Universitat de Girona

FACULTAT DE MEDICINA

KISSING COVERED STENTS VERSUS AORTOBIFEMORAL BYPASS IN PATIENTS WITH LERICHE SYNDROME

RODRIGO FERNÁNDEZ GONZÁLEZ

Tutor: Dra. Patricia Rodríguez Cabeza
Angiology and Vascular Surgery department
H. U. Dr. Josep Trueta, Girona

FINAL DEGREE PROJECT
November 2015

INDEX

Moitas grazas a todo o equipo de Anxioloxía e Cirurxía Vascular do Hospital Dr. Josep Trueta de Girona, pola súa acollida no servizo, implicación e consellos que algún día non moi lonxano espero poder aplicar na miña vida profesional.

<< o verdadeiro heroísmo consiste en trocar os anceios en realidades, as ideias en feitos >>

CASTELAO ····· 1886-1950

1. ABSTRACT

Background: *Leriche syndrome is the most challenging type of occlusive aortoiliac disease for the surgical treatment. Historically, it has been treated by open surgical repair with good results on patency rates. Endovascular surgery appeared as a safe and feasible technique with lower rates of morbimortality than open repair. In the last years, endovascular devices and techniques have evolved as such as the experience of the vascular surgeons. Endovascular approach with kissing covered stents is presented as a safe and reliable alternative to open repair in patients with Leriche syndrome.*

Objectives: *To compare primary patency rates in 5 years term of endovascular with kissing covered stents vs. aortobifemoral bypass in patients with Leriche syndrome. Secondary objectives are to analyse the mortality within the first 30 days, the need for conversion to open surgery, the need for reintervention, the secondary patency and the impairment of kidney function.*

Methods: *Randomized, controlled clinical trial. Patients with Leriche syndrome who meet all the criteria will be randomized for surgical treatment with aortobifemoral bypass or endovascular approach with kissing covered stents.*

Keywords: *Aortobifemoral bypass, kissing stents, Leriche syndrome, aortoiliac occlusive disease.*

Abbreviations: ***PAD*** *(Peripheral Arterial Disease);* ***ABI*** *(Ankle-Brachial Index);* ***CFA*** *(Common Femoral Artery).*

2. INTRODUCTION

Leriche syndrome "is an aortoiliac chronic occlusive disease caused by the progressive occlusion of the terminal aorta affecting gradually its bifurcation and iliac arteries but without involvement of the renal arteries" (1). It is mainly caused by atherothrombotic injuries (1–3). This condition was first described with its triad of symptoms by René Leriche in 1923. Leriche, a French surgeon, associated it with claudication of the buttocks and thighs, erectile dysfunction and decreased femoral pulses or the absence of them (2–7).

Leriche syndrome is a form of peripheral arterial disease (PAD). There are different systems of classification for the aortoiliac occlusive disease and the most common ones are the following (all classifications are provided in ANNEX 1):

- **Trans-Atlantic Inter-Society Consensus II (TASC II).**

  This is the most important classification and it is based on the form, distribution and seriousness of the illness (Fig. 1). It classifies the disease into four types (A-D) and it is mainly used to decide the type of revascularization treatment needed. Leriche syndrome is a TASC II D disease (2,8,9).

- **Anatomical location of the atherosclerotic injuries.**

  It divides the injuries into three different types depending on the degree of the lesion spreading. A small percentage of the patients (5-6%) presents damage on the renal arteries (2).

- **Society of Cardiovascular and Interventional Radiology (SCVIR)** (9)**.**

The exact impact of PAD is very difficult to determine because there are many patients who suffer from this disease in an asymptomatic way, due to collateral circulation development (2).

Some epidemiological studies have shown a prevalence of PAD that changes between the 2-10% in the population under 70 years of age, according to the series. There is a slight predominance among the male gender (1,2,8) (0.7% among women and 1.3% among men (1)). Amongst people over 70 years of age, the prevalence of the PAD is 15-20%.

The aortoiliac sector is affected in the 35% of the cases of PAD in lower limbs (4). Leriche syndrome is an unusual disease (3,10) belonging to this group.

The main cause of chronic aortoiliac occlusion is the formation of atherosclerotic injuries with thrombotic episodes (1–3,8).

As we can see in Figure 1, it has been described several risk factors for the development of PAD but tobacco is claimed to be the most important one, specially in Leriche syndrome (8).

Aortic bifurcation angle is also considered as an independent risk factor for the development of atherosclerosis due to local variations in blood flow and aortic diameter reduction (2).

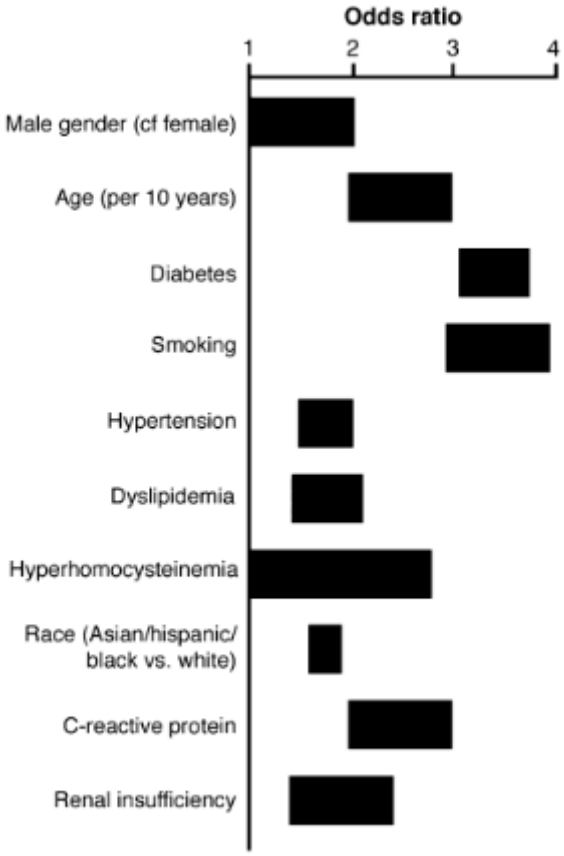


Figure 1. Approximate range of odds ratios for risk factors for symptomatic peripheral arterial disease. (8)

Other possible causes are: the existence of strong adhesions of the tissues around the occlusive vessel due to perivascular inflammatory process (1) or hypoplasia of the aortoiliac segment (11).

Chronic aortoiliac obliteration symptoms in Leriche syndrome depend on the scale of occlusion and the development and existence of collateral circulation (1). The appearance of atheromatosic injuries reduces the arterial light and the blood flow to the pelvic area and the lower extremities. This process produces the typical symptoms of claudication, erectile dysfunction and decreased femoral pulses (1,2). The presence of advanced ischemia is not very frequent (3) and implies risks to the integrity and conservation of the lower limbs (12). Occasionally, the patients may be asymptomatic

(3,8).

The most common symptom is the claudication of hips, thighs and gluteus. Pain usually appears while exercising and diminishes with repose. This is because of the existence of arterial collateral circulation, which also might delay its appearance. This might be the first and only symptom described by the patient (1,2). Pain while resting indicates critical ischemia and it can be seen in very advanced phases of the disease (9).

Men may develop erectile dysfunction as a consequence of reduced blood flow of internal iliac artery (2).

Rare forms of presentation of the aortoiliac obliteration has been presented such as the one described by Yoon et al as a right sciatic neuropathy, or the one described by Kim et al presented as a gradual lumbosacral plexopathy with paraplegia (2).

The diagnosis tends to be clinical through the anamnesis and the physical examination, in which the patients tend to show disproportion of the lower limbs, coldness and paleness in legs and feet and absence or decrease of the femoral pulse (1,4). To clinically measure the grade of ischemia, Fontaine classification (Table 1) can be used (4).

Grade I	Asymptomatic. Detectable by ankle-arm index <0.9
Grade IIa	Intermittent claudication not limiting the patient's life style
Grade IIb	Intermittent claudication limiting for the patient
Grade III	Pain or paresthesias at rest
Grade IV	Established gangrene. Trophic lesions
Grade III and/or IV	Critical ischemia. Threat of loss of limb

Table 1. Fontaine's clinical classification (25).

The ankle-brachial index (ABI)[1] is a non-invasive way to detect and follow the evolution of ischemia in the lower limbs. It is related to the presence of PAD and the seriousness of the occlusion. ABI is calculated with the quotient of maximum systolic pressure in the ankle and the systolic pressure in the arm (13). The interpretation of the obtained values is shown in Table 2.

ABI INTERPRETATION	
>1.30	Incomprehensible
1.00-1.29	Normal
0.99-0.90	Limit values
0.41-0.90	Mild ischemia
<0.41	Severe ischemia

Table 2. Ankle-Brachial Index interpretation (13).

The confirmation of the diagnosis is done by image tests, asked when the revascularization treatment is considered (3,4):

- **CT-Angiography (Computed angiotomography)**: It is the "gold-standard" test nowadays for the aortoiliac occlusion diagnose. It is the most effective test and the one that gives more information. It is a non-invasive and fast test that allows studying the extension of the disease with great accuracy. It also gives information about the arterial condition, the collateral circulation and the surrounding structures (1–4). It can be performed with a minimum amount of intravenous contrast to provide three-dimensional anatomical images. It allows obtaining morphological images of the aortoiliac sector and its branches in order to carry out further measures for endovascular surgery and to plan open repair surgeries (2,4).

