Study of the GORE® EXCLUDER® Endoprosthesis in the treatment Of infra-renal Abdominal Aortic Aneurysms

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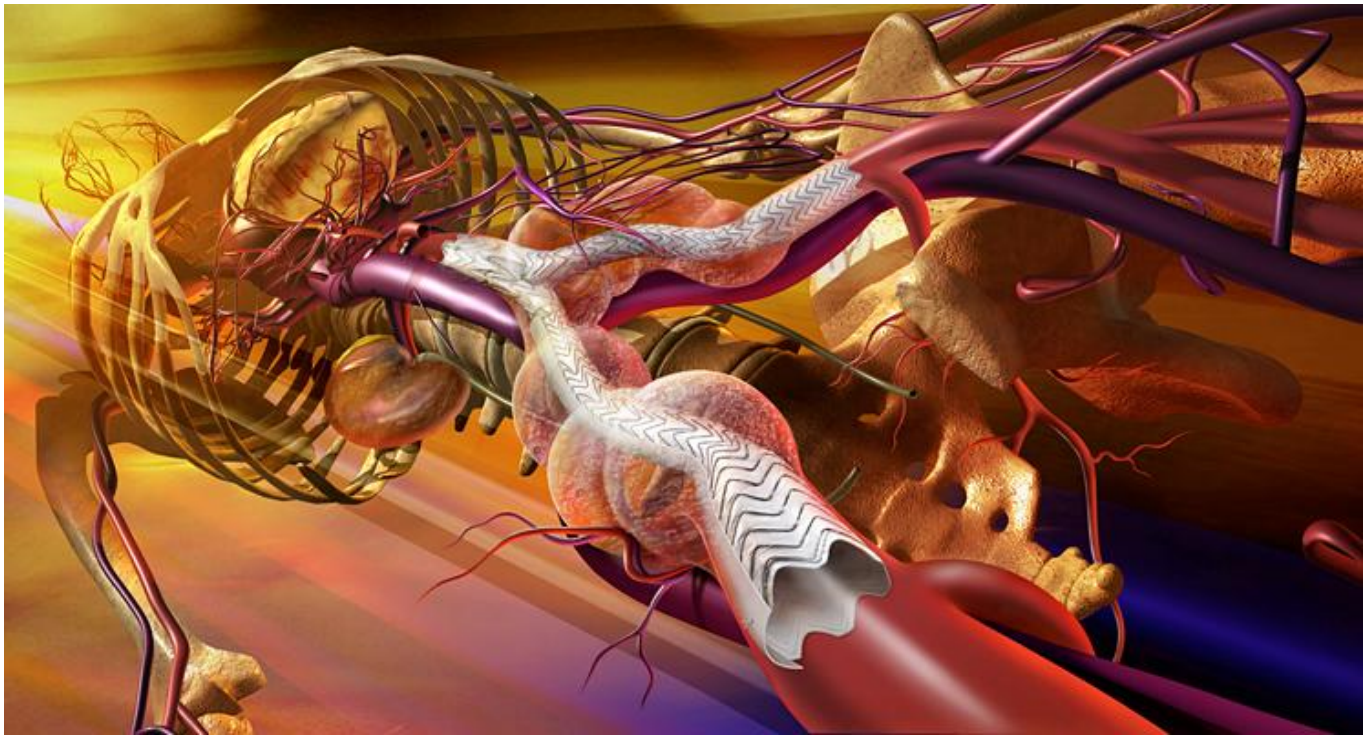
NCT number: NCT02308839

W. L. Gore & Associates, Inc.
Medical Products Division

GORE® EXCLUDER® AAA France Register



Study of the GORE® EXCLUDER® Endoprosthesis in the treatment of infra-renal Abdominal Aortic Aneurysms

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Observational, Prospective, Multicenter Study

Investigator Coordinator:

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CONTACTS & LIST OF INVESTIGATING CENTERS

List and details of the implant centers

SUMMARY OF THE STUDY

Study title :

Study of the GORE® EXCLUDER® Endoprosthesis in the treatment of infra-renal Abdominal Aortic Aneurysms

Introduction :

The treatment of Infra-renal Abdominal Aortic Aneurysms can be effected by abdominal aortic stenting introduced via the femoral artery. This technique is widely used in high surgical risk patients, but may also be recommended for normal surgical risk patients under certain conditions. Given the information available, the French National Authority for Health requires a 5-year follow-up as part of the renewal of reimbursement for these endoprostheses.

Rationale:

The use of abdominal aortic endoprostheses makes the treatment of Infra-renal Abdominal Aortic Aneurysms possible, with implantation via the femoral artery, thus avoiding a very invasive surgical procedure.
However, we lack data on the future of these endoprostheses in the long term.
For this reason, an observational long-term (5 years) study has been put in place.

Objective:

The objective of this study is to assess the usefulness of the technique by documenting overall mortality, complications (endoleak, migration), the rate of surgical conversion, the evolution and rupture of the aneurysm, in the long term, that is, 5 years, on a cohort of patients representative of the population treated in real life conditions.

Judgment criteria:

These criteria are measured postoperatively or within one month after surgery, at 6 months, 12 months and then annually for 5 years, with an annual report issued to be submitted to the French National Authority for Health:

- Overall mortality rate,
- Mortality rate related to the aneurysm,
- Evolution of the diameter of the aneurysm
- Rate of type I, II and III endoleaks,
- Migration rate,
- Rate of surgical conversion,
- Rate of endovascular or surgical re-intervention.

Methodology, type of study:

Observational, Prospective, Multicenter Study

Study Device:

The device concerned in the study is the GORE® EXCLUDER® Endoprosthesis, and any evolution of the range included in the LPP.

Inclusion Criteria:

Any patient requiring abdominal aortic stenting for the treatment unruptured Infra-renal Aortic Abdominal Aneurysm.

Non-inclusion Criteria

Patients whose clinical follow-up is not possible, i.e., patients who cannot return for control visits (e.g. patients living abroad).
A register to document each patient not included in the cohort will be established.

