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Drug-Eluting Stents and Drug-Coated Balloons for Intracranial Atherosclerotic Disease: Reduced Restenosis, But Is It Enough?

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Symptomatic intracranial atherosclerotic disease (ICAD) carries a recurrent stroke risk that can approach 38% despite best medical therapy, and endovascular revascularization has long seemed an attractive adjunct to pharmacotherapy.[1] That attraction was tempered by the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) and Vitesse Intracranial Stent Study for Ischemic Stroke Therapy (VISSIT) trials, which found that percutaneous transluminal angioplasty and stenting (PTAS) with bare-metal or balloon-expandable stents carried an unacceptably high periprocedural risk relative to aggressive medical management alone.[2,3] Subsequent registries such as Wingspan Stent System Post Market Surveillance (WEAVE) and the China Angioplasty and Stenting for Symptomatic Intracranial Severe Stenosis (CASSISS) trial, conducted with more experienced operators and stricter patient selection, suggested that much of this excess risk was modifiable.[4,5] Even so, in-stent restenosis - historically approaching one-third of stented vessels - has persisted as a limitation largely independent of operator skill.

Drug-eluting technology, borrowed from coronary intervention, has been proposed to address this residual problem. Drug-eluting stents (DES) combine a permanent scaffold with an antiproliferative coating (sirolimus or paclitaxel), while drug-coated balloons (DCB) deliver the same class of agent to the vessel wall without leaving a permanent implant, a potentially attractive feature in a circulation of small, tortuous vessels with vulnerable perforating branches. Early feasibility work using repurposed coronary DES suggested acceptable short-term safety,[6] and a subsequent systematic review concluded that DES was a promising, if still under evaluated, option.[7] Intracranial-dedicated DES platforms, rather than repurposed coronary devices, have since entered clinical use,[8] and a large ongoing randomized trial (Drug Eluting Stenting and Aggressive Medical Treatment for Preventing Recurrent Stroke in Intracranial Atherosclerotic Disease Trial (DREAM-PRIDE), NCT04948749), enrolling approximately 792 patients, aims to establish whether DES combined with medical therapy reduces stroke recurrence compared with medical therapy alone.[9]

DCB has generated a parallel, and currently more mature, comparative literature. A 2026 meta-analysis of DCB in symptomatic ICAD reported a consistent restenosis-reduction signal across a still-modest evidence base,[10] and a separate 2025 meta-analysis pooling three studies and 213 patients comparing DCB directly with stent angioplasty found significantly lower odds of overall restenosis (odds ratio 0.22, 95% confidence interval 0.10-0.50) and of recurrent ischemic events (odds ratio 0.20, 95% confidence interval 0.07-0.63) with DCB.[11] The most rigorous test of this comparison to date is the DRug-coated Balloon for Endovascular treatment of sYmptOmatic intracranial stenotic Disease (DR. BEYOND) trial, a multicenter, randomized, open-label, blinded-endpoint study that assigned approximately 198 patients with high-grade (70-99%) symptomatic ICAD to DCB angioplasty or bare-metal (Wingspan) stenting, with six-month angiographic restenosis as the primary efficacy outcome and 30-day stroke or death as the primary safety outcome.[12]

Two caveats deserve emphasis. First, the evidence base for both DES and DCB remains dominated by small, retrospective, single-center cohorts using varying devices, drugs, and restenosis definitions, and powered around angiographic restenosis rather than clinical stroke recurrence; DR. BEYOND is a welcome exception, but it is a single trial comparing one DCB device with one bare-metal stent and does not address how DCB performs against DES. Second, and more fundamentally, drug elution addresses restenosis, a mid- to long-term phenomenon, but does not address the mechanisms - perforator occlusion, dissection, thromboembolism - that most plausibly account for the elevated 30-day stroke and

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death rates seen with intracranial stenting in SAMMPRIS and VISSIT. The improved periprocedural safety achieved with modern operator selection in WEAVE and CASSISS appears attributable to patient selection and technique rather than to drug coating. A favorable restenosis profile should therefore not be read as evidence that DES or DCB have solved the periprocedural risk problem that curtailed enthusiasm for PTAS a decade ago; the two questions are separable and, ideally, should be evaluated as co-primary endpoints within the same randomized trial.

Taken together, the available data support a genuine and biologically plausible reduction in angiographic restenosis with DES and DCB relative to bare-metal or uncoated approaches, but do not yet establish that either technology reduces clinical stroke recurrence, nor do they resolve the periprocedural safety concerns intrinsic to intracranial endovascular intervention. Until adequately powered randomized trials - ideally incorporating stroke or death as a co-primary endpoint alongside restenosis and including head-to-head comparison of DES against DCB - become available, these technologies should be regarded as promising adjuncts rather than default therapy, best offered within a shared decision-making framework to carefully selected patients who remain symptomatic despite maximal medical therapy. The ongoing DES trial (DREAM-PRIDE, NCT04948749) and the recently reported DR. BEYOND trial for DCB represent meaningful progress toward that goal.

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