  The assessment of the longitudinal cuts is useful to see:

[1] In spanish, ITB (Índice Tobillo-Brazo) as shown in ANNEX 7 (Participant data sheet).

- Proximal and distal neck of the thrombosis.
- Beginning, extension and ending of the injury. Measurement for endovascular strategies.
- Renal, intern iliac and visceral arteries.
- Morphology of the viscera (horseshoe kidney, intestinal pathology).
- Periarterial surrounding tissues: hematomas, abscesses, gases, greasy ascites, ganglions, vena cava.
- Good assessment of metallic devices.
- 3D reconstructions.
- High definition, no devices.
- Fast execution.

Disadvantages:

- High dose of radiation
- It does not give a hemodynamic information
- Difficulty of interpretation in much calcified injuries and excessive angulations.
- Bad resolution of small vessels and visceral arteries in a distal level.
- Bad resistance to the iodinated contrasts in patients carrying a chronic renal failure (CRF) because of its nephrotoxicity and it is not good for pregnant women.

- **Doppler ultrasound:** It is an innocuous test that provides good hemodynamic and anatomic information of the aortoiliac sector that may be used as alternative or as a complement to the angiographic study. The most frequent

calculated parameter is the quotient of speed, defined as the speed of the blood flow at the point of maximum acceleration between the speed in an adjacent healthy proximal segment (4,13). Flow speed is measured by cm/sc. We can see the relationship between the quotient of speed and the % of patency in the aortoiliac sector in Table 3. The biggest disadvantages are the operator dependent variability and that it is not useful to plan endovascular interventions (4).

% PATENCY	QUOTIENT OF SPEED
Occlusion	0
30-50%	<2
50-75%	2-3.5
>75%	>3.5

Table 3. Relationship between quotient of speed and % of patency in the aortoiliac sector measured by Doppler ultrasound. Adapted from (13)

- **MR-Angiography (Magnetic resonance angiography)**: This test is used when patients cannot undergo CT-Angiography. The injection of gadolinium as intravenous contrast is necessary. It offers very accurate results, similar to those obtained with the CT (2,4).

Advantages:

- Treatment without radiation.
- Good hemodynamic information and also from the structure of the arterial walls.
- Quick resolution of the 2D and 3D images.

Disadvantages:

- Low availability (high technology equipment).

- Low visceral and surrounding tissues of the aortoiliac sector resolution.
- Devices in the calcified plaques.
- Not good with metallic devices or with pregnant women on their first trimester.
- Long execution time (30 min).

- **DSA (Digital subtraction angiography)**: Not much far away DSA had been the "gold standard" technique in diagnostic work-up of patients with symptomatic disease. However, it is not suitable for patients with diabetes or renal insufficiency due to the use of contrast medium, which increases morbidity. It is currently utilized in conjunction with a planned endovascular intervention (2).

Leriche syndrome's treatment has as main aims to improve the symptoms of the patient, stop the proximal spreading of the thrombus and, in an extreme case, save the limb (14).

The surgical revascularization treatment is performed when lower limbs critical ischemia is present or when disabling symptoms exist (IIb, III or IV grade of Fontaine's scale) (4,14),if the medical treatment has not been successful (14).

Historically and nowadays, the "gold-standard" technique used is the introduction of prosthesis to make an aortobifemoral bypass (8,12,14) that provides an effective recovery and great levels of long term patency (ANNEX 2) (8). Nowadays it is a safe surgery procedure which shows very good results (14). However, although great improves have been achieved, the mortality rate varies between 3-4,6 % and 1-16% for

the morbidity (10,14–16). The possible complications might be cardiopulmonary, sexual dysfunction, intestinal ischemia, ureteral damage or spinal cord's injuries (10).

Following surgical approaches are also used: the endarterectomy, the resection of the occluded segment with grafting of the defect, an unilateral aortofemoral bypass with femoro-femoralis cross-over bypass and the extra-anatomic axilo-bifemoral bypass (5,8). Those techniques suppose an open major surgical intervention, which might aggravate the comorbidities usually shown in Leriche syndrom's patients (3,5).

The endovascular surgery has been developed as a minimally invasive alternative and with less morbidity compared to an open surgery (8,9). It also allows the patient to recover their daily routine (10). The most common complications reported on the literature are aortic rupture, aortic dissection and distal emboli (17,18).

The use of endovascular treatment has increased in the last few years because of the evolution of the endovascular techniques and surgeons' experience (18,19). At the beginning, it was applied for local lesions but recently it has been also proposed as a safety option for extensive lesions (TASC II C/D) (18). Currently guides recommend endovascular approach for TASC II A lesions and open repair for TASC II D lesions. The most recommended approaches for TASC II B/C lesions are controversial (8).

Leriche syndrome is the most complicated type of TASC II for the endovascular treatment and it has been described poorly (10). The most part of the data collected was based on the categories TASC-II C/D of the obstructive aortoiliac pathology, in which the number of patients with Leriche syndrome was not high. Also, many series have mixed the results of endovascular therapy in isolated aortic and aortoiliac lesions

without making differences between them (17).

In 1991 the “kissing stent” technique was introduced as an alternative treatment for the occlusive aortoiliac disease. Two stents are placed simultaneously in the common iliac arteries within overlapping in the distal aorta (20,21). The recommended type of stents for this intervention are the balloon-expandable stents that have more radial strength (4) and it can be further dilated after the initial expansion in order to achieve a haemodynamically satisfying diameter (22). They can be metallic or covered. Up to now, the metallic stents have been used in the most of the studies performed about endovascular treatment for this pathology.

The short-term primary patency values reached using metallic stents have been compared to those obtained with open repair surgery in TASC II C/D injuries (23). Two performed meta-analysis by Ye et al and Jongkind et al show short-term patency rates for endovascular treatment of TASC II C/D injuries (9,24). Nevertheless, the long-term primary patency (4-5 years) after the endovascular treatment for the serious aortoiliac obstructive disease (TASC-II C/D) is less than the one obtained after open repair surgery (60-86% according to Jongkind et al). Data about these short and long-term patency rates are provided in ANNEX 2. These results make open surgery be the elective treatment (3,6). On the other hand, reinterventions after the primary patency loss can be performed with minimally invasive techniques. With them, it is possible to obtain secondary patency rates (ANNEX 2) similar to those achieved with open repair surgery (6,9) (80-98% according to Jongkind et al). Risk factors for restenosis after endovascular surgery were studied by some authors. The only one statistically significative was the lesion length with a p value of 0.035 in a multivariate analysis

(18).

Covered stents have been mainly used in the treatment of endovascular therapy complications (tears or dissections…) in an aortoiliac level and with arteriovenous fistula (4,11).

The limited studies published up to now using covered stents for the aortoiliac occlusive disease treatment have shown improvement in the primary patency rates, if we compared them to the metallic stents. A study carried out by Sabri et al shows primary patency levels of 92% vs 72% in 2 a year term for covered and metallic stents, respectively (p=0.023). Besides, the number of patients classified as TASC II C/D was bigger in the group treated with covered stents (ANNEX 2) (23).

Improving the long term primary permeability is important because it reduces the number of reinterventions (15). The use of covered stents increases patency rates decreasing the hyperplasia via intimal exclusion. They are surrounded by an expanded polytethrafluroethilen (ePTFE) layer (11,15).

With those results, the endovascular surgery with covered stents is presented as a safe and reliable technique for patients with extensive aortoiliac disease, including Leriche syndrome, and with less complications that open surgery. However, long-term studies that compare both techniques are still necessary to define the role of the covered stents in the treatment algorithm of Leriche syndrome.

3. JUSTIFICATION

Leriche syndrome is a chronic disease with low prevalence but a severe impact on a functional level. For its serious consequences, patients with Leriche syndrome often require surgery to prevent the disease to develop to advanced stages. These consequences may include severe limitations in the daily life and limb-threatening symptoms that may lead to loss lower limbs, in the worst situation.

All of the clinical features have not only physical but also psychological impact in the society and it is reflected on the National Care System.

Techniques and devices used in endovascular surgery have evolved to displace conventional open surgery in many cases because of its lower invasiveness, risk of complications and morbimortality. However, open repair remains the technique of choice in the most advanced cases of obstructive pathology of the aortic bifurcation (TASC II C / D).

Leriche syndrome is still the most challenging aortoiliac obstructive disease to endovascular surgery, but nowadays we have the aims necessary to go further in the surgical treatment of this particular disease. Another favourable condition is that vascular surgeons have improved enormously their skills to perform endovascular surgery.

A recent study has shown promising patency values results obtained by implanting covered stents, closer to the results obtained with open surgery and maintaining the

advantages of endovascular surgery.

It is necessary further information and studies that compare both techniques to assess the possibility of endovascular surgery to replace open surgery as the technique of choice in the surgical treatment of patients with Leriche syndrome and complex aortoiliac obstructive disease.

4. BIBLIOGRAPHY

1. Oviedo Gamboa I, Herbas Bernal R, Zegarra Santiesteban W. Diagnóstico por tomografía del Síndrome de Leriche: reporte de un caso clínico. Gac Med Bol. 2013;36(2):105–7.

