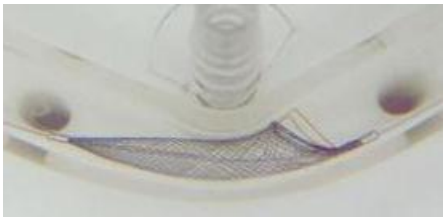
IMPORTANT TRIALS INFLUENCING MEDICAL PRACTICE

- DEFINITE LE and DEFINITE AR give insight in the performance of TURBOHAWK.
- THUNDER, FEM-PAC, LEVANT I, PACIFIER are 4 independent randomized trials demonstrating the efficacy of DEBs. Primary end-points are: late lumen loss (LLL), target lesion revascularization. Intermediate results all show a better outcome from the DEB treated patients than those treated with a regular balloon.
- SPORTS trial compares the use of SILVERHAWK with the IN.PACT
- Rock trial, Pacuba Trial, DEB-IT: all DEB trials that might show important aspects.
- The BASIL-trial has published results on the comparison of the angioplasty with surgical bypass grafting. In this study about 50% of the patients treated were BTK and at 1 and 3 yrs post intervention, no significant difference were found between both treatment arms with respect to vessel patency or mortality.
- COBEST clinical trial is ongoing and will reveal the outcome of the “*COVERED STENT*”. The company ATRIUM makes V12 covered stent. These are typically larger stents (5 mm min diameter). The cover is from PTFE, which need to be extendable and is thus differently constructed then the PTFE eg used for artificial blood vessels.
- Gene therapy (NV1FGF) did not seem successful (Talisman & Tamaris trials), yet cell therapy seems to be effective: in about 10 different trials such a benefit could be demonstrated. Striking example is the BONMOT-CLI study where a significant improvement of the cell-therapy arm above the non-cell-therapy arm was observed.

PICTURES

TURBOHAWK

SPIDER FX



OFFROAD and TRUEPATH of Boston Scientific

V12 covered stent

FLIXENE IFG

PACCOCATH TECHNOLOGY OF THE COTAVANCE DEB

Left: balloon delivers paclitaxel and iopromide to intimal layer which stays on after retrieval of balloon (right)