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Global Collaborators on Advanced Stent-Graft Techniques for Aneurysm Repair (GLOBALSTAR) Project

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Endovascular repair of aortic aneurysms (EVAR) using standard stent-grafts is well established as an alternative to conventional surgery in light of the extensive evidence. However, there are many patients in whom standard stent-grafts are not applicable due to anatomical constraints. A number of advanced endograft technologies have been developed to extend the use of EVAR in circumstances of unfavorable anatomy, including:

1) Stent-graft configurations that extend across and preserve the iliac bifurcation;
2) Fenestrated stent-graft repair of abdominal aortic aneurysms;
3) Endovascular repair of aortic aneurysms using side branches to preserve perfusion of abdominal aortic branches;
4) Endovascular repair combined with debranching of the abdominal aorta and extra-anatomical bypass;
5) Side-branched and fenestrated stent-grafts (including in situ fenestrations) to preserve flow through the branches of the aortic arch; and
6) Stent-graft repair combined with debranching of the aortic arch and extra-anatomical bypass.

The feasibility of all of these techniques has been established, and as a few centers have begun to accumulate clinical experience, it can be anticipated that many more will adopt these techniques in the near future. As in the early days of EVAR, however, enthusiasm and optimism for these techniques needs to be tempered by recognition of

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potential risks, the extent of which is largely unknown.

Methodical and rigorous evaluation of various aspects of these advanced techniques is necessary in order to (1) evaluate their efficacy in relation to the primary clinical objectives, (2) identify and define complications unique to the advanced techniques, (3) identify the potential effects of stent-graft modifications upon stent-graft function, and (4) study complications further to identify solutions. This information is essential before the techniques can be advocated for day-to-day clinical practice. However, there are a number of hurdles to developing such evidence.

The biggest hurdle arises from the fact that, in the early stages of development, new technologies can be applied to a relatively small number of patients in each of the centers using them, and it takes a long time to establish a substantial cohort, even in the busiest of centers. In several ways, the issues facing further evaluation and development of these techniques today are the same as those facing standard EVAR a decade ago. An effective response to this situation was the EUROSTAR registry, a collaborative project.

The EUROSTAR project has played an important role over the last decade in the evaluation of almost every aspect of standard EVAR. EUROSTAR analyses also provided the clinical information that was needed to identify the basic requirements for durable endovascular exclusion of an aneurysm. These data had a significant impact on the evolution of stent-graft design into more effective later iterations.

There is once again a strong case for physicians practicing these techniques to create a joint venture of clinical research. A collective project focusing on advanced techniques is necessary to develop a database that is large enough to allow conclusions to be drawn within a timeframe that will support efficient development and evaluation of these techniques. It is the aim of the Global Collaborators on Advanced Stent-Graft Techniques for Aneurysm Repair (GLOBALSTAR) project to serve this role.

**STANDARD THORACIC EVAR**

Treatment of thoracic aortic pathology using standard stent-graft techniques has been in clinical practice for longer than a decade. There has been a perception that the benefits of EVAR in the thoracic segment considerably outweigh those of conventional surgery, which involves thoracotomy and, often, extracorporeal bypass. Advances in this area, however, have been slow to come due to a number of factors. The incidence of thoracic disease is lower compared to abdominal aneurysms, which prolonged the learning curve and slowed turnaround of the technology cycle. The majority of the published studies included a variety of aortic pathologies treated using various stent-graft iterations, making it somewhat difficult to define the role of EVAR in each type of pathology. Much of the refinement of the concepts of thoracic EVAR has been extrapolated from the infrarenal aneurysm experience. However, this approach has limitations due to differences in the abdominal and thoracic aortic environment. For these reasons, it is essential to continue further evaluation of standard thoracic EVAR, in addition to the aforementioned advanced techniques, with stratified analyses according to the type of pathology treated.

**PROS AND CONS OF REGISTRY-BASED RESEARCH INTO STENT-GRAFT TECHNIQUES**

Registry-based studies have been playing a major role in vascular research over the last decade, and the value of the information generated in this way is understood clearly. Registry data are recognized to represent pragmatic results that are achieved in “real life,” and they allow us to follow the evolution of techniques over time. On the other hand, data from controlled clinical trials reflect results during a specified period of time from patients and centers that have gone through a different type and level of selection processes. The latter data serve specific purposes, and quite often there is no alternative method of collecting such information, e.g., comparison of two different techniques.
Whether such results can be generalized remains questionable because they rarely reflect everyday practice. Mandatory registries are becoming a feature of clinical practice in strongly regulated countries, when the purpose is to determine standards and to provide a benchmark for comparative audit. Observational data are a necessary prerequisite for planning of randomized clinical trials.