2. Wooten C, Hayat M, du Plessis M, Cesmebasi A, Koesterer M, Daly K, et al. Anatomical significance in aortoiliac occlusive disease. Clin Anat [Internet]. 2014 [cited 2015 Oct 20];27(8):1264–74. Available from: http://doi.wiley.com/10.1002/ca.22444

3. West C, Johnson L, Doucet L, Caldito G, Heldman M, Szarvas T, et al. A contemporary experience of open aortic reconstruction in patients with chronic atherosclerotic occlusion of the abdominal aorta. J Vasc Surg [Internet]. 2010 [cited 2015 Oct 20];52(5):1164–72. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0741521410013406

4. Plaza Martínez A, Carrera Díaz S, Alonso Álvarez MI, Escudero JR, Vaquero Puerta C, Cairols Castellote M, et al. Tratamiento endovascular de la patología obstructiva aortoiliaca. Angiologia. 2011;63(2):75–94.

5. Krankenberg H, Schlüter M, Schwencke C, Walter D, Pascotto A, Sandstede J, et al. Endovascular reconstruction of the aortic bifurcation in patients with Leriche syndrome. Clin Res Cardiol. 2009;98(10):657–64.

6. Setacci C, Galzerano G, Setacci F, De Donato G, Sirignano P, Kamargianni V, et al. Endovascular approach to Leriche syndrome. J Cardiovasc Surg (Torino). 2012;53:301–6.

7. Ellis H. René Leriche : the Leriche syndrome. J Perioper Pract. 2013;23(6):147–8.

8. Norgren L, Hiatt W, Dormandy J, Nehler M, Harris K, Fowkes F, et al. Inter-Society Consensus for the management of peripheral arterial disease (TASC II). Int Angiol [Internet]. 2007 [cited 2015 Oct 20];26(2):82–157. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0741521406022968

9. Jongkind V, Akkersdijk GJM, Yeung KK, Wisselink W. A systematic review of endovascular treatment of extensive aortoiliac occlusive disease. J Vasc Surg [Internet]. 2010 [cited 2015 Oct 20];52(5):1376–83. Available from: http://dx.doi.org/10.1016/j.jvs.2010.04.080

10. Schmalstieg J, Zeller T, Tübler T, Sixt S, Schwencke C, Sandstede J, et al. Long term data of endovascularly treated patients with severe and complex aortoiliac occlusive disease. J Cardiovasc Surg (Torino). 2012;53:291–300.

11. Mwipatayi BP, Surg M, Sa FCS, Thomas S, Hons M, Wong J, et al. A comparison of covered vs bare expandable stents for the treatment of aortoiliac occlusive disease. J Vasc Surg [Internet]. 2011 [cited 2015 Oct 20];54(6):1561–70.e1. Available from: http://dx.doi.org/10.1016/j.jvs.2011.06.097

12. Kashyap VS, Pavkov ML, Bena JF, Sarac TP, O'Hara PJ, Lyden SP, et al. The management of severe aortoiliac occlusive disease: Endovascular therapy rivals open reconstruction. J Vasc Surg. 2008;48(6):1451–7.e3.

13. March García J, Fontcuberta García J, de Benito Fernandez L, Marti Mestre X, Vila Coll R. Guía básica para el estudio no invasivo de la isquemia crónica de miembros inferiores. Vascular SE de A y C, editor. Madrid;

14. Llaneza Coto J, Carreño Morrondo J, Herrero Menéndez M. Tratamiento quirúrgico de la enfermedad obstructiva del sector aortoiliaco. Derivación protésica. In: Vascular F de la SE de A y C, editor. Tratado de las enfermedades vasculares. Barcelona: Viguera Editores, S.L.; 2006. p. 549–542.

15. Humphries MD, Armstrong E, Laird J, Paz J, Pevec W. Outcomes of covered versus bare-metal balloon-expandable stents for aortoiliac occlusive disease. J Vasc Surg [Internet]. Society for Vascular Surgery; 2014 [cited 2015 Oct 20];60(2):337–43. Available from: http://dx.doi.org/10.1016/j.jvs.2014.02.055

16. Groot Jebbink E, Grimme F a. B, Goverde PCJM, van Oostayen J a., Slump CH, Reijnen MMPJ. Geometrical consequences of kissing stents and the Covered Endovascular Reconstruction of the Aortic Bifurcation configuration in an in vitro model for endovascular reconstruction of aortic bifurcation. J Vasc Surg [Internet]. Society for Vascular Surgery; 2015;61(5):1306–11. Available from: http://linkinghub.elsevier.com/retrieve/pii/S074152141302301X

17. d'Othée BJ, Haulon S, Mounier-Vehier C, Beregi JP, Jabourek O, Willoteaux S. Percutaneous endovascular treatment for stenoses and occlusions of infrarenal aorta and aortoiliac bifurcation: Midterm results. Eur J Vasc Endovasc Surg [Internet]. 2002 [cited 2015 Oct 20];24(6):516–23. Available from: http://linkinghub.elsevier.com/retrieve/pii/S107858840291751X

18. Ichihashi S, Higashiura W, Itoh H, Sakaguchi S, Nishimine K, Kichikawa K. Long-term outcomes for systematic primary stent placement in complex iliac artery occlusive disease classified according to Trans-Atlantic Inter-Society Consensus (TASC)-II. J Vasc Surg [Internet]. 2011 [cited 2015 Oct 20];53(4):992–9. Available from: http://dx.doi.org/10.1016/j.jvs.2010.10.069

19. Hans SS, DeSantis D, Siddiqui R, Khoury M. Results of endovascular therapy and aortobifemoral grafting for Transatlantic Inter-Society type C and D aortoiliac occlusive disease. Surgery. 2008;144(4):583–90.

20. Grimme FAB, Goverde PCJM, Verbruggen PJEM, Zeebregts CJ, Reijnen MMPJ. First Results of the Covered Endovascular Reconstruction of the Aortic Bifurcation (CERAB) Technique for Aortoiliac Occlusive Disease. Eur J Vasc Endovasc Surg [Internet]. 2015 [cited 2015 Oct 20];1–10. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1078588415005407

21. Goverde PCJM, Grimme FAB, Verbruggen PJEM, Reijnen MMPJ. Covered endovascular reconstruction of aortic bifurcation (CERAB) technique: a new approach in treating extensive aortoiliac occlusive disease. J Cardiovasc Surg (Torino) [Internet]. 2013 Jun [cited 2015 Sep 22];54(3):383–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23640357

22. Laganà D, Carrafiello G, Mangini M, Lumia D, Caronno R, Castelli P, et al. Endovascular treatment of steno-occlusions of the infrarenal abdominal aorta. Radiol Med [Internet]. 2006 [cited 2015 Oct 20];111(7):949–58. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17021687

23. Sabri SS, Choudhri A, Orgera G, Arslan B, Turba UC, Harthun NL, et al. Outcomes of Covered Kissing Stent Placement Compared with Bare Metal Stent Placement in the Treatment of Atherosclerotic Occlusive Disease at the Aortic Bifurcation. J Vasc Interv Radiol [Internet]. 2010 [cited 2015 Oct 20];21(7):995–1003. Available from: http://dx.doi.org/10.1016/j.jvir.2010.02.032

24. Ye W, Liu CW, Ricco JB, Mani K, Zeng R, Jiang J. Early and late outcomes of percutaneous treatment of TransAtlantic Inter-Society Consensus class C and D aorto-iliac lesions. J Vasc Surg. 2011;53(6):1728–37.

25. Serrano Hernando FJ, Martín Conejero A. Peripheral Artery Disease: Pathophysiology, Diagnosis and Treatment. Rev Española Cardiol [Internet]. 2007 [cited 2015 Oct 20];60:969–82. Available from: http://www.revespcardiol.org/en/peripheral-artery-disease-pathophysiology-diagnosis/articulo/13114115/

5. HYPOTHESIS

In the surgical treatment of Leriche syndrome, endovascular surgery with kissing covered stents appears to be a safe and feasible alternative to aortobifemoral bypass of the aortoiliac sector for obtaining acceptable patency rates.

6. OBJECTIVES

6.1. PRIMARY OBECTIVE

This study aims to compare primary patency rates in 5 years term of endovascular with kissing covered stents vs. aortobifemoral bypass in patients with Leriche syndrome who have undergone surgery, at Hospital Universitari Dr. Josep Trueta.

6.2. SECONDARY OBJECTIVES

To analyse and study:

- The mortality within the first 30 days.
- The need for reintervention
- The secondary patency
- The need for conversion to open surgery
- The impairment of kidney function

7. METHODS

7.1. STUDY DESIGN

A randomized clinical trial: aortobifemoral bypass or endovascular approach with kissing covered stents.

Blinding can't be used in this study. The intervention has to be known by the vascular surgeon in order to perform it. The scars will be noticed by the patient.

7.1.1. RANDOMIZATION METHODS

Patients' randomization will be performed using the "Epidat 4.1" software. The vascular surgeon will not have access to information on the type of surgery for each patient up to 48 hours before surgery to minimize any selection bias.

7.2. STUDY POPULATION

Patients diagnosed with Leriche syndrome from January 2016 at H. U. Dr. Josep Trueta, tributaries of surgery and suitable for 2 types of intervention: aortobifemoral bypass and endovascular approach with kissing covered stents. They must meet all of the inclusion and the exclusion criteria.

7.2.1. INCLUSION CRITERIA

- Men and women over 18 years.
- Patients diagnosed with Leriche syndrome by the vascular surgery team of H. U. Dr. Josep Trueta, tributaries of surgery treatment according to their decision.