Conduct of the Study:

Following the same schedule as that of patient routine follow-up, that is, with a postoperative follow-up or within one month after surgery, at 6 months, 12 months and then annually, for 5 years.

	Post-operative follow-up (D1 to D30)	**Follow-up at 6 months.**	**Follow-up at 1, 2, 3, 4 and 5 years**	**Follow-up intermediate *****
Clinical examination	**X**	**X**	**X**	**X**
Radiography of the abdomen without preparation in 3 effects (front, profile and ¾)	**X**[1]	X*	X*	X*
CT with contrast medium	**X**	**X**	**X**	**X**
MRI	X*	X*	X*	X*
Vascular Doppler	X**	X**	X**	X**

* if CT with contrast medium cannot be performed

** if RMI cannot be performed

*** interim follow-up carried out only in case of leakage, deterioration of the endoprosthesis or scalability of the aneurysm on the previous control examination. Follow-up to be carried out 3 months after the control where the anomaly was observed.

[1] Radiography in postoperative follow-up will not be necessary in case of 3D reconstruction performed during the CT.

Expected Benefits:

The expected benefit of this Study is to have a long-term evaluation of Abdominal Aortic GORE® EXCLUDER® Endoprosthesis, thus making it possible to assess the long term usefulness of the technique with this endoprosthesis.

[redacted]

Known Risks:

The protocol does not affect patient management, so there is no risk posed by the research.

Duration of the inclusion period:

Inclusion period of 180 patients: 12 months

Duration of participation of each patient:

The requirement of the French National Authority for Health is long-term patient follow-up, that is, 5 years. In this context, there is no maximum follow-up duration for this study.

Total duration of the Research:

In this context, there is no maximum follow-up duration for this Study (12 months inclusion period and a minimum of 5 years of follow up).

[redacted]

1 SCIENTIFIC JUSTIFICATION AND GENERAL DESCRIPTION OF THE RESEARCH

1.1 Rationale [1]

1.1.1 General Description of the Disease and of its Management

Definition

There is no unambiguous definition of an Abdominal Aortic Aneurysm (AAA). For Johnston *et al.*[2], AAA is a localized and permanent dilation of the aorta of more than 50% compared to the normal expected diameter, with a loss of parallelism of its edges, bag-shaped (saccular aneurysm) or spindle (fusiform aneurysm). This definition helps to differentiate an AAA from an "Arteriomegaly" (diffuse enlargement affecting several arterial territories with a diameter exceeding 50% of the expected arterial diameter). The normal diameter of the aorta is fundamental data. It depends on age and sex.
Other definitions have been used in the literature. For Cronenwett *et al.*[3], an Infra-renal Abdominal Aortic Aneurysm is an enlargement of its transverse or anteroposterior diameter by more than one and a half times that of the interrenal aorta. Collin *et al.*[4] proposed the following definition: "An abdominal aortic aneurysm is present when the maximum external diameter of the infrarenal abdominal aorta is either (1) greater than 4.0 cm or (2) exceeds the maximum diameter of the aorta between the origin of the superior mesenteric and left renal arteries by at least 0.5 cm."

The risk of progression of AAA has been studied mainly in relation to its maximum outside diameter, a value commonly used to determine the rate of growth, the risk of rupture of an AAA, and to define the surgical indications.

Similarly, descriptions of "small," "medium" or "large" are based on commonly accepted figures[5]:

- A 'small' AAA has a diameter smaller than 5 cm.
- An 'average' AAA has a diameter between 5 and 7 cm.
- A 'large' AAA has a diameter of more than 7 cm.

Severity[1]

The progressive growth of an AAA is inevitable, but the pace of this growth is difficult to predict in a given patient. Thanks to diagnosis and monitoring methods, surgery is increasingly programmed at an early stage[6,7]. This helps prevent rupture which is a progressive form evaluated at 7 per 100,000. This is a common cause of death in patients with Abdominal Aortic Aneurysm.

1.1.2 Treatment

There are two types of treatments:

- **Endovascular treatment with stenting.** The principle of endovascular treatment of AAA is based on the exclusion of the aneurysm with an endoprosthesis inserted via the femoral artery and attached to the artery walls upstream and downstream.
The theoretical advantages of this alternative to conventional therapy are the absence of laparotomy, aortic clamping and reduced blood loss. This technique is less invasive than conventional surgery[8]. This technique is accompanied by the need for a significant number of additional procedures. Initially, uncertainties existed on the durability of implants and evolution of the AAA towards rupture even though aortic endoprosthesis implantation is still possible[8]. However, the publication of long term results of the EVAR1[9] and 2[10] Studies in 2010 as well as the DREAM Study[11], dispelling these uncertainties to a large extent by providing long term results.

- **Surgery by flattening transplant** with opening of the aneurysm sac and implantation of a synthetic or bifurcated tube, whose perioperative mortality is currently less than 5% in the majority of unruptured AAA series[12,13]. Mortality increases significantly, up 15%, in high surgical risk patients. This surgery may be combined with treatment of associated lesions of visceral arteries.
The treatment of Abdominal Aortic Aneurysms by laparoscopic surgery is a new technique currently being evaluated.

1.1.3 Requirements of the French National Authority for Health

The opinion of the National Commission for the Evaluation of Medical Devices and Health Technologies (CNEDiMTS) of July 13, 2010 (Appendix 1) indicates that:

Terms of renewal:

> CNEDiMTS subjects the renewal of registration of each endoprosthesis to the presentation of results of a specific follow-up study implemented on a cohort of patients representative of the population treated in real life conditions.
> The objective of each study is to evaluate the usefulness of the technique by documenting overall mortality, complications (endoleak, migration), the rate of surgical conversion, evolution and rupture of the aneurysm, in the long term, that is, beyond 5 years.
> This prospective cohort study shall involve at least 150 patients implanted after registration on the LPPR [List of Reimbursable Products and Services].
> The results of the follow-up study shall be forwarded to CNEDiMTS once a year, for consideration.
> The follow-up evaluation may lead CNEDiMTS to recommend that reimbursement for the abdominal aortic endoprosthesis concerned be maintained or suppressed.