Some advanced endovascular technologies have applications that are unlikely ever to be subjected to randomized clinical trials despite uncertainties regarding the overall performance of such techniques. There are a number of reasons for this, e.g., the lack of widespread application of such techniques, making it difficult to sustain randomized trials; a lack of equipoise in relation to certain subsets of patients or certain techniques; variance of opinion among physicians as to the circumstances that should create equipoise in the choice of treatment, particularly when the alternative treatment modality is conservative management or a much higher risk operation, etc. For all these reasons, a dedicated registry is essential for the evaluation of advanced stent-graft techniques.

Registries, particularly voluntary registries, do have drawbacks: absence of data monitoring, drop-off in follow-up data registration, absence of a core laboratory, and heterogeneity of factors relating to patients, physicians, and technical aspects, to name a few. However, lessons have been learned in running large registries, e.g., in the areas of securing funding, maintaining collaborator satisfaction, encouraging proactive scientific participation from collaborators, achieving expeditious dissemination of information, etc. The GLOBALSTAR project will benefit from this experience to enable it to overcome or mitigate these limitations.

GLOBALSTAR

Intended Purposes

- Create follow-up protocols for each of the advanced techniques;
- Standardize investigations that are part of follow-up protocols;
- Set reporting standards for advanced techniques and compile definitions and lists of potential complications associated with these techniques;
- Evaluate the techniques in terms of primary and non-primary endpoints;
- Establish an archive of all preoperative and follow-up imaging;
- Develop a core laboratory for image evaluation to aid identification of mechanisms of function and failure;
- Provide an early warning system of complications specific to advanced techniques; and
- Develop a method of evaluating the techniques when used in emergency situations.

Organization, Data Collection, and Analyses

The GLOBALSTAR project is organized as a network of physicians with established or developing experience of advanced EVAR techniques. Collaborators are expected to propose and lead specific studies. An International Advisory Board will discharge the following responsibilities: (1) proposing or approving registry protocols; (2) overseeing data collection, data protection, and ethical responsibilities; (3) developing and verifying reports and publications; (4) ensuring freedom from conflict of interest and bias and overseeing financial arrangements; and finally (5) approving applications from new participating centers. The project will also be supported by registry advisors, a data manager, and a health scientist. The principal investigator will take responsibility for the day-to-day functioning of the registry under the supervision of the International Advisory Board.

Performed at the time of enrollment, the consenting process involves informing the patients of the purposes of the registry and the manner in which the data will be treated. For reasons of confidentiality, the data registry needs to be absolutely secure. In order to best serve the purposes of the participating collaborators, it should also be convenient and easy to use, with minimal impact upon
local resources. To fit these requirements, the registry will be Internet-based, incorporating security features equivalent to those of financial transactions. (The technical details of the Internet security setup will be available for inspection on specific enquiry.) Using secure access, authorized individuals will be able to input data via the Internet directly; they will also be able to freely view all data accumulated from their particular center at any time and download it into various popular software packages (e.g., SPSS, Microsoft Excel). This could serve the purpose of a secure database for each center and may be used for their clinical and academic purposes in an appropriate manner. Patients must be registered before treatment to reduce reporting bias influenced by outcomes. The entire registry data will be included in periodic analyses and for specific studies.

Core Laboratory

The increasing complexity of stent-graft design calls for increasing attention to detail in their further evaluation. Understanding the mechanisms of stent-graft failure often involves careful analysis of computed tomographic (CT) images using a robust and consistent methodology. The importance of a dedicated core laboratory to perform this function is particularly great in relation to advanced EVAR techniques since minor changes in stent-graft configuration, structure, or position have the potential to initiate significant clinical complications, e.g., target vessel loss after fenestrated EVAR. Resolution of routine CT scans in the majority of the centers will be adequate for the purposes of the core laboratory, whose database will also use an Internet-based system of data collection. Once uploaded to the registry, patient details from the imaging files will be replaced with case-record identifiers so that images can be stored anonymously, while preserving the ability to link them with corresponding clinical data when required.

Relationship With Industry

Commercial manufacturers of stent-grafts and related technologies stand to benefit from scientific evaluation of advanced EVAR techniques, without which it would not be possible to improve these techniques or to define their role in disease management. The registry will foster a mutually beneficial partnership between physicians and industry representatives who will be consulted on the evolution and strategic planning of the program. There will be opportunities for industry partners to be granted access to registry data by agreement, provided confidentiality of contributing physicians and patients is preserved.

It is one of the functions of the International Advisory Board to ensure transparency of registry function and freedom from bias or adverse influence from individual companies or from the industry as a whole, so that the credibility of the data published will not be undermined.

FUTURE DIRECTIONS

The overall aim of the GLOBALSTAR project is to make an important contribution to the continuing evolution of EVAR technologies and to ensure maximal benefit for patients with aneurysm disease. Success will depend upon the enthusiastic and committed support of physicians and industrial partners around the world.

REFERENCES