- Suitable patients for the 2 types of surgery: aortobifemoral bypass and endovascular approach with kissing covered stents.
- Patients must be properly informed and sign the informed consent in order to participate in the study.

7.2.2. EXCLUSION CRITERIA

- Patients who will not perform the follow up and monitoring at H. U. Dr. Josep Trueta.
- Allergy to any of the devices used in the interventions.
- Contraindication to aspirine or clopidogrel usage.
- Life expectancy <1 year.
- Previous surgery in the aortoiliac segment.
- Extensive common femoral artery disease or multiple groin incision
- Medical contraindications: Grade 3-4 COPD (GOLD scale); Grade 3-4 cardiac failure (NYHA scale); renal insufficiency grade 3-5.
- Anatomical Contraindications: disease affecting 2 cm of the abdominal aorta below the renal arteries; unsuitable femoral access due to excessive calcification of the arterial wall, aneurysm or arteriovenous fistula in the femoral artery.

7.3. SAMPLING

7.3.1. PACIENT SELECTION

Patients are selected at H. U. Dr. Josep Trueta. They must meet all the inclusion and

the exclusion criteria. A consecutive non-probabilistic sampling will be performed.

If the patient meets all the requirements, an informative document, where the study is explained, will be given. If the patient is interested to participate in the study, informed consent sheet must be signed.

7.3.2. SAMPLE SIZE

Accepting an alpha risk of 0.05 and a beta risk of 0.05 in a two-sided test, 13 subjects are necessary in first group and 13 in the second one in order to recognize as statistically significant a difference greater or equal than 15 units. The common standard deviation is assumed to be 10. It has been anticipated a drop-out rate of 10%.

We have assumed a standard deviation of 10 units according to previous data from aortobifemoral bypass and endovascular surgery with metallic stents. No data with endovascular approach with covered stents in 5 years term was available. For this reason the standard deviation will be reviewed after the first results and recalculated if it is necessary.

According to the vascular surgery service data at H. U. Dr. Josep Trueta, the number of patients who require surgical treatment for Leriche syndrome in our hospital per year is about 20. We have estimated 2 year period is needed to collect all patients.

Sample size has been calculated with GRANMO software.

7.4. VARIABLES

7.4.1. INDEPENDENT VARIABLE

The independent variable in this study is the performance of an endovascular

approach with kissing covered stents versus an aortobifemoral bypass for the treatment of Leriche syndrome. It is a nominal dichotomous qualitative variable.

7.4.2. DEPENDENT VARIABLE

The percentage of primary patency in the aortoiliac sector in a 5 years period after the surgery. Primary patency is defined as uninterrupted permeability in absence of restenosis or occlusion, without any further procedures performed on the vessel or stent. Quotient of speed will be measured by Doppler ultrasonography and associated with its related value of patency (see 2. : Introduction. Table 3).

It is a continuous quantitative variable.

7.4.3. SECONDARY VARIABLES

- **Mortality**

It is defined as the death of the patient in the first 30 days after surgery. It is a nominal dichotomous qualitative variable (YES/NO).

- **The need for reintervention**

The need for reintervention is determined by a change in a previously palpable pulse, recurrent symptoms, drop in the ABI >0.15, findings in the Doppler ultrasound indicating a >50% stenosis defined as >2 increase in the quotient of speed, or any combination of these findings.

It is a nominal dichotomous qualitative variable (YES/NO).

- **Secondary patency**

Secondary patency is defined as the percentage of permeability achieved by all

procedures that aimed reanalysing an occluded stent, thereby preserving the endograft. It will be measured as primary patency.

It is a continuous quantitative variable.

- **Conversion to open surgery**

It is defined by the need to perform an open repair surgery during the endovascular approach.

It is a nominal dichotomous qualitative variable (YES/NO).

- **Impaired renal function**

It is defined by a serum creatinine (Cr) rise of 0.5 mg/dL or greater after the procedure. Recovery of the renal function was based on serum Cr in mg/dL values measured at the discharge; renal function recovery is defined as "recovered" if the serum Cr levels return to baseline or serum Cr is <1.2 mg/dL.

It is a nominal dichotomous qualitative variable (YES/NO).

7.4.4. COVARIATES

- Lesion length (mm)

It is measured by CT-Angiography. It is a continuous quantitative variable.

7.5. DATA COLLECTION

FIRST VISIT

Patients come to the vascular surgery consult at H. U. Dr. Josep Trueta to be evalued

on the suspicion of Leriche syndrome.

A complete medical history will be made in order to collect patient's data needed. The physical examination will include:

- Ischemia assessment according to the scale of Fontaine.
- Ankle-brachial index (ABI).
- Abdominal Doppler ultrasound to assess the state of the aorta and the aortic bifurcation.

The vascular surgeon will indicate the need for surgical treatment.

On this visit, a CT angiography and the assessment by the anesthesiologist (PREOPERATIVE), will be scheduled. The preoperative will include a pulmonary and cardiac assessment and a general blood analysis with hematocrit, hemoglobin and creatinine values.

SECOND VISIT

The results of the CT angiography and the anesthesiology report will be reviewed. Once the patient has been identified as eligible to participate in the study by meeting all the criteria, the details of the study will be explained, the information sheet for participants will be given and all questions will be resolved. If the patient voluntarily agrees to participate in the study, informed consent must be signed.

At this time, the patient will be randomized for the type of surgery. The vascular surgeon will not know the result immediately to avoid selection bias.

HOSPITALIZATION

All patients will enter the vascular surgery service of H. U. Dr. Josep Trueta and should

fast 6 hours prior to surgery.

In case of open repair, patients should be admitted the day before the surgery in the morning. It will be administered a digestive cleaning enema as previous preparation to the surgery.

In case of endovascular surgery, patients should be admitted the same day of the surgery, in the morning. If the serum creatinine values in preoperative are > 1.5 mg/dl, they will be admitted the evening before surgery and will receive a regimen of 500 ml of normal saline solution every 8 hours and acetylcysteine 1200 mg every 12 hours as a surgical renal preparation.

SURGICAL INTERVENTION

During the surgery, an operating room nurse will record the operating time and the blood volume lost.

Moreover, in case of endovascular surgery, irradiation time and contrast volume administered will be registered.

POSTOPERATORY

In the immediate postoperative period all patients will be admitted into the intensive care unit for 2 hours in case of endovascular surgery and 48 hours in case of open repair, before returning to vascular surgery service. A blood analysis including at least hematocrit, hemoglobin and serum creatinine values will be done in the 24 hours postoperative period and before the discharge.

A daily medical evaluation will be conducted to determine the possibility of discharge.

All patients will receive antiplatelet therapy for life after the discharge: AAS in case of

open repair and dual antiplatelet therapy with AAS and clopidogrel in case of endovascular surgery.

FOLLOW UP

Controls will be made in the vascular surgery consult at H. U. Dr. Josep Trueta. Clinical evaluation and abdominal Doppler ultrasound with Philips Sparq ultrasound system will be done to assess the aortoiliac sector patency. A nurse will also record the ABI.

The first checks will be carried out one week, one month, six months and one year post-intervention. Since then, a check every 1 to 5 years post-intervention will be done.

SUMMARY

1ST VISIT	**-Diagnose and surgical treatment indication** **-CT scan and preoperative scheduling**
2ND VISIT	**-CT scan and preoperative results assessment** **-Eligibility, information sheet and informed consent** **-Randomization**
HOSPITALIZATION INTERVENTION POSTOPERATIVE	**-Kidney function assessment** **-Need for conversion to open repair** **-Mortality**
FOLOW UP	**-Patency rates** **-Need for reintervention** **-Mortality**

7.6. INTERVENTIONS

Interventions will be performed in a conventional operating room in case of aortobifemoral bypass. In case of endovascular approach a high quality fluoroscopy and a suitable mobile operating table for radiological work and long measure devices are needed. All patients will be monitored with continuous electrocardiographic control, blood pressure, oxygen saturation and pulse. Heparinization full dose is recommended during the procedure. Afterwards a protamine sulfate neutralization will be done. The interventions will be always performed by the same vascular surgeon.

7.6.1. AORTOBIFEMORAL BYPASS (OPEN REPAIR)

The procedure is done under general anesthesia. Endotracheal intubation is required.

A dose of 2 g of cefazolin ev. is administered as a prophylactic antibiotic. It is recommended to administer the antibiotic at the time of anesthesia induction in order to achieve a proper blood level at the time of the skin incision. Prophylaxis should last for 24-48 hours. Vancomycin, aztreonam and clindamycin are other alternatives if allergy to cephalosporines.

All these patients need radial artery cannulation. A central line and Swanz-Ganz catheter will be selectively placed in high-risk patients according to the preoperative study.

The surgical approach to the aorta can be performed in 2 ways:

- Transperitoneal approach through median laparotomy with xiphopubic incision. It will be the approach of choice because it allows a quick and easy

exposure of the surgical field.

- Retroperitoneal approach through an oblique incision from the tip of the last rib to the paramedian abdominal area immediately below the umbilical area. It is performed with the patient's torso rotated about 45 degrees to the right, keeping the hips and lower limbs as horizontally as possible. This approach is reserved for patients with hostile abdomen because of irradiation or previous midline laparotomy, intestinal adhesions, extreme obesity, inflammatory bowel disease, colostomy, ileostomy or ureterostomy.

