Clin Neuroradiol (2016) 26:387–389
DOI 10.1007/s00062-016-0550-z

EDITORIAL

Intracranial Stenting in Germany

The Reimbursement Decision has been made, but the Scientific Debate Continues

Bernd Eckert[1]

Published online: 28 November 2016

The results of the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) [1] and the Vitesse Stent Ischemic Therapy trial (VISSIT) [2] have changed the current clinical and reimbursement practice in the endovascular treatment of intracranial atherosclerotic disease (ICAD) for stroke prevention. After the initial clinical alert, due to the termination of the SAMMPRIS trial on 11 April 2011 the National Institute of Neurological Disorders and Stroke (NINDS) restricted reimbursement of intracranial stenting with the Wingspan stent to patients:

- between 22 and 80 years of age,
- who have had two or more strokes despite aggressive medical treatment, if the most recent stroke occurred more than 7 days prior to a planned Wingspan treatment,
- who have a stenosis >70% and have shown a recovery from previous stroke (modified Rankin scale [mRS] $\leq$ 3).
- Furthermore, the Wingspan Stent System should *not* be used for the treatment of transient ischemic attacks (TIA).

In other words, the U.S. Food and Drug Administration (FDA) allows stenting in patients who have survived two (or more) strokes in good conditions (mRS $\leq$ 3), if the next stroke will not occur within 7 days after the most recent stroke. SAMMPRIS may justify the restriction of stenting as first line treatment in cases of symptomatic ICAD; however, ICAD patients develop clinical symptoms in a very heterogeneous manner with regard to the concerning etiology, severity of symptoms and variation in time. Hence, the SAMMPRIS trial listed 29 exclusion criteria, including tandem extracranial and intracranial stenosis, bilateral intracranial vertebral stenosis and progressive neurological signs within 24 h before stenting; however, the FDA generalized the SAMMPRIS results to the entire ICAD patient population cohort without evident proof of these indications [3]. Many experts especially criticized the criteria of two or more strokes, the strict interval of 7 days and the general exclusion of TIA.

In Germany, the public health insurances (*Gesetzliche Krankenversicherungen*, GKV) called for an investigation into intracranial stenting conducted by the Federal Joint Committee (*Gemeinsamer Bundesausschuss*, G-BA), the resolution authority within the German self-regulated healthcare system. The debate was influenced by political intentions far beyond the specific issue of intracranial stenting. Further, the decision-making process was influenced by the intended restriction of the approval for new "high-risk" devices in the context of the Medical Devices Act (*Medizinproduktegesetz*, MPG), and by a political discussion concerning the decision-making quorum within the G-BA itself. A two-year process of intense G-BA discussion between the GKV on the one side and the German Hospital Society (*Deutsche Krankenhausgesellschaft*, DKG) on behalf of the clinical community on the other, ended on 15 September 2016 with the following G-BA decision that reimbursement of ICAD stenting be restricted to the following indications:

a) Recurrent infarction despite aggressive medical treatment due to an intracranial stenosis >70%. The intervention should be performed within a sufficient time interval to the most recent clinical event.

✉ Bernd Eckert
b.eckert@asklepios.com

[1] Institut für Radiologie und Neuroradiologie, Asklepios Klinik Altona, Paul-Ehrlich-Str. 1, 22763 Hamburg, Germany

b) Patients with an acute occlusion due to a high-grade stenosis lacking alternative therapeutic options.

Compared to the FDA rules, this decision reflects some arguments put forward by the neuromedical experts (the German Society of Neuroradiology, DGNR and the German Society of Neurology, DGN); however, the DGNR and DGN still complain that patients with relapsing TIA/stroke without infarct detection in computed tomography (CT) or magnetic resonance imaging (MRI) cannot be stented, despite the fact that nearly one third of patients with nondisabling stroke do not show relevant findings on diffusion-weighted imaging MRI (DWI-MRI) [4]. This obvious gap between the decision and clinical realities particularly applies in the rare but very real cases of patients with relapsing symptoms due to severe bilateral vertebral or basilar artery stenosis [5].

To understand the G-BA decision we have to analyze the decision-making process. The Institute for Quality and Economy in the Public Health System (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*, IQWIG), an independent board exclusively serving for the G-BA, was instructed to provide a report on the scientific evidence of intracranial stenting in ICAD. According to German jurisdiction, this report is automatically assumed to be correct (*Richtigkeitsvermutung*). The review process for establishing evidence differed between institutional review and expert review. According to the IQWIG algorithm, the conclusions of the Rapid Report were drawn exclusively from the results of randomized clinical trials [6]. Beside the SAMMPRIS trial, three other low recruiting trials were cited, including a Chinese study of 35 patients, which was translated from Chinese into German language exclusively for this report [7]. In contrast, clinical experts tend to use well-designed observational studies involving homogeneous populations and often scrutinize the conclusions of poorly designed randomized trials [8]. The IQWIG Rapid Report excluded patients with hemodynamic stenosis from its conclusions, especially those in unstable condition, because these patients were namely excluded in the studies cited. This exclusion reveals the general dilemma concerning the variety of patients who were excluded from the trials. The therapeutic concept in these patients is still below the evidence level. The institutional experts stressed the potential harm of intracranial stenting in general, while the neuromedical experts underlined its potential benefits under specific conditions. The neuromedical experts were required to provide evidence in favor of stenting these patients, but the institutional experts did not accept the results of any observational trials below the randomized level.

