CLINICAL AND EPIDEMIOLOGICAL ASSESSMENT CONCERNING HYBRID REVASCULARIZATION TECHNIQUES IN THE TREATMENT OF MULTILEVEL ARTERIAL OCCLUSIVE DISEASE

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CLINICAL AND EPIDEMIOLOGICAL ASSESSMENT CONCERNING HYBRID REVASCULARIZATION TECHNIQUES IN THE TREATMENT OF MULTILEVEL PERIPHERAL ARTERIAL OCCLUSIVE DISEASE (Abstract): Aim of the study was to report a novel hybrid technique for multilevel arterial lesions of the lower extremities and to evaluate the clinical outcomes. In patients with multilevel arterial disease, the combined (hybrid) treatment, consisting of endovascular intervention and classical surgical intervention on the same vascular axis seems to be the most indicated treatment in order to obtain an adequate inflow and outflow. Material and methods: we have performed a non-randomized study during a 44-month period (January 2010 – September 2013) in a number of 94 patients treated by hybrid revascularization techniques. All the patients included in the study have been post-surgically surveyed at well established intervals (1, 3, 6, 9, 12, 24 and 36 months) by: clinical examination, laboratory tests, Duplex ultrasound, and, as needed, CT or MR Angiography. Results: the 6 months primary patency in each studied group (corresponding to the years of 2010, 2011 and 2012) was 58.69%, 68.42%, and 62.06%, respectively; the 12 months primary patency was 45.65%, 57.89%, and 34.48%, respectively. Clinical improvement has been noticed in 83 patients (88.29%). There have been registered 19 amputations (20.21% of the cases): 11 majors (thigh and below the knee), representing 11.7% of the total number of cases and 8 minors (toe or transmetatarsal), representing 8.51% of the total number of cases. The amputation-free survival period ranged between 7 days and 24 months, with an average of 7.66 months. Conclusions: the hybrid techniques are a feasible option for the multilevel arterial disease, with favorable patency and limb salvage rates. Keywords: MULTILEVEL ARTERIAL DISEASE, HIBRID REVASCULARIZATION

Multilevel involvement is typically observed in peripheral arterial occlusive disease (PAOD). A staged approach to multilevel occlusive disease was the standard for numerous years, consisting of balloon angioplasty of the iliac artery followed by interval infrainguinal surgery (1, 2). This approach was a rational strategy at a time when open and endovascular surgical techniques were only performed in separate settings.

Multilevel revascularization, using a combination of endovascular and open techniques, was first reported in the early
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1990s (3). Hybrid surgery is ideal for multilevel lesions, as it allows the application of minimally invasive treatment on complex anatomy in high-risk patients. Usually, the procedures are performed simultaneously, although individual patient anatomy plays a part in the decision of whether to perform the two procedures simultaneously or not. The aim of the treatment is to obtain an improvement of both the inflow and the outflow (4, 5).

The rate of hybrid interventions has progressively increased during the last decade and it is estimated to be around 5-20% of all vascular reconstructions (6).

In the hybrid technique, the endovascular stage can be an inflow procedure, an outflow procedure, a combination of the two, or a bypass revision.

The open techniques consisted of an autologous or synthetic bypass graft and/or endarterectomy.

MATERIAL AND METHODS

We have performed a non-randomized study in two centers. The data was gathered retrospectively for a 20-month period (January 2010 – September 2011), and prospectively for a 24-month period (September 2011 – September 2013) for a number of 94 patients treated by hybrid revascularization techniques at the Cardiovascular and Thoracic Surgery Clinic, “Imelda” Hospital, Bonheiden, Belgium.

The including criteria for the patients were: aged 18 and over, multilevel peripheral arterial disease in any of the Leriche-Fontaine stages, with uni- or bilateral pathology, and had an indication of hybrid revascularization by both endovascular therapy (either balloon angioplasty, stenting or endoprosthesis insertion), and an open technique (bypass or endarterectomy, with or without angioplasty). The study included 94 patients (female 35.1%, male 64.9%, mean age 70.68 years).

The patients were divided into two groups: 1 – included patients who had the hybrid techniques done in one procedure; 2 – included patients treated in two successive procedures.

The second group was divided into two sub-groups of patients: one for which the open revascularization technique was done first, followed by an endovascular procedure; and the second, for which the initial procedure was the endovascular one, followed by the open technique.

Peripheral arterial disease was localized at a minimum of two levels on the same vascular axis: aortic, iliac, inguinal (involving the common, deep femoral artery and the origin of the superficial femoral artery), or infrainguinal (supra- or infragenicular).