The femoral approach will be performed by two longitudinal incisions on both inguinal folds. The lymphatic tissue must be respected to prevent postoperative lymphorrhea. Dissection of the femoral tripod will spread according to surgical planning based on previous imaging tests and palpation during surgery. Two separate tunnels are performed to pass the Dacron prosthesis inside the abdominal cavity by blunt dissection. By using the fingertips of both index fingers, sliding them across the upper outer surface of the femoral and iliac arteries we will prevent venous lesions. We must go as close as possible to the arterial wall and try to pass under the ureter to avoid its entrapment, which can generate postoperatively hydronephrosis. Prosthetic tunneling will be made avoiding twisting of the prosthesis. It is advisable to wash it with abundant serum to prevent clot formation inside.

The next step is a general heparinization and aortic clamping below the left renal vein.

The proximal anastomosis will be performed side to end, because it allows maintaining the flow of the permeable visceral arteries.

The distal anastomosis will be performed in the femoral tripod end to side (usually in

the deep femoral artery).

Finally, aortic clamp will be removed to check the blood flow and all the incisions will be closed in layers.

7.6.2. ENDOVASCULAR APPROACH WITH "KISSING" COVERED STENTS

It will be performed percutaneously. This procedure can be done under local anesthesia, but the epidural one is used in case of necessity to make an inguinal incision for the approaching of the common femoral artery (CFA).

Two covered stents are implanted bilaterally. Now the technique is described for each side:

First, the CFA is punctured retrogradely below the inguinal ligament with an Abocath® puncture system. The artery can be detected by touching or with an ultrasound system.

The next steps involve the placement of a "J" guide and a sheath to reach the lesion that will be identified then by arteriography.

To cross the lesion, a Terumo hydrophilic guide is placed under fluoroscopic control.

Once we have crossed the lesion, a ballon predilation is performed. At this time a new check is done by a new arteriography.

Then a Be Graft balloon-expandable covered stent is placed in each side and deployed simultaneously into the lesion (occasionally we need to place 3 stents if the lesion is very long). They will be overlapped with the typical shape of the "kissing". We must verify preoperatively the diameter of the aorta to be equal to or greater than the total diameter of the two stents used. The stent delivery catheters will be removed and a

new angiography will confirm their position.

Finally, a percutaneous closure system Exoseal ™ is introduced by specific device for haemostasis. This device emits a polymer that is placed on the puncture site in the arteria wall. The device is removed and a slight compression of the area is done.

If percutaneous approach is not possible (for example in case of obesity, severe subcutaneous tissue fibrosis ...) the approach will be performed by an inguinal incision and exposure of the femoral triangle. The closure of the artery wall will be made by using Prolene™ suture. Finally, the incision is closed in layers.

8. STATISTICAL ANALYSIS

UNIVARIATE ANALYSIS

Categorical data will be expressed as absolute numbers and percentages. Continuous data will be presented as mean and standard deviation or median (quartiles) depending on whether or not they are normally distributed.

BIVARIATE ANALYSIS

Differences between continuous data and type of surgery will be compared with Student's t test for independent data if data are normally distributed or with Mann-Whitney test for not normally distributed data. Normality will be checked using Kolmogorov-Smirnov test.

Categorical variables will be compared using Chi-square test or Fisher's test, as appropriate.

MULTIVARIATE ANALYSIS

To add the covariates to the statistical analysis for not disturb the main association we want to analyse (5 years term primary patency with each surgical technique), we will use a multiple linear regression.

Values of $P < 0.05$ will be considered significant. Statistical analysis will be performed with the "SPSS 19.0" software (Social Package for Statistical Sciences).

9. ETHICAL CONSIDERATIONS

- This clinical trial must have been approved by the "Comitè d'Ètica d'investigació Clínica" (CEIC) of Hospital Universitari Doctor Josep Trueta, de Girona in order to ensure the protection of the rights, safety and welfare of patients participating in the study.
- The basic ethical principles will be accomplished according to the recommendations contained in the Declaration of Helsinki and subsequent revisions: the Belmont Report, the Convention of Oviedo, ethical and methodological aspects of the Good Clinical Practice of the European Union, as well as other guidelines for the methodology of the WHO Research.
- To ensure the confidentiality of the information regarding the identity of the subjects involved in this trial, the "Ley Orgánica de Protección de Datos" 15/1999 must be accomplished.
- This clinical trial will follow the Royal Decree 1591/2009 of 16 October, which regulates medical devices and the Royal Decree 1616/2009 of 26 October, which regulates the active implantable medical devices.
- The safety and feasibility of the two surgical techniques that belong to this clinical trial have been proved in several studies.
- Patients who want to participate in this study must be informed and understand the procedures. Also they have to sign the consent form file.

10. STUDY LIMITATIONS

- This clinical trial can't be blinded because the vascular surgeon must know the type of intervention to carry on it. Also the patient will know that because of the kind of incisions or punctures performed on it.
- No randomized controlled trials have been published on open repair versus endovascular approach in Leriche syndrome or aortoiliac extensive disease.
- Most of the studies regarding surgical treatment of extensive aortoiliac obstructive disease include not only Leriche syndrome but patients with several different lesions. For these two last reasons, exact model information couldn't be treated. However, this was an encouraging situation to carry on this study.
- The results may not be extrapolated to other populations mainly because one of the key points in this study is the surgeon's experience. Regarding to this, the surgeon who will perform all the interventions is familiarized with both surgical approaches.
- To carry out this study, the sample size was calculated only for the primary objective, so it is possible not to achieve feasible conclusions for the secondary objectives.
- This study will be conducted with a small sample size. This implies that the results may not be statistically significant and would need further validation with studies with a larger sample.
- The sample size was calculated according the previous data from open repair and endovascular surgery with metallic stents. No data with endovascular

approach with covered stents in 5 years term was available. We have assumed a standard deviation of 10 units to collect the values of primary patency. For this reason the standard deviation should be reviewed after the first results and recalculated if it is necessary.

11. WORK PLAN

Investigators: Rodrigo Fernández González, Dra. Patricia Rodríguez Cabeza.

Collaborators: Vascular surgeons, anaesthetists and nurse staff of H. U. Dr. Josep Trueta of Girona, statisticians.

1. **Bibliography research and protocol development (2 months)**

   Conducted by the investigators.

   We will make the study protocol and errors will be corrected. For its approval it will be submitted to CEIC review.

2. **Coordination phase (1 month)**

   Conducted by the investigators and collaborators (except the statisticians).

   We will define the schedule and the role of each of the researchers and collaborators in each phase of the study. Vascular surgeons must know in detail the protocol in order to perform a correct patient selection and data collection. All the information will be shared with the anaesthetists and nurses.

   A meeting every six months to clarify possible doubts will take place. If there is any change in the collaborators during the study, the new one will be informed in detail for the correct conduct of the study.

3. **Patients selection and interventions (24 months)**

   Conducted by the investigators and the vascular surgeons.

Patients will be assessed for suspected Leriche syndrome in vascular surgery outpatient consults at H. U. Dr. Josep Trueta.

Once the necessary data is collected, researchers and collaborators will verify that all patients met the criteria for the participation in the study.

Interventions will always be held on the same vascular surgeon and the nursing staff.

4. Data collection and processing database (7 years)

Conducted by the investigators, vascular surgeons and nursing staff.

The vascular surgeon who will perform the interventions will record the incidents that happened during it.

Vascular surgeons will review the patients daily until discharge.

The nursing staff will perform the necessary tests to collect all the data needed to cover all the objectives of the study.

After the discharge, patients will attend vascular surgeon outpatient consults at H. U. Dr. Josep Trueta for an appropriate follow-up up to 5 years post-intervention.

At the same time, the data will be recorded in the database and reviewed by researchers.

5. Data analysis (3 months)

Conducted by the investigators and the statistician.

All data collected will be analysed by a professional statistician.

6. Interpretation and conclusions (4 months)

Conducted by the investigators.

A final report with the evaluation and interpretation of al outcomes will be drafted.

7. Dissemination plan (3 months)

The results will be written and edited aiming to publish them in different journals and congresses.

The chronogram is available in the ANNEX 6.

12. FEASIBILITY

12.1. RESEARCH TEAM

We need vascular surgeons and nursery staff trained in both surgical techniques of the study. Our main vascular surgeon who will perform all the interventions has been performing these surgeries during the last fifteen years. Al the vascular surgeons of the department are responsible of the patient's follow up with ultrasound monitoring. This technique is submitted to an operator-dependent variability, though.

IdIBGi will provide a statistician to carry out the data analysis.

12.2. AVAILABLE MEANS

For diagnosing and patient's follow up we need blood pressure cuffs, a CT scan and a Doppler ultrasound scan.

For the interventions we need surgical devices, Be Graft covered stents, bifurcated prosthesis. A fluoroscopy and an adapted table for endovascular surgery will bw needed.

All of these means are available in our hospital.

12.3. PATIENTS

In our hospital, about 20 patients need surgical treatment for Leriche syndrome every year. We assume that not all the patients will meet all the criteria to participate in the

study. We expect to collect our sample size (26 patients) in 2 years. If it is not possible, this period should be enlarged.

13. BUDGET

All the research team is employed by the institution. For these reason their services are not included in the budget.

