IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Stents for the treatment of intracranial artery stenosis[1]

Executive Summary

[1] Translation of the executive summary of the rapid report N14-01 *Stents zur Behandlung intrakranieller arterieller Stenosen* (Version 1.0; Status: 10 September 2014). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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This report was prepared in collaboration with external experts.

The responsibility for the contents of the report lies solely with IQWiG.

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Executive summary

On 28 February 2014 the Federal Joint Committee (G-BA) wrote to the Institute for Quality and Efficiency in Health Care (IQWiG) to commission the assessment of stents for the treatment of intracranial artery stenosis.

Research question

The aim of this investigation was to assess the benefit of stent placement in intracranial vessels in patients with symptomatic intracranial artery stenosis. As comparison intervention any other treatment option was used. Patient-relevant outcomes were considered.

Methods

To process the research question mentioned above, only randomized controlled trials (RCTs) were included that investigated stents in intracranial stenosis with regard to patient-relevant outcomes.

For this purpose, a systematic literature search was performed in the following databases: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (Clinical Trials). In addition, a search for relevant systematic reviews took place in the databases MEDLINE and EMBASE in parallel with the search for relevant primary studies. Searches were also conducted in the databases Cochrane Database of Systematic Reviews (Cochrane Reviews), Database of Abstracts of Reviews of Effects (Other Reviews), and the Health Technology Assessment Database (Technology Assessments). The search was conducted on 14 April 2014.

In addition, systematic reviews and publicly accessible trial registries were searched, and publicly accessible trial registries and approval documents as well as documents sent by the G-BA were also screened.

Moreover, the websites of the manufacturers Obex, Stryker, BostonScientific and Biotronik were searched for relevant studies, and the authors of relevant study publications were contacted in order to clarify important questions.

The selection of relevant studies was performed by 2 reviewers independently of each other for the result from the bibliographic literature search, from the search in publicly accessible trial registries and from documents sent by the G-BA. The selection of relevant studies from the remaining search sources was performed by one reviewer and checked by a second reviewer.

Data extraction was conducted in standardized tables. To evaluate the certainty of results, the risk of bias at study and outcome level was assessed and rated as low or high respectively. The results of the individual studies were described, organized by outcomes.

Results

A total of 4 RCTs that included patients with symptomatic intracranial artery stenosis were identified. In 3 studies (SAMMPRIS, Miao 2012 and Gao 2013), percutaneous transluminal angioplasty and stenting (PTAS) and medical treatment was compared with medical treatment. In the 4th study (Qureshi 2013), PTAS and medical treatment was compared with percutaneous transluminal angioplasty without stenting (PTA) and medical treatment. All studies had a high risk of bias both at study and at outcome level.

Medical treatment consisted of dual antiplatelet therapy (clopidogrel and acetylsalicylic acid) in all studies. This dual antiplatelet therapy is not approved in Germany for the therapeutic indication "stroke". No data were available for approval-compliant medical treatment.

PTAS and medical treatment versus medical treatment

For the outcomes "all-cause mortality" and "cerebrovascular mortality", only data from the SAMMPRIS study were available. In total, of the 224 patients in the PTAS group, and of the 227 patients in the group with medical treatment, 13 patients (6%) died in each group. 6 of these (2.7%) died from their cerebrovascular disease in the PTAS group, and 2 patients (0.9%) in the comparator group. In summary, there was no hint of benefit for the treatment group with PTAS and medical treatment for the outcomes "all-cause mortality" and "cerebrovascular mortality".

For the outcome "stroke", only the data from the SAMMPRIS study were evaluable because Miao 2012 and Gao 2013 only recorded strokes in the territory of the treated artery or in the affected hemisphere and did not present the overall rate of stroke.

The rate of stroke in the total observation period (median: 32.4 months) was differentiated from periprocedural stroke (within 30 days of the intervention) for the report.

In the SAMMPRIS study, stroke occurred in 59 patients (26.3%) in the PTAS group, and in 42 patients (18.5%) in the group with only medical treatment during the total observation period. The difference was statistically significant ($p = 0.048$, odds ratio = 1.58; 95% confidence interval [CI] [1.01; 2.46]). A hint of harm to the disadvantage of the PTAS group can therefore be derived.