1.1.4 Description of the GORE® EXCLUDER® Endoprosthesis

The device concerned in the study is the GORE® EXCLUDER® Endoprosthesis, and any evolution of the range included in the LPP.

The GORE® EXCLUDER Endoprosthesis® is an aortic, modular, bifurcated Endoprosthesis composed of two elements:

- the Trunk-ipsilateral Leg Endoprosthesis. (trunk) (Fig. 1 and 2)
- the Contralateral Leg Endoprosthesis (Fig. 3 and 4)

The prosthesis is in expanded polytetrafluoroethylene (ePTFE), supported by a Nitinol wire along its outer surface. Nitinol anchors and an ePTFE sealing cuff are located at the aortic end of the trunk. An ePTFE sleeve is used to constrain the endoprosthesis on the leading end of the delivery catheter (fig. 5, 6, 7 and 8).

Figure 1: Trunk-ipsilateral leg endoprosthesis; (aortic diameters of 23, 26 or 28.5 mm)

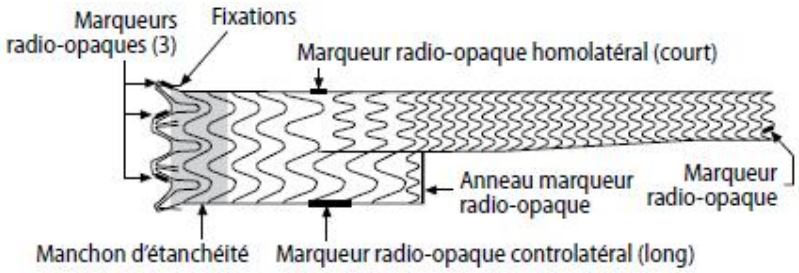


Figure 2: Trunk-ipsilateral leg endoprosthesis; (aortic diameters of 31 mm)

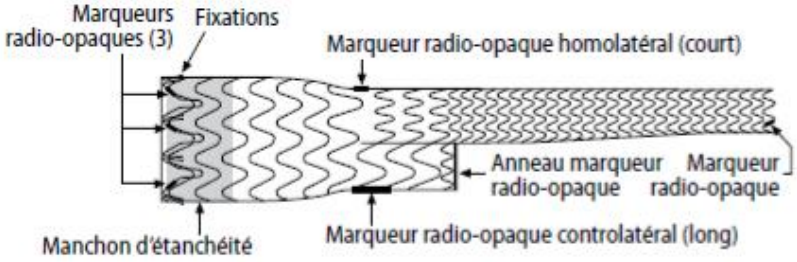
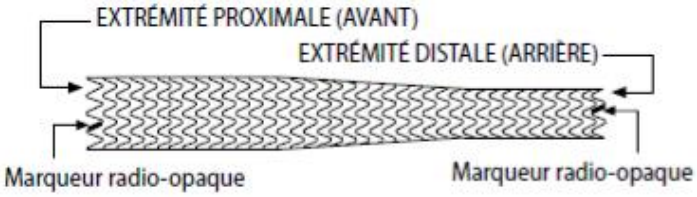


Figure 3: Contralateral leg endoprosthesis; (distal iliac diameters of 12 and14.5 mm)



Marqueurs radio-opaques de l'endoprothèse jambage controlatéral :

- Un (1) marqueur à chaque extrémité

Figure 4: Contralateral leg endoprosthesis; (distal iliac diameters of 16, 18 and 20 mm)

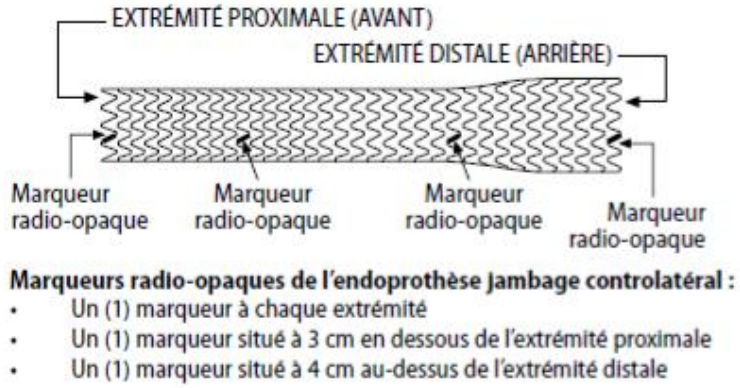


Figure 5: GORE EXCLUDER® AAA Endoprosthesis Delivery Catheter

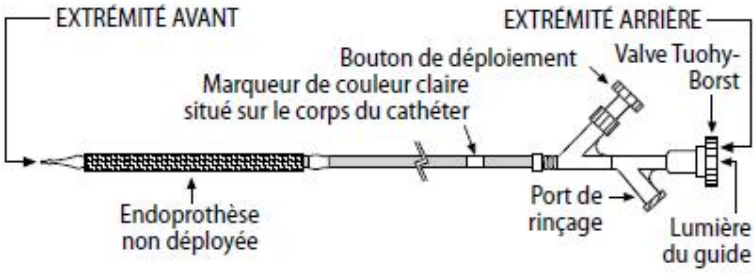


Figure 6: (Trunk-ipsilateral leg) GORE ® EXCLUDER AAA Endoprosthesis undeployed on catheter with radiopaque markers

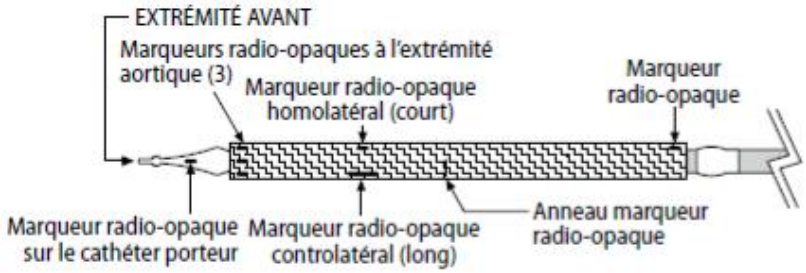


Figure 7: (Distal contralateral iliac diameters of 12 and 14.5 mm) GORE EXCLUDER® AAA Endoprosthesis constrained delivery catheter with radiopaque markers

