STENT GRAFT UPDATE

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Chapter 10

A PATHOLOGIST'S VIEW OF STENTING: BARE STENTS AND STENT GRAFTS

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The relatively high incidence of restenosis following arterial balloon angioplasty and the less frequent, but clinically important complication of abrupt vessel closure have directly lead to the development of intraarterial stents. A stent is a prosthetic intraluminal scaffolding device designed to maintain lumen patency in the setting of an underlying intrinsic or extrinsic disease state. Currently, stent placement is being increasingly utilized for the treatment of atherosclerotic coronary and peripheral vascular disease. In the heart, emergency coronary artery stent placement is used as a bailout procedure for abrupt or threatened artery closure due to arterial dissection following percutaneous transluminal coronary angioplasty (PTCA) and has reduced the need for urgent coronary bypass surgery [27, 33, 58]. The use of stents as primary therapy for atherosclerosis has gained wide acceptance, with reports of reduced restenosis rates in selected coronary lesions compared with PTCA [20, 21, 24, 62].

Keywords: *Stent, stent graft, artery, atherosclerosis, pathology*

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In the peripheral circulation, stents have become an accepted treatment for atherosclerosis of the iliofemoral arteries. Recently, stent grafts have been introduced for revascularization of atherosclerotic lesions as well as treatment for aneurysms of the aorta and its major branches, traumatic aneurysms, and arteriovenous fistulas [29]. With the presence of a graft in addition to a stent, it is hoped that there will be a reduction in restenosis that occurs secondary to neointimal growth from the surrounding vessels [17]. In the treatment of peripheral aneurysms, the purpose of the stent graft is to isolate the aneurysmal segment from blood flow thereby reducing the risk of aneurysmal rupture and embolization of atherothrombotic material from the aneurysm sac [17].

While stents reduce restenosis rates in carefully selected lesions [24, 63], in-stent restenosis remains a recognized clinical problem [31] and can be expected to increase in incidence as stenting becomes more frequent and is utilized in less ideal lesions [55]. Despite the tremendous expansion of the use of stents, there has been little published data on the pathology of stents deployed in human atherosclerotic arteries [2, 32, 67]. Most experimental studies of stenting in large animals employ normal, non-atherosclerotic vessels. In these studies, thrombus formation and acute inflammation have been identified early after stenting; smooth muscle cells and scattered chronic inflammatory cells predominate in the intima 2-4 weeks post-deployment [7]. When stents have been used in atherosclerotic models (mostly rabbit aorta and iliac arteries), early thrombus formation followed by smooth muscle cell proliferation has been observed [45, 50, 65]. Studies in normal arteries in experimental models suggest a relationship between the severity of arterial injury and subsequent neointima formation [51, 52, 59].

In this chapter, a general overview of stents and stent grafts will be presented. The pathology of stenting with and without grafts in experimental animals and in human atherosclerotic coronary arteries will be described to highlight stent-vessel wall interaction.

STENTS

The development of stents was pioneered in the experimental work of Dotter (stainless steel and nitinol wire coil) [19], Cragg (nitinol coil stent) [14], Maass (self-expanding stainless steel coil stents) [36], Gianturco (spring-loaded zigzag stainless steel and interdigitating coil stents) [53, 74], and Palmaz (stainless steel slotted tube stent) [43] which was followed by initial stent implants in humans by Sigwart (self-expanding mesh stent) [64].

The metals used in intravascular stents include surgical-grade stainless steel, nickel-titanium alloy (nitinol), titanium, and gold-coated stainless steel alloys [66]. Stainless steel has excellent tensile strength and is resistant to corrosion, but is relatively thrombogenic compared to the other metals. Titanium has high strength per unit density allowing for lighter devices, is corrosion-resistant, and has excellent biocompatibility. The shape memory property of nitinol allows for devices to be highly compressed and resume original shape upon warming. Nitinol exerts a strong radial expanding force and good biocompatibility. Gold coating of stainless steel adds visibility via enhanced radio-opacity and inhibits corrosion and infection. The basic designs of stents currently in use are the coil, slotted tube, mesh, and corrugated ring.

BIOLOGIC RESPONSES TO STENTING

Stent placement elicits the following sequence of local vascular events: thrombus formation and inflammation early after deployment with subsequent neointimal growth. These events are affected by changes in local shear stress, blood flow velocity, stent design, vessel injury, and the presence or absence of underlying pathology in the artery in which the stent is deployed. The biologic responses to stent grafts can be expected to be similar to those found after placement of bare stents.

Thrombosis

Damage to the vessel wall endothelial lining, either by a bare stent or stent graft, induces platelet activation and aggregation accompanied by fibrin deposition resulting in thrombus formation. The stent wires themselves produce turbulence proximal and distal to the strut resulting in focal low shear stress areas which can precipitate increased thrombus formation. Thrombus deposition on stent struts is a uniform finding following device deployment, but thrombus size may be affected by stent design [51]. Tubular slotted stents implanted in normal canine coronary arteries show thrombus composed of platelets, fibrin and trapped erythrocytes with an immature endothelial layer at 1 week [56]. In the porcine restenosis model, thrombus adjacent to mesh stent struts is composed of platelets, fibrin, acute inflammatory cells, and trapped erythrocytes [7]. In human atherosclerotic arteries, stent-associated thrombus is common, particularly early after stenting, consisting of platelets, fibrin, and inflammatory cells (Figure 1) and is seen with all stent designs evaluated (Palmaz-Schatz, Gianturco-Roubin, Gianturco-Roubin II, Multi-Link, and Wiktor) [22].