If one differentiates between the types of stroke, there was no statistically significant difference between the groups for the overall rate of ischaemic stroke (PTAS group 21.4%, group with only medical treatment: 18.1% $p = 0.425$, odds ratio 1.24; [95% CI: 0.78; 1.97]). There was a statistically significant difference between the groups in the overall rate of haemorrhagic stroke ($p = 0.003$, odds ratio 11.67; CI [1.49; 91.18]). A total of 11 strokes (4.9%) occurred in the PTAS group. A total of 1 haemorrhagic stroke (0.4%) occurred in the group with only medical treatment. Due to the effect size, an indication of an effect to the disadvantage of the PTAS group can be derived. There was no statistically significant

difference between the groups in the SAMMPRIS study with regard to the outcome "severe stroke" (PTAS group 6.7%, group with only medical treatment 7% p = 0.912).

In the SAMMPRIS study, periprocedural ischaemic stroke occurred in 23 patients (10.3%) in the PTAS group, and in 12 patients (5.3%) in the group with only medical treatment. The difference was statistically significant (p = 0.049, odds ratio = 2.05; 95% CI [0.99; 4.23]) to the disadvantage of the PTAS group. Hence a hint of an effect can be derived to the disadvantage of the group who received PTAS and medical treatment. Moreover, in the SAMMPRIS study, periprocedural haemorrhagic stroke occurred in 10 patients (4.5%) in the group who received PTAS and medical treatment. No haemorrhagic stroke occurred in the comparator group with medical treatment (p = 0.001, odds ratio = 22.27; CI [1.30; 382.42]). Due to the effect size, an indication of an effect can be determined to the disadvantage of the group who received PTAS and medical treatment.

With regard to the outcome "repeated revascularization of the target vessel or other vessels", one event was reported in the group with medical treatment and PTAS in the Miao 2012 study. The difference was not statistically significant so that no hint of a benefit can be determined for the treatment group that received medical treatment and PTAS.

Relevant data on adverse effects and treatment complications were reported in the SAMMPRIS study. More bleeding events that did not result in stroke were reported in the PTAS group (16 patients [7%] versus 9 patients [4%]); however, this difference was not statistically significant (odds ratio = 1.86; 95% CI [0.81; 4.31]). Myocardial infarction occurred in 5 patients (2%) in the PTAS group, and in 9 patients (4%) in the group with only medical treatment. However, this numerical difference to the disadvantage of the group with medical treatment was not statistically significant (odds ratio = 0.55; 95% CI [0.18; 1.68]). In summary, there was no hint of harm for the treatment group that received medical treatment and PTAS.

No data were reported on further patient-relevant outcomes, particularly hospitalization, health-related quality of life, physical endurance and performance of daily activities or ability to work.

PTAS and medical treatment versus PTA and medical treatment

For the comparison of PTAS and medical treatment versus PTA and medical treatment, data could only be extracted from Qureshi 2013. Due to the small sample size (n = 18) and the low number of events, the Institute did not perform its own calculation of effect estimate and CI for any of the outcomes.

With regard to the outcomes "all-cause mortality" and "cerebrovascular mortality" as well as "stroke", one event (11.1%) was reported in the PTA group in Qureshi 2013. With regard to the outcome "repeated revascularization of the target vessel and other vessels", one event occurred in the PTAS group.

In Qureshi 2013, data on the outcome "dependence on others or requiring care" were available for the modified Rankin Scale. The scores of the 2 treatment groups were comparable.

Hence no hint of benefit or harm of the 2 treatment options could be derived for any of these outcomes.

No data were reported on further patient-relevant outcomes, particularly hospitalization, health-related quality of life, physical endurance and performance of daily activities or ability to work.

Conclusions

In the comparison of PTAS and medical treatment versus medical treatment, there was a hint of greater harm in the PTAS group for the outcome "stroke". This harm particularly resulted from the considerable increase in the rate of periprocedural stroke. For all other patient-relevant outcomes considered, no hint of benefit or harm of PTAS and medical treatment in comparison with medical treatment could be determined.

The available studies were conducted with dual antiplatelet therapy consisting of acetylsalicylic acid and clopidogrel (medical treatment). This combination is not approved in Germany for the secondary prevention of stroke. No study data were available for the drug treatment approved in Germany.

Keywords: stents, intracranial arteriosclerosis, benefit assessment, systematic review

The full report (German version) is published under https://www.iqwig.de/de/projekte-ergebnisse/projekte/nichtmedikamentoese-verfahren/n14-01-stents-zur-behandlung-intrakranieller-arterieller-stenosen-rapid-report.5989.html#overview.