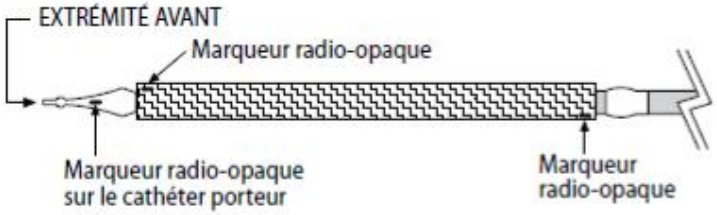


Figure 8: GORE EXCLUDER® AAA Endoprosthesis (Contralateral iliac diameters of 16, 18 and 20 mm) constrained delivery catheter with radiopaque markers

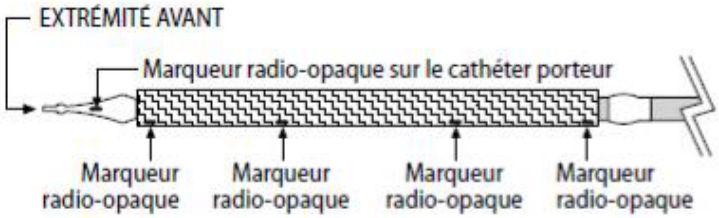


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Figure 9: Aortic Extender Endoprosthesis

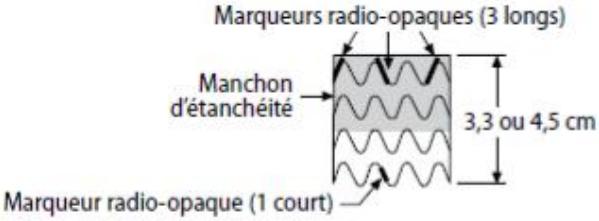


Figure 10: Aortic Extender Endoprosthesis Delivery Catheter

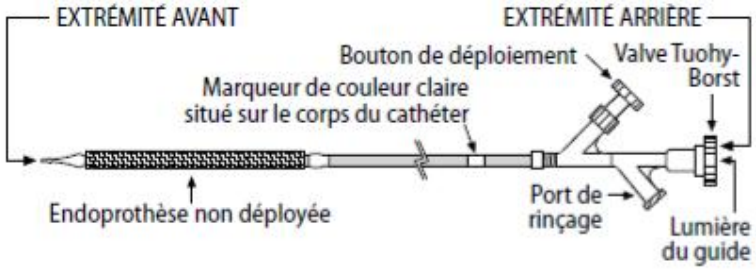
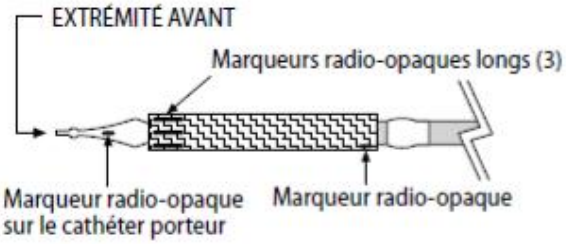
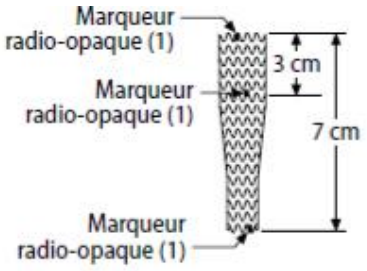


Figure 11: Constrained Aortic Extender Endoprosthesis



The Iliac Extender Endoprosthesis provides an extension of up to 4 cm of either the ipsilateral or contralateral limb. The extender component can be placed at variable extension lengths from 4 cm to 0 cm, allowing a customization of extender treatment length based on patient anatomy. The graft material is ePTFE/FEP, supported by a Nitinol wire along its external surface. A radiopaque marker is located 3 cm from the proximal end (fig. 12). An ePTFE/FEP sealing cuff is used to constrain the endoprosthesis on the leading end of the delivery catheter (fig. 13). Deployment of the Iliac Extender initiates from the leading end and proceeds toward the trailing end of delivery catheter. Following deployment, the ePTFE / FEP remains *in situ* between the endoprosthesis and the vessel wall.

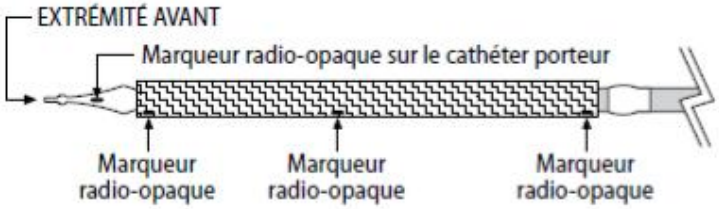
Figure 12: Iliac Extender Endoprosthesis



Marqueurs radio-opaques de l'extension iliaque (3 au total) :

- Deux (2) marqueurs d'extrémité : un (1) à chaque extrémité
- Un (1) marqueur situé à 3 cm en dessous de l'extrémité proximale
- Remarque : Toutes les dimensions sont nominales.

Figure 13: Constrained Iliac Extender Endoprosthesis (distal iliac diameters of 10, 12 and 14.5 mm)



1.1.5 Using the GORE® EXCLUDER® Endoprosthesis

The prescription and usage modalities are as follows:

- The abdominal aortic stenting should be performed in accordance with recommendations of the French Health Products Safety Agency and the French National Authority for Health (HAS) in the July 2009 report [1].

- Follow-up should be conducted in accordance with the follow-up procedure established by Afssaps and the analysis of the follow-up data shall be transmitted by W. L. Gore & Associates to HAS annually

1.2 Expected Benefit

The expected benefit of this study is to have a long-term evaluation of the GORE® EXCLUDER Abdominal Aortic Endoprosthesis® thus allowing to evaluate the long term usefulness of the technique with this endoprosthesis.
This study will make it possible meet the HAS requirements for any renewal of registration on the LPPR of the GORE® EXCLUDER® Endoprosthesis (Appendix 1).

1.3 Foreseeable and known risks for persons participating in the research

The research is observational; it does not lead to any change in patient management. Consequently, there is no risk associated with the research for patients.