Unfortunately, this means that if there is a lack of evidence from randomized clinical trials, the institutional review may overrule expert opinion in the institutional process. To avoid a growing gap between institutional review and expert opinions we have to provide further study results. In the context of intracranial stenting the next step will be the technical optimization of the procedure and the definition of subgroups who might benefit from stenting; however, the G-BA decision impedes further studies beyond the defined restrictions, especially in the subgroup of patients with hemodynamic disorders. The AcandiS Stenting of Intracranial STENosis regisTry (ASSISTENT) may represent a promising start. However, in the approval process for this new stent system the notified body demanded instructions for use (*Zweckbestimmung*) that are identical to those for the FDA Wingspan [9]. Thus the centers participating in the ASSISTENT registry now have to act in the twilight zone between the G-BA decision and the instructions for use. On the other hand, the strict indications also represent an opportunity to increasingly put neuroradiologists at the helm of further research in this field. As such, we can view it as a challenge to renew our efforts and to carefully reassess the ongoing search for evidence.

References

1. Derdeyn CP, Chimowitz MI, Lynn MJ, Fiorella D, Turan TN, Janis LS, Montgomery J, Nizam A, Lane BF, Lutsep HL, Barnwell SL, Waters MF, Hoh BL, Hourihane JM, Levy EI, Alexandrov AV, Harrigan MR, Chiu D, Klucznik RP, Clark JM, McDougall CG, Johnson MD, Pride GL Jr, Lynch JR, Zaidat OO, Rumboldt Z, Cloft HJ. Stenting and aggressive medical management for preventing recurrent stroke in Intracranial stenosis trial investigators. Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial. Lancet. 2014;383(9914):333–41.
2. Zaidat OO, Fitzsimmons BF, Woodward BK, Wang Z, Killer-Oberpfalzer M, Wakhloo A, Gupta R, Kirshner H, Megerian JT, Lesko J, Pitzer P, Ramos J, Castonguay AC, Barnwell S, Smith WS, Gress DR, VISSIT Trial Investigators. Effect of a balloon-expandable intracranial stent vs medical therapy on risk of stroke in patients with symptomatic intracranial stenosis: the VISSIT randomized clinical trial. JAMA. 2015;313(12):1240–8.
3. FDA. Neurological Devices Panel of the Medical Devices Advisory Committee Meeting Announcement. March 23. Silver Spring: FDA; 2012.
4. Makin SD, Doubal FN, Dennis MS, Wardlaw JM, Makin SD, Doubal FN, Dennis MS, Wardlaw JM. Clinically confirmed stroke with negative diffusion-weighted imaging magnetic resonance imaging: longitudinal study of clinical outcomes, stroke recurrence, and systematic review. Stroke. 2015;46(11):3142–8.
5. Maier IL, Karch A, Lipke C, Behme D, Mpotsaris A, Kabbasch C, Liebig T, Faymonville A, Reich A, Nikoubashman O, Buhk JH, von Schoenfeld P, Weber W, Mikolajczyk RT, Bähr M, Knauth M, Kallenberg K, Liman J. Transluminal angioplasty and stenting versus conservative treatment in patients with symptomatic basilar artery stenosis: Perspective for future clinical trials. Clin Neuroradiol. 2016; doi:10.1007/s00062-016-0528-x.
6. IQWiG. Stents zur Behandlung intrakranieller arterieller Stenosen – Rapid Report. 2014, p N14–01.
7. Gao HH, Gao LB. Stent implantation combined with drug therapy versus pure drug therapy for symptomatic severe stenosis of middle cerebral artery: a randomized and comparative study. J Interv Radiol (China). 2013;22(2):89–92.

8. Fiehler J. Evidenzbasierte Medizin in der interventionellen Neuroradiologie. Clin Neuroradiol. 2015;25(Suppl 2):103–8.
9. Möhlenbruch MA, Pfaff J, Herweh C, Bösel J, Rizos T, Nagel S, Ringleb PA, Bendszus M, Pham M. One-pass endovascular treatment of intracranial atherosclerotic stenosis with a novel PTA balloon and self-expanding microstent. Neuroradiology. 2016;58(9):893–9.