All patients were pre-operatively evaluated by physical examination, blood tests, duplex scan, CT or MR Angiography. Also, the risk factors and associated co morbidities were noted.

Postoperative surveillance at well established time intervals (1, 3, 6, 9, 12, 24 and 36 months), consisted of: blood tests and Duplex scans, clinical examination (improvement of the claudication distance, amelioration of rest pain, healing of trophic lesions).

We evaluated the primary patency, assisted primary patency and secondary patency of all procedures, initial technical success, complication rate, morbidity and mortality associated with each technique, amputation-free survival rate, symptomatic improvement, and the risk factors that influenced the postoperative outcome and recovery period.

The statistic analysis and epidemiologi-
Statistical data were performed in SPSS 15.0 (SPSS Inc., Chicago, IL, USA). A p value of less than 0.005 was considered statistically significant.

During the study, the primary and secondary patency were analyzed using the Kaplan-Meier estimator.

RESULTS
Thirty-three patients (35.10%) were revascularized by simultaneous hybrid procedures and 61 patients (64.89%) by successive hybrid procedures: the open technique of 42 patients (44.68%) was followed by an endovascular procedure and in 19 patients (20.21%) the endovascular technique was followed by an open procedure (fig. 1).

The majority of patients treated by simultaneous hybrid procedures were classified as stage II Leriche-Fontaine (fig. 2).

![Fig. 1. The distribution of cases according to the revascularization procedure sequence](image1)

![Fig. 2. The distribution of hybrid procedures according to the disease stage.](image2)

For the studied period of time, there were 49 bypass procedures performed, 37 common femoral artery endarterectomies and angioplasties, 23 desobstructions using the Fogarty catheter, 97 thrombolysis procedures, 164 endovascular angioplasties
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and 100 endovascular angioplasties followed by stenting.

Elective procedures were performed for 61.7% of the patients and emergency procedures for the rest of 38.3% of the patients, with acute or subacute ischemia. Emergency procedures consisted of thrombolysis, bypass, or native artery thrombectomies, with or without a bypass or supra/subjacent percutaneous angioplasties (PTA) on the same arterial axis.

The initial technical success for all procedures was 100%.

We had 19 early artery or bypass occlusions (less than 30 days) and one case with a postoperative local haematoma which required a reintervention for haemostasis and evacuation.

We had one severe graft infection (for which a myoplasty was performed, with favorable postoperative recovery) and 78 late occlusions (after more than 30 days), which entailed follow-up procedures for reestablishing the patency.

We had 7 intra-stent stenoses at the level of the superficial femoral artery, which were solved by angioplasty and restenting or femoro-popliteal bypass.

There were 19 (20.21%) amputations recorded: 11 majors (thigh or below-knee), representing a rate of 11.7% of the total number of cases and 8 minors (toe or trans-metatarsal), representing a rate of 8.51% of all cases. The major amputations were 10 unilateral and one bilateral (successive). Limb salvage rate for the patients in stage III and IV Leriche-Fontaine was 73.17%. Clinical improvements was noticed in 83 (88.29%) patients. After six months primary patency in each studied group (corresponding to the years of 2010, 2011, and 2012) was 58.69%, 68.42%, and 62.06% respectively, comparable with those published in the literature. After twelve months primary patency was 45.65% in the 2010 studied group, 57.89% in the 2011 group of patients, and 34.48% for the 2012 group (fig. 3, 4, 5).

We did not find statistically significant differences between the averages of the primary patency of various disease stages. The mortality rate for the entire period studied was 0%.

![Fig. 3. The Kaplan-Meyer diagram of primary patency for the 2010 patient group](image)
In regards to the influence of the hybrid procedure type on the primary patency (PP), we found that in the case of successive endovascular and open procedures, the average PP is significantly higher compared to the PP of open technique followed by an endovascular procedure (Fig. 6).

The statistic analysis identified the only risk factors which significantly influenced the primary patency in the studied group: obesity and renal insufficiency.
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Fig. 6. The influence of the type of hybrid procedure on the primary patency

**DISCUSSION**

Implementing hybrid techniques in the vascular surgery practice and the possibility of performing them in hybrid operating rooms offer therapeutic options that come to meet the needs of the patients with multilevel lesions and high surgical risk.

For the cases treated in a simultaneous hybrid manner, the main role was played by the common femoral artery (CFA), and its suitability for supra- or subjacent endovascular angioplasty. Endarterectomy, with or without patch angioplasty has been performed on this artery in 28 cases.