Inflammation

Stent placement invariably involves injury to the underlying artery by the stent itself, that is embedded in the arterial wall, and by adjunctive PTCA,

which is associated with plaque disruption (in atherosclerotic arteries) and medial dissection or rupture (in normal and atherosclerotic arteries). Plaque compression by stent struts is uniformly seen in experimental studies and in human arteries [2, 22, 45]. In animal models, acute inflammatory cells are observed at 24 hours post-stenting with macrophage infiltration by 7 days [7]. In human atherosclerotic coronary arteries, neutrophils accumulate in the first week after deployment, begin to decline in number by 1 month, and then are no longer seen beyond 30 days [22, 67]. The extent of inflammation increases with greater arterial injury and with the penetration of stent struts into the necrotic core of atherosclerotic plaques (Figure 2). Chronic inflammation (lymphocytes and macrophages) around stent struts is also commonly seen at all time points post-stenting and probably reflects the chronic inflammatory response already commonly seen in atherosclerotic lesions that is further augmented by the presence of the stent acting as a foreign body [22, 30].

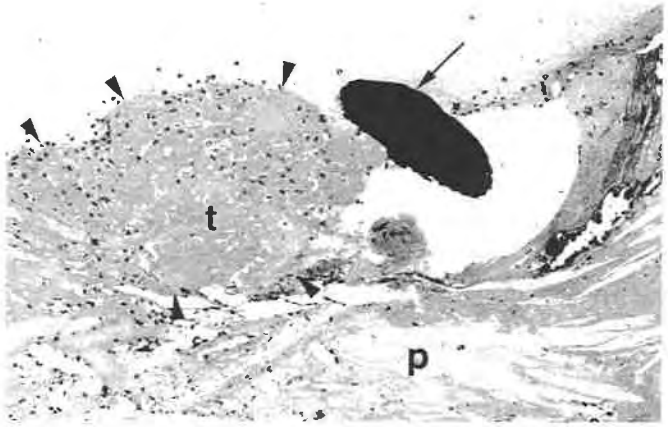

FIGURE 1

A fibrin and platelet-rich thrombus (t, outlined by arrowheads) containing inflammatory cells is present adjacent to an AVE stent strut (arrow) 8 hours post-deployment. A ruptured fibrous cap overlying the plaque (p) necrotic core is present below the strut. (Hematoxylin-eosin stain)

Cellular Proliferation

In the porcine coronary artery restenosis model, Carter et al showed maximal cellular proliferation 7 days after stent placement (18.6 ± 3.5%

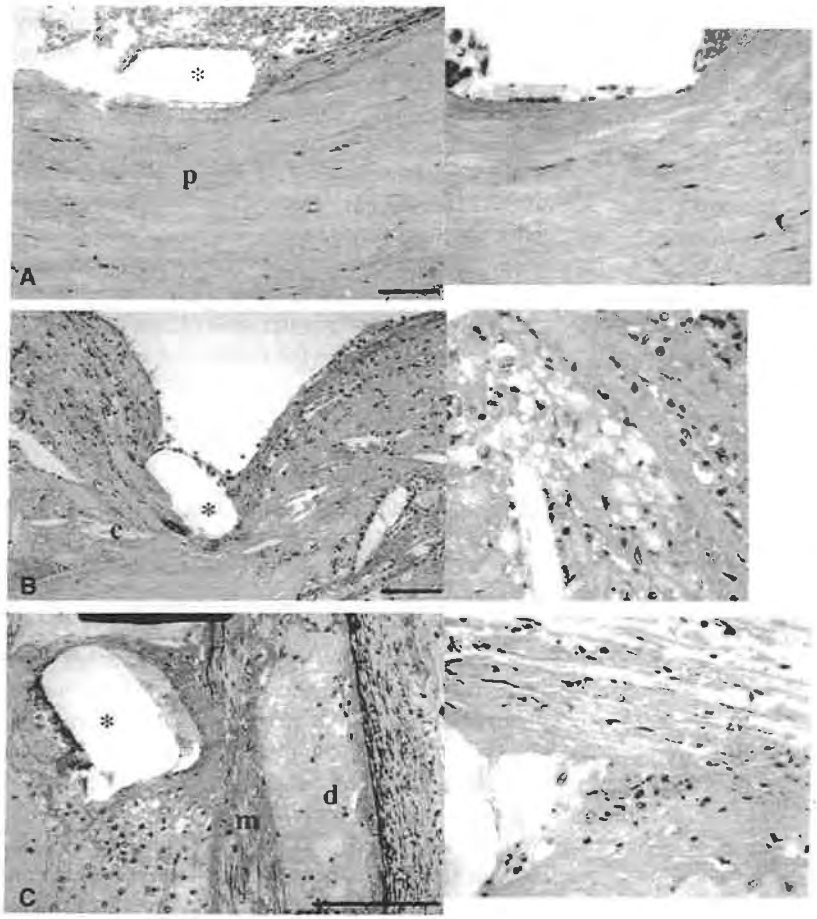

FIGURE 2

Arterial inflammation in coronary arteries with stents placed ≤3 days antemortem. Movat pentachrome stains are presented in the left panels with higher power hematoxylin-eosin from same section shown in the right panels. In A, few inflammatory cells are present adjacent to Palmaz-Schatz strut (*) in contact with fibrous plaque (p). In B, increased numbers of inflammatory cells are associated with a Palmaz Schatz strut (*) that penetrates into a necrotic core (c). In C, a Palmaz Schatz strut (*) is in contact with damaged media (m) with dissection (d) and numerous associated inflammatory cells. (A and B scale bars 0.10 mm; C scale bar 0.14 mm). *Reproduced with permission from reference 22.*

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