In case of an open repair with the implantation of an aortobifemoral bypass we need:

- 1 bifurcated prosthesis of Dacron: 800€/unit.
- Surgical devices: 200€/unit.

In case of an endovascular approach with kissing covered stents we need:

- Covered stents of Be Graft. According with their length measures there are 3 types of stents: 15cm (3000€/unit), 10cm (2500€/unit) and 5cm (1700€/unit). Two stents every intervention (3 stents occasionally) are needed. We can assume a medium cost of 5000€ for each intervention.
- Perishable devices: 1000€/unit.
- 2 percutaneous close system Exoseal™: 250€/unit (500€/intervention).

We also have to take into account the medium stay in the different hospital departments:

- Intensive care unit: 50€/hour. Two hours in case of endovascular (100€/intervention) and 48 hours in case of open repair (2400€/intervention).
- Vascular surgery service: 300€/day. We assume 2 days for endovascular (600€) and 7 days for open repair (2100€) including the admission prior to the surgery and the postoperative period.

The cost of this study is showed in the following table for 26 patients (13 for each intervention).

	CONCEPT	AMOUNT	COST
SURGICAL MATERIAL	Bifurcated prosthesis of Dacron (units)	13	10.400€
	Surgical devices (units)	13	2.600€
	Be Graft stents (interventions)	13	65.000
	Perishable devices (units)	13	13.000€
	Perclose Exoseal™ system (units)	26	6.500€
STAY AT HOSPITAL	Intensive care unit (hours)	650	32.500€
	Vascular surgery service (days)	117	35.100€
		TOTAL COST	165.100€

14. PROJECT IMPACT AND APLICABILITY

The aim of this study is to achieve more information about what is the currently role of the covered stents in the treatment algorithm of Leriche syndrome.

There are only a few studies comparing some of the available techniques for the surgical treatment of this particular patology and more relevant features to improve evidence are needed.

Leriche syndrome is the most challenging aortoiliac occlusive disease to solve with endovascular surgery.

If the results of this study are favourable to our aim, on the one hand, we will add more evidence to confirm that endovascular surgery may be a great and safe alternative for the treatment of all the variety of aortoiliac occlusive injuries.

On the other hand, patients with Leriche syndrome need a lot of health-cares because of the chronic condition of this disease. Endovascular surgery may lead more patients to be treated because of its low amount of contraindications and complications compared with the currently gold-standard techniques.

Al of these conditions should be taken account by the National Health Care System. Then, more studies about cost-efficacy will be needed. But first, we have to verify the patient's benefit.

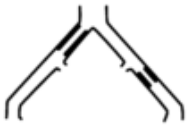
15. ANEXES

15.1. CLASIFICATIONS

TRANSATLANTIC INTER-SOCIETY CONSENSUS II (TASC II)

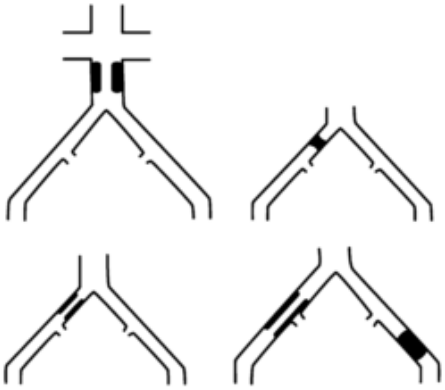
Type A lesions

- Unilateral or bilateral stenoses of CIA
- Unilateral or bilateral single short (≤3 cm) stenosis of EIA



Type B lesions:

- Short (≤3cm) stenosis of infrarenal aorta
- Unilateral CIA occlusion
- Single or multiple stenosis totaling 3–10 cm involving the EIA not extending into the CFA
- Unilateral EIA occlusion not involving the origins of internal iliac or CFA



Type C lesions

- Bilateral CIA occlusions
- Bilateral EIA stenoses 3–10 cm long not extending into the CFA
- Unilateral EIA stenosis extending into the CFA
- Unilateral EIA occlusion that involves the origins of internal iliac and/or CFA
- Heavily calcified unilateral EIA occlusion with or without involvement of origins of internal iliac and/or CFA

Type D lesions

- Infra-renal aortoiliac occlusion
- Diffuse disease involving the aorta and both iliac arteries requiring treatment
- Diffuse multiple stenoses involving the unilateral CIA, EIA, and CFA
- Unilateral occlusions of both CIA and EIA
- Bilateral occlusions of EIA
- Iliac stenoses in patients with AAA requiring treatment and not amenable to endograft placement or other lesions requiring open aortic or iliac surgery

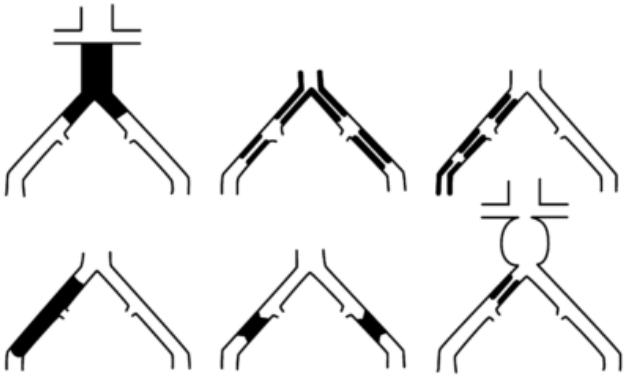


Fig. F1. TASC classification of aorto-iliac lesions. CIA – common iliac artery; EIA – external iliac artery; CFA – common femoral artery; AAA – abdominal aortic aneurysm.

ANATOMICAL LOCATION OF THE ATHEROSCLEROTIC INJURIES

TABLE 1. Classification System of Aortoiliac Occlusive Disease—Based on Anatomical Location of the Lesions

Class	Vessels of involvement
Type I	Infrarenal abdominal aorta and common iliac arteries.
Type II	Infrarenal abdominal aorta, common iliac arteries, external iliac arteries and femoral (common femoral) bifurcation.
Type III	Infrarenal abdominal aorta, common iliac arteries, external iliac arteries, femoral (common femoral) bifurcation, popliteal, or tibial arteries.

Reference: Reddy and Shepard (2006).

SOCIETY OF CARDIOVASCULAR AND INTERVETIONAL RADIOLOGY (SCVIR)

SCVIR
type 1 Short segment (<2 cm) stenoses of the infrarenal aorta, with minimal atherosclerosis of the aorta otherwise. Iliac stenoses less than 3 cm in length that are concentric and noncalcified.
type 2 2-4 cm stenoses of the infrarenal aorta, with mild atherosclerosis of the aorta otherwise Iliac stenoses 3-5 cm in length or calcified or eccentric stenoses less than 3 cm in length
type 3 Long segment (>4 cm) stenoses of the infrarenal aorta Aortic stenosis with atheroembolic disease Medium length (2-4) stenoses of the infrarenal aorta, with moderate to severe atherosclerosis of the aorta otherwise Iliac stenoses 5-10 cm in length
type 4 Iliac stenoses greater than 10 cm in length Chronic iliac occlusions greater than 4 cm in length after thrombolytic therapy Extensive bilateral aortoiliac atherosclerotic disease Aortic or iliac stenoses in patients with AAA or other lesions requiring aortic or iliac surgery

15.2. DATA OF PATENCY RATES

AORTOBIFEMORAL BYPASS LONG TERM PATENCY RATES

Table F4. Patency at 5 and 10 years after aortobifemoral bypass[191]

Indication	5-year % patency (range)		10-year % patency (range)	
	Claudication	CLI	Claudication	CLI
Limb based	91 (90–94)	87 (80–88)	86 (85–92)	81 (78–83)
Patient based	85 (85–89)	80 (72–82)	79 (70–85)	72 (61–76)

CLI – critical limb ischemia.

Eur J Vasc Endovasc Surg Vol 33, Supplement 1, 2007

SHORT AND LONG TERM PATENCY RATES WITH METAL STENTS (JONGKIND ET AL)

Table IV. Primary and secondary patency rates

		1 year		*2 year*		*3 year*		*4 year*		*5 year*	
First author	*Year*	*PP (%)*	*SP (%)*	*PP (%)*	*SP (%)*	*PP (%)*	*SP (%)*	*PP (%)*	*SP (%)*	*PP (%)*	*SP (%)*
Nyman	2000	97	100[a]								
Scheinert	2001	84	88	81	88	78	86	76	85	66	80
Ali	2003			84	95[b]						
Greiner	2003		91[a]		65[a]						
Rzucidlo	2003	70	88								
Domanin	2005	70	88								
Lagana	2006	89	100								
Ballzer	2006					90	96				
De Roeck	2006	94	100	89	94	89	94	77	94	77	94
Park	2007	C 94	C 97			C 94	C 97[a]			C 78	C 74[a]
		D 93	D 94			D 74	D 85[a]			D 74	D 85[a]
Piffaretti	2007	92		86						81	
Bjorses	2008	97	100	88	97	83	95	74	91	65	83
Chang	2008									60	98
Gandini	2008	95	97	93	96	91	94	88	93	86	90
Hans	2008							69	89		
Sixt	2008	C 86	C 98								
		D 85	D 98								
Sharafuddin	2008							81	94[a]		
Kashyap	2008	90	97	82	97	74	95				
Moise	2009	85	100			66	90				

C, Results for patients with TASC type C lesions; *D*, results for patients with TASC type D lesions; *PP*, primary patency; *SP*, secondary patency.
[a]primary assisted patency.
[b]limb salvage rate.