1.4 Description of the Study Population

The study population corresponds to 180 consecutive patients treated with bifurcated GORE® EXCLUDER Endoprosthesis® for unruptured Infra-renal Abdominal Aortic Aneurysm.

Patient recruitment shall be a consecutive recruitment of 180 patients. Each center is multidisciplinary, combining surgical and radiological activities.

2 OBJECTIVE OF THE STUDY

The objective of this Study is to evaluate the usefulness of the technique by documenting:

- Overall mortality,
- Complications (endoleak, migration),
- The surgical conversion rate,
- The evolution and rupture of the aneurysm,

in the long term, that is, 5 years, on a cohort of patients representative of the population treated in real life conditions.

3 RESEARCH DESIGN

3.1 Study Methodology

Observational, Prospective, Multicenter Study

3.2 Conduct of the Study

The Study is conducted according to the usual management schedule for these patients.

After inclusion of the patient, there will be postoperative follow-up or in the months following the procedure and at 6 months, 12 months and annually, for 5 years.

The clinical and radiological follow-up will be performed according to the follow-up protocol recommended by HAS and by Learned Societies (Société de Chirurgie Vasculaire [Society for Vascular Surgery] – Société Française de Radiologie [French Society of Radiology]) [1].

	Post-operative follow-up (D1 to D30)	**Follow-up at 6 months.**	**Follow-up at 1, 2, 3, 4 and 5 years**	**Follow-up intermediate *****
Clinical examination	**X**	**X**	**X**	**X**
Radiography of the abdomen without preparation in 3 effects (front, profile and ¾)	**X**[1]	X*	X*	X*
CT with contrast medium	**X**	**X**	**X**	**X**
MRI	X*	X*	X*	X*
Vascular Doppler	X**	X**	X**	X**

* if CT with contrast medium cannot be performed

** if RMI cannot be performed

*** interim follow-up carried out only in case of leakage, deterioration of the endoprosthesis or scalability of the aneurysm on the previous control examination. Follow-up to be carried out 3 months after the control where the anomaly was observed.

[1] Radiography in postoperative follow-up will not be necessary in case of 3D reconstruction performed during the CT.

An annual report will be forwarded to CNEDiMTS.

3.3 Evaluation Criteria

These criteria are measured postoperatively or within one month after surgery, at 6 months, 12 months and then annually for 5 years, with an annual report issued to be submitted to the French National Authority for Health:

- Overall mortality rate,
- Mortality rate related to the aneurysm,
- Evolution of the diameter of the aneurysm
- Rate of Endoleaks for Type I, II and III
- Migration rate,
- Rate of surgical conversion,
- Rate of endovascular or surgical re-intervention.

3.4 Evaluation Parameters

General Data

- Age
- Gender
- Diameter of Abdominal Aortic Aneurysm
- Patient status (normal or high surgical risk according to the Afssaps criteria, Appendices 3 and 4)
- All references and evolution of the range of the GORE® EXCLUDER Endoprosthesis®

Data related to the procedure (at all control times):

- Death from all causes
- Aneurysm-related death
- Evolution of the diameter of the aneurysm
- Types I, II and III endoleak
- Migration
- Surgical conversion
- Re-intervention related to the initial procedure

Definitions :

Death related to the aneurysm shall be defined as any death occurring as a result of a ruptured Abdominal Aortic Aneurysm or following any procedure intended to treat Abdominal Aortic Aneurysm.
If the death occurred within 30 days of any procedure intended to treat Abdominal Aortic Aneurysm, then it will be considered as related to the aneurysm unless proven otherwise. Deaths occurring beyond 30 days of any procedure intended to treat Abdominal Aortic Aneurysm and that are related to the procedure should be considered as related to the aneurysm.

Distal migration is defined by a distal displacement strictly greater than 10 mm. Proximal migration is defined either by proximal displacement strictly greater than 10 mm, or by proximal displacement which covers one of the renal arteries; the reference examination being the first postoperative CT performed.

An increased aneurysm diameter is defined as an increase strictly greater than 5 mm of the largest measurable diameter of the aneurysm; the reference diameter being the diameter of the first post-operative check-up.

3.5 Duration of the Study

Duration of the inclusion period:

Inclusion period of 180 patients: 12 months

Duration of participation of each patient:

The requirement of the French National Authority for Health is long-term patient follow-up, that is, 5 years.

Total duration of the Research:

In this context, there is no maximum follow-up duration for this Study (12 months inclusion period and a minimum of 5 years of follow up).

4 SELECTION AND EXCLUSION OF PEOPLE FROM THE RESEARCH

4.1 Inclusion Criteria

Any patient requiring GORE® EXCLUDER stenting® for the treatment of an unruptured Infra-renal Abdominal Aortic Aneurysm.

4.2 Non-inclusion Criteria

Patients whose clinical follow-up is not possible i.e., patients unable to return for monitoring visits (e.g., patients living abroad).

4.3 Explanation of the Endoprosthesis

Any patient for whom the GORE® EXCLUDER Endoprosthesis® has been withdrawn will be monitored for up to 5 years.
A minimum of one clinical follow-up will be carried out.

4.4 Premature discontinuation of the research for the patient

The following cases will be considered premature discontinuation of the study:

- Patient withdrawing his non-opposition
- Death
- Failure to Return

A patient who does not show up at the scheduled visit will be considered **temporarily** as having failed to return if the Investigator does not get any information about the patient:

- after having tried to contact him by phone several times (at least two documented phone calls)
- and after having sent him an invitation letter without any reply for 1 month.

All contact attempts will be documented.

If the Investigator obtains news about a temporarily-failed-to-return patient before the end of the study, that patient will no longer be considered failed-to-return; otherwise, he will be permanently categorized as having failed to return at the end of the study.

4.5 Procedures put in place to avoid failure-to-return

Several measures will be taken to avoid failure-to-return.

The study documents handed over to investigators during study set up highlight the fundamental importance of patient follow-up and data collection during the entire study.

The investigator will seek the means to contact the attending physician or the nearest trusted relation.

