

Trial Design Issues Associated with Evaluation of Stents in Diseased Iliac Arteries

1. Introduction

Percutaneous transluminal angioplasty (PTA) is described as a well-established treatment modality for atherosclerotic peripheral artery disease.¹⁻⁶ However, PTA can lead to dissections, vessel recoil, or intimal flaps which limit flow, or an unfavorable residual stenosis. Restenosis has been reported in up to 20 percent of the patients who have had a prior PTA procedure.^{2, 3, 4, 7, 8, 9}

In 1996, the Transatlantic Inter-Society Consensus (TASC) working group consisting of representatives from several American, Canadian and European medical societies was formed to develop a consensus document on the management of peripheral arterial disease. The TASC consensus document, Management of Peripheral Arterial Disease, was published in the January 2000, issue of the Journal of Vascular Surgery. The TASC consensus document noted the availability of stents and attributed this factor for the improvement in the immediate hemodynamic PTA results in the iliac artery and the effective management of recoil and PTA related flow-limiting dissections.¹⁰

Currently there are only two stent systems approved by FDA for use in the iliac artery. Both stent systems are indicated for use following suboptimal PTA and were evaluated in registry studies with PTA, and/or the approved competitor stent, as a historical control. Following approval of the second stent in 1996, most IDE applications submitted to FDA incorporated a randomized controlled study design to evaluate the safety and effectiveness of stenting in the iliac artery following suboptimal PTA. In view of the on-going clinical trials, FDA required the use of a randomized trial design, or a well described historical control that could provide an appropriate comparison.

All of the clinical trials currently in progress use a randomized control trial with an approved iliac stent as the control. However, slow patient enrollment, despite expansion of the investigational site limits, has substantially delayed the completion of these trials. The main cause for this slow enrollment seems to be the availability of a variety of stents that are now available for other indications.

FDA acknowledges the difficulties of conducting a randomized study to evaluate a new stent for the suboptimal use indication in the iliac artery. To this end the Division of Cardiovascular and Respiratory Devices (DCRD) is seeking Panel input on the following questions regarding the design of these studies.

II. Questions

Iliac Stenting Following Suboptimal Angioplasty

Currently FDA recommends that clinical trials of new stent systems for the treatment of atherosclerotic disease in the iliac artery following suboptimal PTA use a composite primary endpoint of freedom from peri-procedural death and freedom from target lesion revascularization and restenosis (>50%) at nine months. FDA has accepted duplex ultrasound as a method for determining patency at nine months, with angiography if the ultrasound quality is inconclusive or indicative of restenosis. FDA has also recommended that sponsors follow the definitions for success, improvement and patency as outlined in the Reporting Standards for Clinical Evaluation of New Peripheral Arterial Revascularization Devices.⁹

1. Given the current understanding of stenting the iliac artery following suboptimal angioplasty, please discuss the need for a randomized control trial to evaluate a new iliac stent system for a suboptimal indication.
2. If randomization is not considered necessary, please discuss the adequacy of a non-randomized concurrent control, historical control or the development of objective performance criteria (OPC) in the assessment of this technology.

Primary Stenting for the Treatment of Iliac Artery Occlusions

The TASC consensus noted the widespread use of primary stenting for the treatment of iliac artery occlusions but believed that this “practice needs to be subjected to rigorous clinical evaluations.” FDA has informed sponsors who are conducting randomized iliac trials that a separate registry study for an occlusion indication would be acceptable.

3. Please discuss the adequacy of a registry trial design, the use of a historical control or objective performance criteria and the length of follow-up in the assessment of stents for this application.

III. References

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4. Becker GJ, Palmaz JC, Rees CR et al. Angioplasty-induced dissections in human iliac arteries: management with Palmaz balloon-expandable intralumen stents. *Radiology* 1990; 176:31-38.
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8. TASC Working Group. Management of Peripheral Arterial Disease (PAD). *J Vasc Surg* 2000; S1-S296.
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