SHORT TERM PRIMARY PATENCY RATES WITH METAL AND COVERED STENTS (SABRI ET AL)

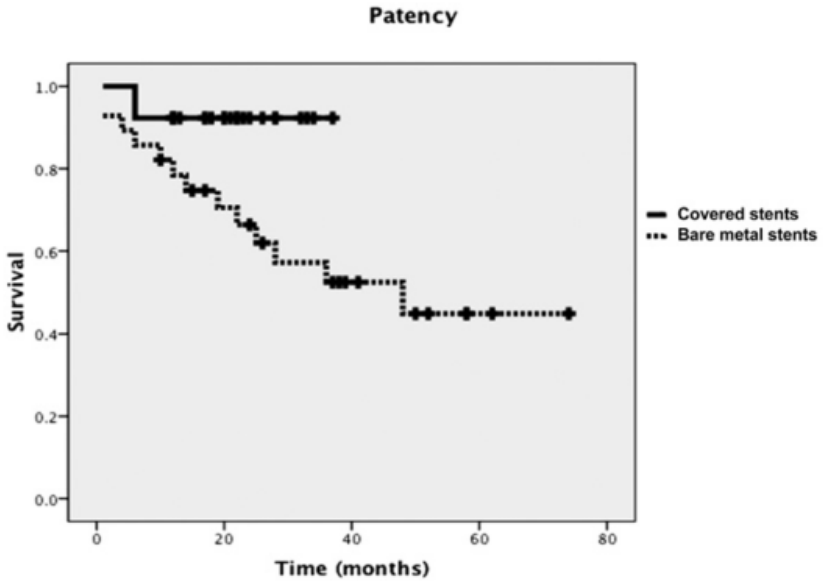
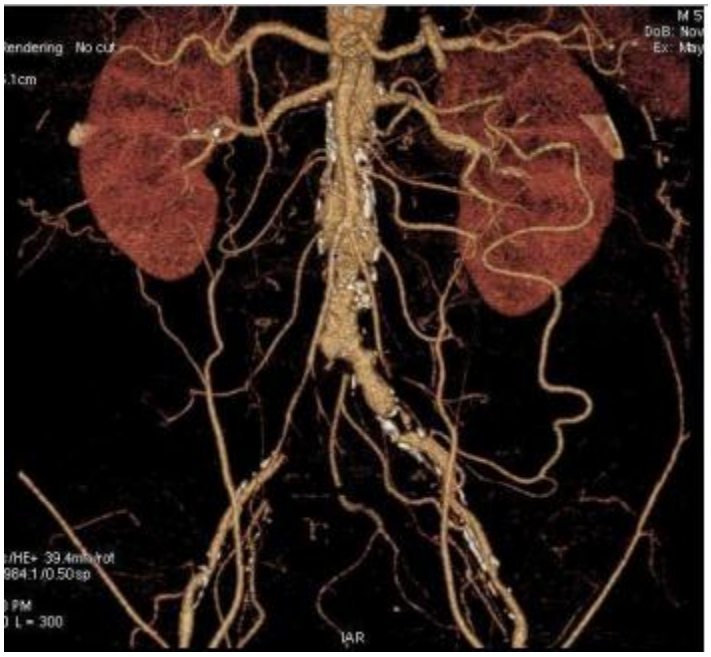


Figure 3. Kaplan Meier survival curve shows improved patency of the covered stents versus the bare metal stents at 1 and 2 years (92 and 92% vs 84 and 72%, respectively).

15.3. DIAGNOSE IMAGING

3D CT-ANGIOGRAPHY[2]

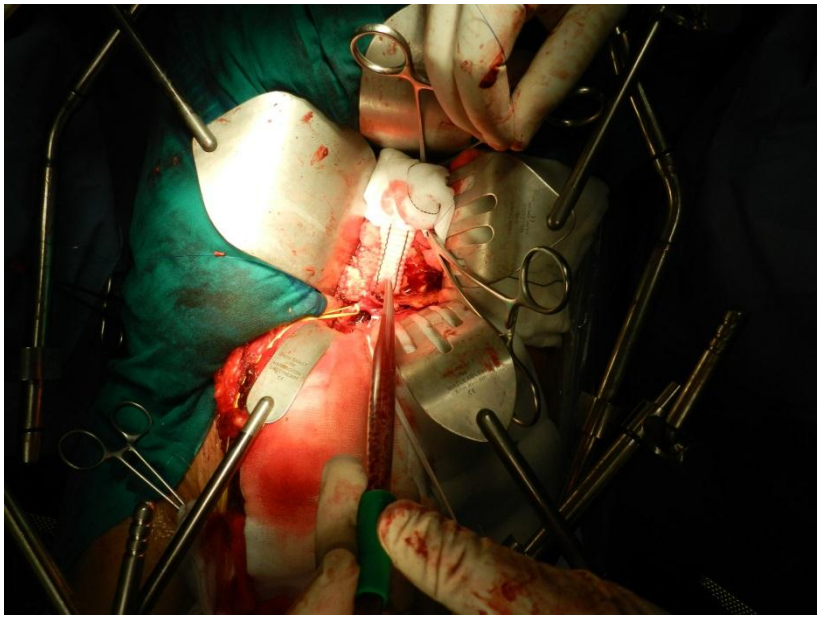


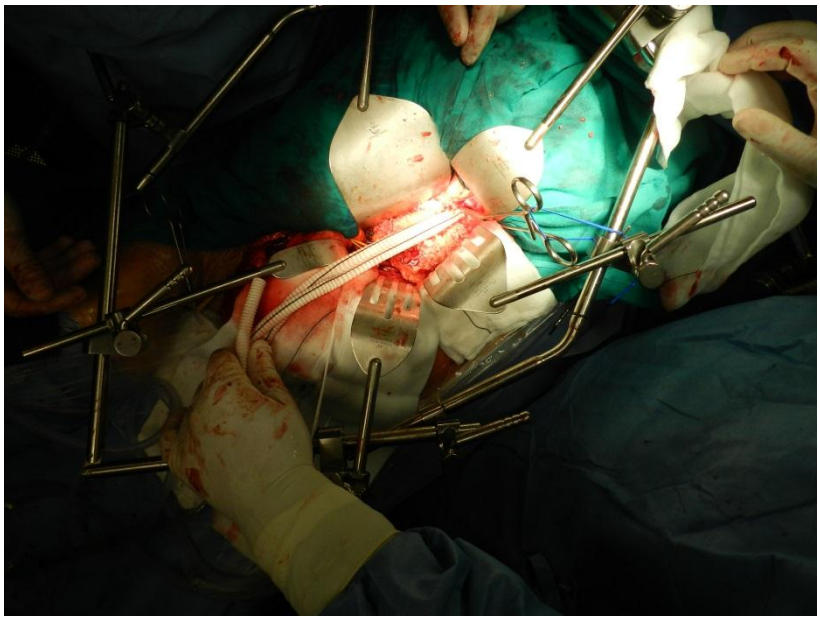
http://eurorad.org/eurorad/case.php?id=11084

[2] Atheromatous disease of the infrarenal aorta, occlusion of the right common iliac artery and tight stenosis of the left common iliac artery. Is not exactly a Leriche syndrome but this image leads us to notice about the CT-Angiography results.