In the event of absence from a visit, the center investigator will contact him by phone several times (at least two documented calls) and send him an invitation letter. In the absence of a response, the attending physician will be contacted in a bid to obtain information on the patient's status and on all the elements needed to trace a possible clinical event related to the endoprosthesis (hospitalization, etc.).
In the absence of results from the procedures below, the patient living/deceased status will be documented by investigation in the municipality of birth by the Investigator.

5 TREATMENT ADMINISTERED TO RESEARCH SUBJECTS

5.1 Drugs authorized and prohibited under the Protocol including rescue medication

No medications are prohibited. Medications are used under usual conditions of surgery. The study does not involve any restriction or recommendation.

5.2 The medical device used

The device is the GORE® EXCLUDER Endoprosthesis® detailed in paragraph 1.1.4

A copy of the instructions for use supplied with each device is found in the investigator's file (Appendix 5).

5.3 Scientific Committee

A Scientific Committee common to all manufacturers has been established (Appendix 6).
This multidisciplinary and independent Scientific Committee is composed of one methodologist and six practitioners (Cardiac Surgeon, Vascular Surgeon, Interventional Radiologist).
This committee is the guarantor of scientific and methodological validity of the Protocol.

6. STATISTICAL ANALYSIS

[redacted]

6.2 Strategy for analyzing collected data

6.2.1 Patient characteristics and follow-up

Patient demographic and medical data and descriptive follow-up data will be described on the patient population included. Qualitative parameters will be described by their distribution frequency and bilateral confidence intervals associated at 95%, quantitative parameters by their average, minimum, maximum, median and quartiles standard deviation, number of missing values.

6.2.2 Criteria Studied

Main analyses:

The criteria studied are as follows:

- Death from all causes
- Aneurysm-related death
- Evolution of the diameter of the aneurysm.
- Types I, II and III endoleaks
- Migration
- Surgical conversion
- Re-intervention related to the initial procedure

Definitions :

- Death related to the aneurysm shall be defined as any death occurring as a result of a ruptured Abdominal Aortic Aneurysm or following any procedure intended to treat Abdominal Aortic Aneurysm.
  If the death occurred within 30 days of any procedure intended to treat Abdominal Aortic Aneurysm, then it will be considered as related to the aneurysm unless proven otherwise.
  Deaths occurring beyond 30 days of any procedure intended to treat Abdominal Aortic Aneurysm and that are related to the procedure should be considered as related to the aneurysm.

- Distal migration is defined by a distal displacement strictly greater than 10mm. Proximal migration is defined either by proximal displacement strictly greater than 10mm, or by proximal displacement which covers one of the renal arteries; the reference examination being the first postoperative CT performed.

- An increase in the diameter of the aneurysm is defined by an increase strictly greater than 5 mm of maximum diameter of the highest measurable diameter of the aneurysm; the reference diameter being the diameter of the first post-operative check-up.

Each of the rates that match the Study criteria will be analyzed by calculating frequency distributions and bilateral confidence intervals of 95% (IC95) associated.

Event rates over time are described by survival curve according to the Kaplan-Meier method and the related Kaplan-Meier estimators will be calculated.

Additional Analyses:

All the analyzes may be stratified by center if recruitment in each center participating in the study is sufficient for such analyzes to be of interest. However, it must be emphasized that this Protocol in no way aims to compare the centers.

For exploratory purposes, the study criteria will also be analyzed depending on patient baseline characteristics:

- Age (in categories)
- Gender
- Diameter of Abdominal Aortic Aneurysm
- Patient status (normal or high surgical risk according to the Afssaps criteria, Appendices 3 and 4)

6.3 Statistical criteria for discontinuing the research

No discontinuation criterion

6.4 Method of management of missing, unused or invalid data

Missing data will be listed and presented in a tabulated form.

Patients will be considered as censored at the date of the last observation.

6.5 Choice of persons to be included in the analyses

All the patients in the register will be considered in the analysis.

6.6 Data Analysis Manager and Working Software

The Manager of data analysis performed by W. L. Gore & Associates is: MedPass International.

All the analyses will be managed under the responsibility of Marie-Christine Reymond located at MedPass International, 95 bis boulevard Pereire, 75017 PARIS.

All the analyses will be managed with SAS software.

A detailed statistical analysis plan will be prepared by MedPass for W. L. Gore & Associates.

7 RIGHT OF ACCESS TO DATA AND SOURCE DOCUMENTS

Individuals with direct access in accordance with current legislative and regulatory provisions, notably articles L.1121-3 and R.5121-13 of the Public Health Code (for example, investigators, individuals responsible for quality control, and any individuals appointed to collaborate in trials) take all the necessary precautions with a view to ensuring the confidentiality of information relating to experimental drugs, trials, subjects involved in trials, particularly as regards their identity, and results obtained. Data collected by these people are then anonymized.

8 LOGISTICS AND QUALITY ASSURANCE

The research will be supervised according to the Manager's standard operating procedures.
The conduct of the research in the investigation centers and management of the subjects will be done in accordance with the ethical and medical guidelines.

Transcribing data into the case report form

eCRF

The study data will be recorded by participating physicians (investigators) on a eCRF. Information provided in the study questionnaire should be a reflection of those in the patient record.

- Monitoring

In order to ensure data quality, a monitoring plan is put in place. Among other things, this plan details the frequency of site visits and the proportion of monitored data. It is expected that at least 10% of the data be verified.

Monitoring elements regarding the quality of filling eCRF are performed by a CRA.

Participating physicians may be contacted in case of absence of filling of data after inclusion of patients or date of scheduled visit.

- Data Management

Systematic coherence control procedures are set up and documented. Correction procedures are traced. For the study data, Queries are issued and sent to different centers for resolution.

- Quality Assurance Procedure

Quality control is carried out continuously during the various stages of error correction, according to the Manager's standard operating procedures.

9 LEGAL AND ETHICAL CONSIDERATIONS

In this research, W. L. Gore & Associates and/or MedPass International are the Managers and are responsible for regulatory tasks.