The most common endovascular procedure user was balloon angioplasty followed by stenting. Combined open and endovascular revascularization may be performed with either a staged or simultaneous approach. Endovascular surgery has been enthusiastically embraced by a large number of vascular surgeons, leading to increased experience with these types of procedures. In numerous hospitals, hybrid operating rooms have been constructed, making it possible to use both open and endovascular techniques. It is both easy and comfortable to perform simultaneous hybrid surgery in this environment. The hybrid approach has several advantages (7).

Firstly, there is no delay in providing complete revascularization to the ischemic limb. Secondly, the length of hospital stay is reduced and finally, puncture-site complications are eliminated since the target artery is accessed through the surgical field and the access site becomes the location of proximal anastomosis.

Cotroneo *et al* (8) reported on 2-year results of hybrid revascularization. The technical success rate was 100% whilst the primary patency rate was 86.2% at 6 months and 79.1% at 24 months. Hybrid surgery has a theoretical advantage com-
pared with open or endovascular revascularization performed separately, in terms of patency rate. With hybrid surgery, inflow or outflow arteries may be revascularized, which may affect the patency rate.

Antoniou et al (9) also reported on 3-year results of hybrid revascularization. The technical success rate was 100%. Primary patency rate was 71%.

The annual number of hybrid procedures is increasing. Aho and Venermo (10) reported that this number ranges between 4, in 2004, and 73, in 2011. Out of this total number of hybrid procedures, the proportion performed by vascular surgeons increased from 0% in 2004 to 86.3% in 2011. Relatively young vascular surgeons have adopted endovascular surgery and became familiar with it. According to a survey conducted by the Society for Vascular Surgery (11), younger vascular surgeons (aged <50 years) frequently reported that >50% of their workload is endovascular, compared with older vascular surgeons (aged ≥50 years) (P<0.001). The endovascular skills of vascular surgeons have improved through education and simulator-based endovascular skills training (12, 13, 14, 15).

**CONCLUSIONS**

Hybrid interventions have become a well-accepted strategy for revascularization in patients with critical limb ischemia due to multilevel arterial occlusive disease. Technical success and short- and long-term limb salvage outcomes of hybrid interventions have been shown to be at least comparable to the conventional endovascular and surgical revascularization procedures. Hybrid revascularization offers the efficiency and convenience of a single-stage therapy without added risks for those with lower extremity ischemia.

In our study hybrid procedures are a feasible option for multilevel peripheral arterial occlusive disease, with favorable patency and limb salvage rates. The observations of the current study indicate that femoral endarterectomy plays an important role in hybrid surgery.

**REFERENCES**

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**ROLE OF OSTEOPROTEGERIN CGA HAPLOTYPE IN PATIENTS WITH RHEUMATOID ARTHRITIS**

Osteoprotegerin (OPG) has been associated with increased risk of atherosclerotic disease in the general population and have been described several polymorphisms in the OPG gene with functional effects on cardiovascular disease in non-rheumatic individuals. A group of researchers from Spain aimed to analyze the effect of three of functional OPG polymorphisms on the risk of cardiovascular disease in a large and well-characterized cohort of patients with rheumatoid arthritis. Three OPG gene variants (rs3134063, rs2073618 and rs3134069) were genotyped by TaqMan assays in 2027 patients with rheumatoid arthritis. Anti-cyclic citrullinated peptide (anti-CCP) antibody testing was positive in 997 of 1714 tested. Also, 18.3% of the whole series had experienced cardiovascular events, including 5.4% with cerebrovascular accidents. The relationship between OPG variants and cardiovascular events was assessed using Cox regression. No association between OPG gene variants and cardiovascular disease was observed in the whole group of rheumatoid arthritis patients or in anti-CCP positive patients. Nevertheless, a protective effect of CGA haplotype on the risk of cardiovascular disease in general, and specifically in the risk of cerebrovascular complications after adjusting for sex, age at disease diagnosis and traditional cardiovascular risk factors was disclosed in anti-CCP negative patients. They concluded that their results indicated a protective effect of the OPG CGA haplotype on cardiovascular risk, mainly due to a protective effect against cerebrovascular events in anti-CCP negative rheumatoid arthritis patients. (Genre F, López-Mejías R, García-Bermúdez M et al. Osteoprotegerin CGA Haplotype Protection against Cerebrovascular Complications in Anti-CCP Negative Patients with Rheumatoid Arthritis. *PLoS One.* 2014 Sep 3; PMID:25184828).

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