15.4. IMAGES OF INTERVENTIONS

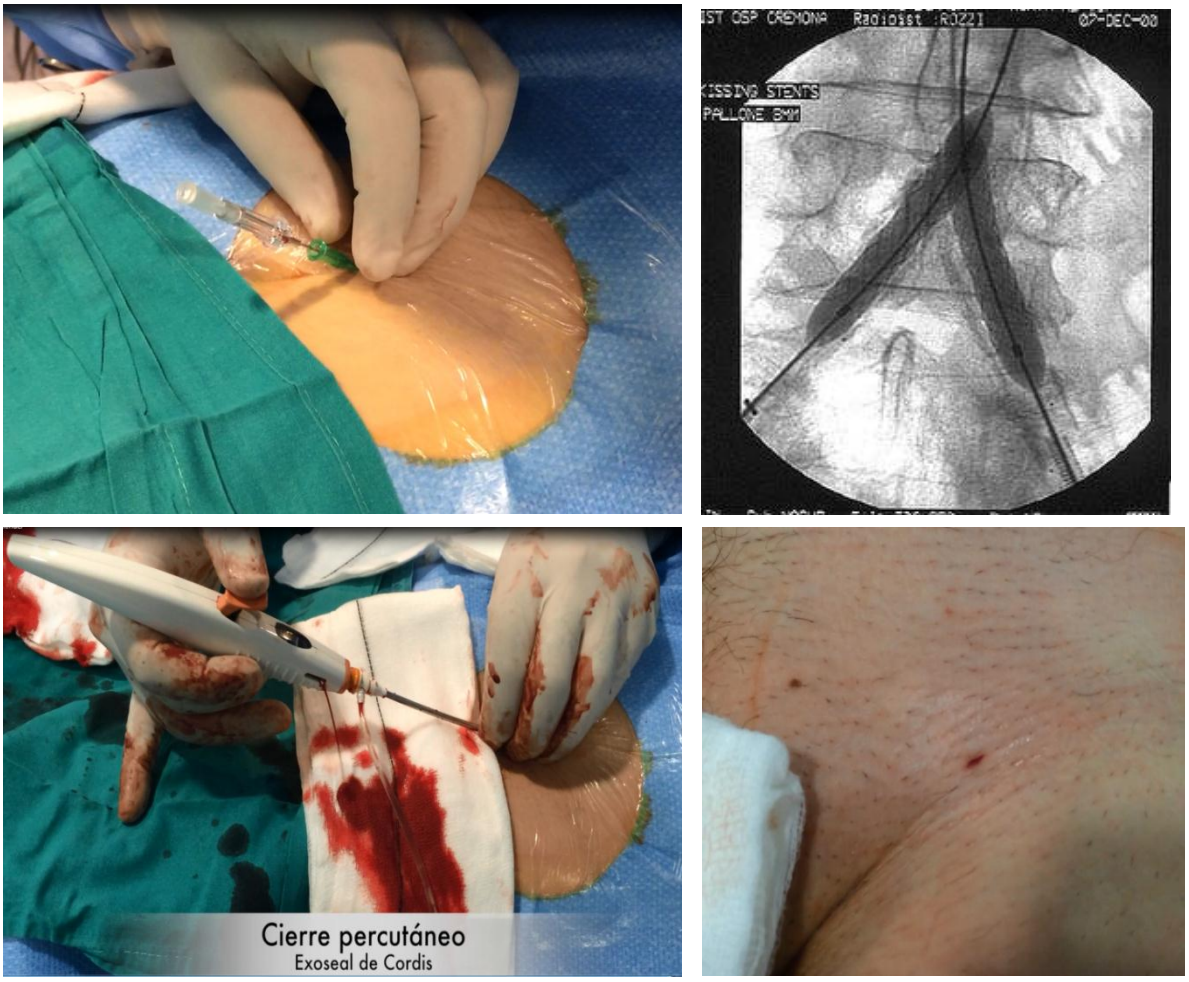
AORTOBIFEMORAL BYPASS





H. U. Dr. Josep Trueta operating room

ENDOVASCULAR APPROAC WITH "KISSING" COVERED STENTS



H. U. Dr. Josep Trueta operating room

http://www.radiologiacremona.it/casi_angio/caso

15.5. INFORMATION SHEET FOR PARTICIPANTS

HOJA DE INFORMACIÓN AL PACIENTE

INTRODUCCIÓN

Usted padece síndrome de Leriche, una enfermedad obstructiva arterial severa del sector aortoilíaco. Diversos estudios han demostrado la seguridad y fiabilidad del bypass aortobifemoral y de la cirugía endovascular con stents cubiertos como tratamiento de revascularización de esta patología. Ambas técnicas compiten actualmente por ser la técnica de elección en el tratamiento quirúrgico de la enfermedad que usted padece, pero son necesarios estudios comparativos entre ambas para determinar cuál de las dos es la más apropiada en cada caso.

OBJETIVO

Comparar la permeabilidad primaria del sector aortoilíaco en un periodo de 5 años tras cirugía endovascular con stents cubiertos vs. bypass aortobifemoral, en pacientes con síndrome de Leriche en el Hospital Universitari Dr. Josep Trueta de Girona.

PROCEDIMIENTO

Si acepta participar en el estudio, se le asignará aleatoriamente una de las dos técnicas quirúrgicas como tratamiento para su patología.

Además, se le realizará un seguimiento clínico y ecográfico en 1 semana, 1 mes, 6 meses, 1 año y anualmente hasta 5 años después de la intervención.

POSIBLES BENEFICIOS

Se espera que comparando los resultados de permeabilidad primaria de las dos técnicas quirúrgicas, se pueda definir con mayor precisión el papel de la cirugía endovascular con stents cubiertos en el tratamiento del síndrome de Leriche.

PARTICIPACIÓN VOLUNTARIA

Su participación en el estudio es totalmente libre y voluntaria. Usted puede no aceptar participar en el mismo. Además, debe saber que usted puede abandonar el estudio en cualquier momento sin necesidad de dar ninguna explicación. Ninguna de estas circunstancias va a influir sobre los cuidados que usted reciba en el futuro.

CONFIDENCIALIDAD

El acceso a sus datos clínicos se realizará guardando la más estricta confidencialidad, de forma que no se viole su intimidad ni la de los demás participantes en el estudio. Sus datos clínicos estarán a disposición de los monitores del estudio y se incluirán (junto con los de los otros pacientes que participen en el mismo) en las publicaciones derivadas del estudio, pero de forma anónima, de manera que su nombre e identidad se mantendrán siempre en secreto. Durante la realización del estudio se le garantiza el estricto cumplimiento de la Ley 15/1999, del 13 de Diciembre de Protección de Datos Personales.

INVESTIGADORES PRINCIPALES

Rodrigo Fernández González. Estudiante 6º curso de medicina. Universitat de Girona.

Dra. Patricia Rodríguez Cabeza. Servicio de Angiología y Cirugía Vascular. Planta 4ªB H. U. Dr. Josep Trueta de Girona.

15.6. INFORMED CONSENT FORM

CONSENTIMIENTO INFORMADO

Título del estudio: **"KISSING COVERED STENTING VS. AORTOBIFEMORAL BYPASS IN PATIENTS WITH LERICHE SYNDROME"**

Declaro bajo mi responsabilidad que yo,

……..

- He leído la hoja de información que se me ha entregado.
- He podido preguntar acerca del estudio todas las dudas que he tenido.
- Comprendo que mi participación es voluntaria y que puedo retirarme del estudio cuando quiera sin tener que dar explicaciones y sin que ello repercuta en mis cuidados médicos.
- Consiento en que el monitor del estudio tenga acceso a mis datos médicos que serán absolutamente confidenciales y que podrán ser incluidos, de forma anónima, en las publicaciones que deriven del estudio.
- Presto libremente mi conformidad para participar en el estudio.

Girona,…….. de ……. Del 20…….

Firma del paciente Firma y nombre del investigador

15.7. PARTICIPANT DATA SHEET

HOJA DE DATOS DEL PACIENTE

NOMBRE: _____ **APELLIDOS:** _____

EDAD: _____ **SEXO:** _____

RAZA: _____ **FECHA DE INTERVENCIÓN:** _____

FACTORES DE RIESGO:

Tabaquismo ☐ HTA (en tratamiento médico) ☐

DM ☐ Dislipemia ☐

Arteriopatía periférica ☐ Insuficiencia Renal ☐

Hiperhomocisteinemia ☐ Otros _____

ENFERMEDADES RELEVANTES:

ALERGIAS:

MEDICACIÓN PREVIA:

Antiagregantes ☐ Otra: _____

Anticoagulantes ☐

DATOS PREOPERATORIOS

CLÍNICA (grado de isquemia según clasificación de Fontaine):

Grado I ☐ Grado IIb ☐ Grado IV ☐

Grado IIa ☐ Grado III ☐

EXPLORACIÓN FÍSICA:

ITB: _____ **ECO-DOPPLER ABDOMINAL** (cociente de velocidad): _____

ANGIO-TC:

Longitud de la lesión (cm) _____

Longitud segmento sano infrarrenal (mm) _____

Diámetro aorta abdominal (mm) _____

ANALÍTICA:

Creatinina (mg/dl) _____

Hemoglobina (mg/dl) _____

Hematocrito (%) _____

DATOS INTRAOPERATORIOS

Tipo de intervención: **Bypass aortobifemoral** ☐ **Endovascular "kissing"** ☐

Tiempo quirúrgico (min) _____

Tiempo de fluoroscopia (seg) _____

Cantidad de contraste (cc) _____

Stents utilizados _____

Otras complicaciones _____

Conversión a cirugía abierta ☐

DATOS POSTOPERATORIOS

ANALÍTICA:	**24h**	**Alta**
Creatinina	_____	_____
Hemoglobina	_____	_____
Hematocrito	_____	_____

Estancia en unidad de rehabilitación (horas) _____

Estancia en servicio de cirugía vascular (días) _____

SEGUIMIENTO

EXPLORACIÓN FÍSICA:

	1 SEM	1 MES	6 MES	1 AÑO	2 AÑO	3AÑO	4 AÑO	5 AÑO
PULSOS								
COLORACIÓN								
Tª								

NECESIDAD DE REINTERVENCIÓN* ☐ **Fecha:** _____

	1 SEM	1 MES	6 MES	1 AÑO	2 AÑO	3 AÑO	4 AÑO	5 AÑO
Permeabilidad 1ª								
Permeabilidad 2ª								
ITB								
Grado de Fontaine								

***en caso de reintervención, se rellenará la fila de permeabilidad 2ª y se dejará de rellenar la fila de permeabilidad 1ª, a partir de la fecha de la misma.

15.8. CHRONOGRAM

STARTING MONTH ENDING MONTH	Sep 2015 Nov 2015	Dec 2015 Dec 2015	Jan 2016 Dec 2017	Jan 2018 Dec 2022	Jan 2022 Mar 2022	Apr 2022 Apr 2022	May 2022 Jul 2022	RESPONSIBLES
1.Biliography research & protocol developement								Investigators
2.Coordination phase								Investigators, vascular surgeons, nursing staff, anaesthetists
3.Patients´selection								Investigators, vascular surgeons
4.Data collection & processing database								Investigators, vascular surgeons, nursing staff
5.Data analysis								Investigators, statistician
6.Interpretation and conclusions								Investigators
7.Dissemnation plan								Investigators