9.1 CNIL [French Data Protection Agency] Declaration

This research is subject to the law of January 6, 1978 relating to Data Protection, as amended.
Before its actual commencement, the processing of data collected in research is subject to referral to the French Advisory Committee on Information Processing in Material Research in the Field of Health (**CCTIRS**), and then the French Data Protection Agency (**CNIL**).

9.2 Information and Non-opposition Form

When selecting the subject, the physician will verify the selection and non-selection criteria and will inform the subject of the Study principle and his/her role.

The investigating physician should inform the patient and answer all his/her questions.
The patient must be informed of his/her rights to be able to object to, if he/she so wishes, the analysis of data concerning them, before any action necessary to research.
In this context, an Information and Non-opposition Form is prepared.
This Information Form includes the data requested by Afssaps and HAS in Appendix II of the report dated July 7, 2009 (Appendix 2).

9.3 Final report on the Research

The final report on the research will be written by W. L. Gore & Associates. This report will be sent to each of the investigators.

10 DATA PROCESSING AND STORAGE OF DOCUMENTS AND DATA RELATING TO THE RESEARCH

Documents pertaining to research must be stored by all parties involved for a period of 15 years after the end of the research.

This indexed storage will comprise at least:

- Successive versions of the Protocol (identified by the version No. and date),
- The letters of correspondence with the Manager,
- A completed and validated case report form for each subject enrolled,
- All appendices specific to the study,
- The final report of the study.

The database from which the statistical analysis was drawn must also be stored by the Analysis Manager (paper or electronic medium).

11 RULES RELATING TO PUBLICATION

- W. L. Gore & Associates is the proprietor of all data, analysis and results relating to the GORE® EXCLUDER Endoprosthesis® and no use or transmission to a third party may be made without its prior consent.

However, the consultant is free to independently use and develop data from the medical records of his own patients and also data and information:

- that were known to the consultant prior to their disclosure by manufacturers;
- that are or become legally accessible to the public;
- that are released from confidentiality status by written agreement of the manufacturer.

Appendix 1: Opinion of HAS dated July 13, 2010

HAUTE AUTORITÉ DE SANTÉ

NATIONAL COMMISSION FOR EVALUATION OF MEDICAL DEVICES
AND HEALTH TECHNOLOGIES
OPINION OF THE COMMISSION

July 13, 2010

Devices : Abdominal Aortic Endoprosthesis (Title III - Chapter 1 - Section 1 - Subsection 2 - paragraph 4 of the list of products and services mentioned in Article L. 165-1 of the Social Security Code)

Pursuant to:

- Decree No. 2004-1419 of 23 December 2004 on the management of products and services mentioned in Article L. 165-13 of the Social Security Code authorizing the Evaluation of Products and Services Commission (CEPP), on its own initiative or at the request of Ministers in charge of Social Security, to reevaluate the expected or actual services of the products or services listed as provided for in Article L. 165-1 (Article 13 of the Decree);

- self-referral to CEPP dated April 5, 2006 relating, in particular, to post-registration study objectives required within the framework of the renewal of registration of Abdominal Aortic Endoprostheses listed under brand name;

- the proposals of the mandated Working Group;

the National Commission for Evaluation of Medical Devices and Health Technologies recommends amending the conditions for renewal of registration of Abdominal Aortic Endoprostheses, listed under the brand name, in the following manner.

Terms of Renewal

CNEDiMTS subjects the renewal of registration of each endoprosthesis to the presentation of results of a specific follow-up study implemented on a cohort of patients representative of the population treated in real life conditions.
The objective of each study is to evaluate the usefulness of the technique by documenting overall mortality, complications (endoleak, migration), the rate of surgical conversion, evolution and rupture of the aneurysm, in the long term, that is, beyond 5 years.
This prospective cohort study shall involve at least 150 patients implanted after registration on the LPPR [List of Reimbursable Products and Services].
The results of the follow-up study shall be forwarded to CNEDiMTS once a year, for consideration.
The evaluation of this follow-up may lead CNEDiMTS to recommend that reimbursement for the EPA concerned be maintained or suppressed.

APPENDIX 2: Information note to patients / HAS Guide

Data that should appear in the patient information note
(Appendix II of the HAS Report dated July 7, 2009)

Dear Sir/Madam,

You have an Infra-renal Abdominal Aortic Aneurysm that requires treatment.
This treatment is necessary: when the largest diameter of the aneurysm reaches 50 mm, or when the diameter has increased by at least 10 mm in one year, or when the aneurysm is painful, or when the aneurysm is a sac-like.
Your physician recommends treatment of the Infra-renal Abdominal Aneurysm with an aortic endoprosthesis.
This treatment can be used to treat your aneurysm since it has an anatomy adapted to conditions of use of the GORE® EXCLUDER Endoprosthesis®.
In this case, the standard treatment of Abdominal Aortic Aneurysm is currently the "classic" surgery that involves opening the abdomen. The postoperative mortality risk (death) of conventional treatment is low, but treatment with endoprosthesis reduces that risk. In return, the durability of treatment by endoprosthesis is less well known and one or more additional procedures might be needed subsequently. This will most often be a minor operation but conventional surgery will sometimes be necessary. Despite treatment with endoprosthesis, rupture of the aneurysm may also occur.
Using this type of endoprosthesis requires regular clinical and radiological monitoring.
The following tests should be performed:

- **Immediately after surgery or within 30 days after implantation:**
  - radiography of the abdomen without preparation in 3 effects (front, profile and three-quarters);
  - CT scan with early and late acquisitions after injection of contrast medium (according to SFR recommendations);
  - if the CT scan cannot be done, an examination by magnetic resonance imaging (MRI);
  - if the MRI cannot be performed, a vascular Doppler ultrasound.
- **At the 6th month, 12th month and then annually, indefinitely,** repeating the examination in the first 30 days (computed tomography or vascular Doppler ultrasound).

Data collected will be included in a follow-up study of the GORE® EXCLUDER Endoprosthesis® requested by HAS.
Your information will remain strictly confidential. This data can be processed by computer; you will only be identified by the first three letters of your family name and the first 2 letters of your first name. The right of access provided for by the "Data Protection" Law (Article 40), shall be exercised at all times with your physician and you can exercise your right of rectification with him. Follow-up data concerning you will be assessed respecting data confidentiality and anonymity.

APPENDIX 3: Normal surgical risk patient

Definition of normal surgical risk patient
eligible for abdominal aortic stenting

HAS Report dated July 7, 2009

The reassessment of the benefit-risk balance can help lift the high-risk patient restrictions. Endovascular treatment can be offered as first-line surgery for **normal surgical risk and favorable anatomic criteria patients** and after informing patients of the benefits and risks of both methods.
The treatment may be recommended for a normal surgical risk patient only if the following anatomical criteria are met:
- neck without thrombus or major circumferential calcification
- proximal neck with parallel edges > 15 mm
- angle of the proximal neck: - < 40°
- or between 40° and 60°, provided that the length of the neck is more than 20 mm

The diameter of the proximal neck, the state of the distal neck (iliac anchor point(s)), the iliofemoral accesses must be compatible with the implantation system and the endoprosthesis used.
It should be noted that the introduction of an EPA in a patient with normal surgical risk should not lead to the voluntary exclusion of functional visceral arteries including the hypogastric artery, apart from the inferior mesenteric artery.

APPENDIX 4: High surgical risk patient

Definition of high surgical risk patient

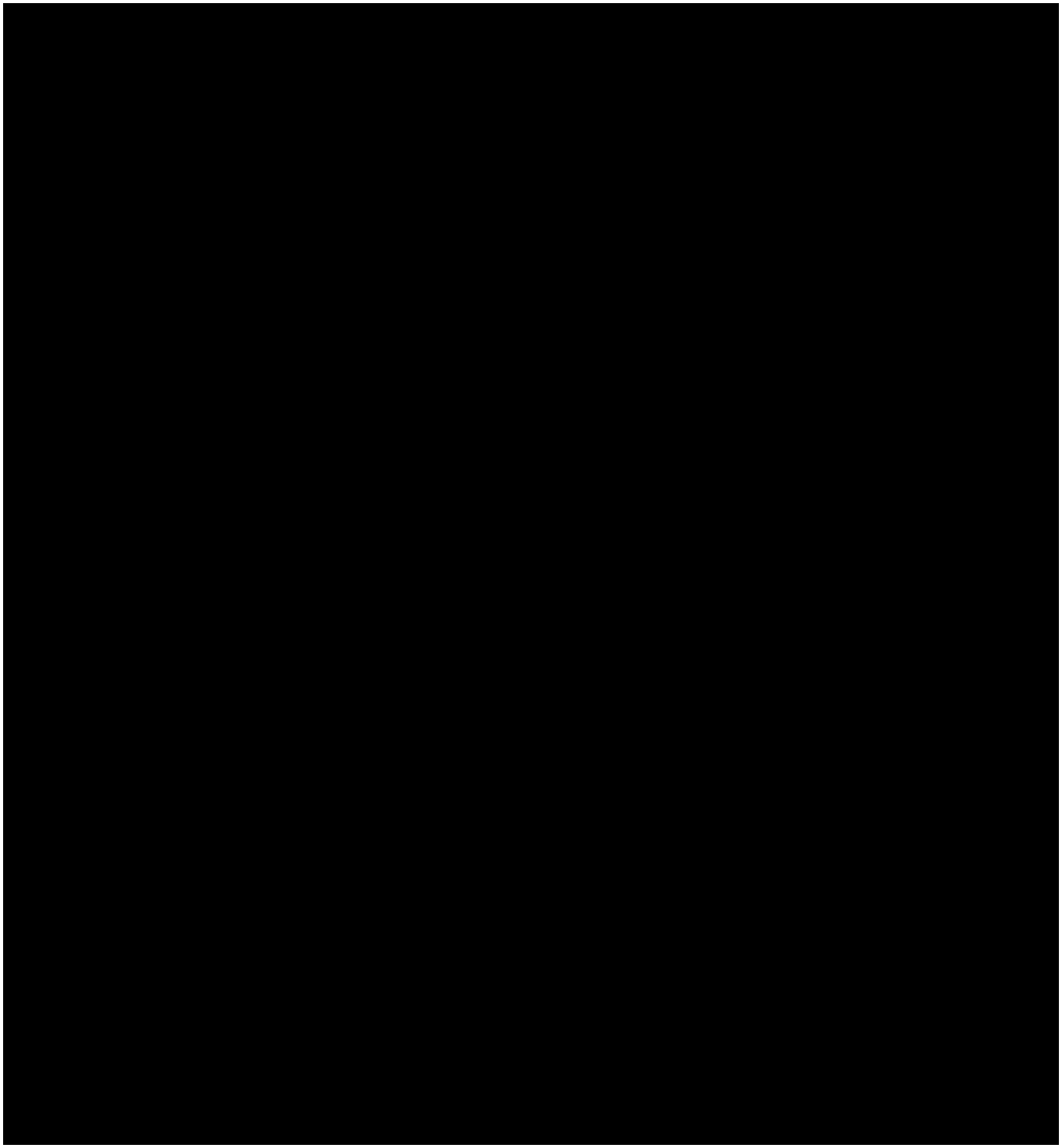
HAS Report dated July 7, 2009

Patients at high surgical risk must present one of the following factors:

– Age greater than or equal to 80 years.
– Coronary artery disease (history of myocardial infarction or angina) with positive functional testing and coronary lesions for which revascularization is impossible or not indicated.
– Cardiac failure with patent clinical manifestations.
– Inoperable aortic stenosis.
– LVEF < 40 %.
– Chronic respiratory failure objectified by one of the following criteria:
  - FEV < 1.2 l/sec ;
  - VC <50% of the predicted value according to age, sex and weight;
  - Arterial blood gases in the absence of oxygen: $PaCO^{2}$> 45 mm Hg or PaO^{2} < 60 mm Hg;
  - oxygen therapy at home.
– Renal impairment if creatinine > 200 µmol/l before injection of contrast medium.
– Hostile abdomen, including the presence of ascites or other signs of portal hypertension.

[redacted]

[redacted]



APPENDIX 8: References

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