Does Carotid Stent Cell Design Matter?

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Background and Purpose—Carotid stent cell design has recently been suggested to be a determinant of periprocedural and early postprocedural neurologic complications. We investigated the impact of closed- versus open-cell stent design on neurologic adverse events and mortality after carotid artery stenting.

Methods—We studied 1684 consecutive patients (1010 asymptomatic, 674 symptomatic) from 10 European centers who underwent carotid artery stenting with either closed-cell (n=859, 51%) or open-cell (n=825, 49%) design stents. Rates of transient ischemic attack, stroke, and death on the day of the procedure (acute events) and from day 1 to day 30 after the procedure (subacute events) were analyzed (95% CIs).

Results—Combined transient ischemic attack, stroke, or death rates, and stroke or death rates within 30 days of treatment were 6.1% (95% CI, 5.0 to 7.2) and 3.1% (95% CI, 2.3 to 3.9) for the closed-cell design versus 4.1% (95% CI, 3.2 to 5.0) and 2.4% (95% CI, 1.7 to 3.1) for the open-cell design stents (P=0.077, P=0.38), respectively, without significant differences in asymptomatic and symptomatic patients. By propensity-score–adjusted multivariable analysis, the open-cell carotid stent design was not associated with a differential risk for combined acute and subacute neurologic complications compared with closed-cell stents (adjusted odds ratio=0.84, P=0.53). When analyzed separately, the risk for acute events on the day of the procedure (adjusted odds ratio=0.83, P=0.57) and the risk for subacute events at days 1 to 30 (adjusted odds ratio=1.61, P=0.51) also were not significantly different between the groups.

Conclusions—Current data do not support the superiority of a specific carotid stent cell design with respect to neurologic complications, stroke, and mortality risk. (Stroke. 2008;39:905-909.)

Key Words: stents ■ carotid artery

The safety and efficacy of carotid artery stenting (CAS) remain debatable, particularly since recent randomized trials revealed unfavorably high complication rates within the endovascular treatment arms.1,2 Nevertheless, several experienced centers continue to report excellent low rates of neurologic adverse events from thoroughly monitored CAS registries.3–6 Discrepancies between studies not only may be due to the effects of a learning curve and operator experience7 but also may arise from device-related differences. In this context, Bosiers et al8 recently reported a potential impact of carotid stent cell design on the risk for neurologic complications. Different carotid stent designs yield different vessel wall scaffolding and plaque stabilization properties, depending on the size of the free cell area between the struts of stents. Stents with small cell sizes have a dense, metallic mesh and therefore may provide more effective plaque coverage and reduce the risk for embolization of particles compared with stents with large cell sizes. Currently available “closed-cell design stents” are characterized by small free cell areas between the metallic struts compared with “open-cell design stents,” which leave larger gaps uncovered; typical examples are given in Figure 1. Notably, in the nonrandomized study by Bosiers et al,8 patients who received closed-cell carotid stents exhibited a substantially lower risk for subacute neurologic events, particularly when symptomatic patients were treated, supporting the hypothesis that stents with a small free cell area and dense, metallic meshes improve the safety of CAS. As a shortcoming, however, closed-cell design stents are less flexible and less conformable to carotid anatomy and therefore may be even disadvantageous in certain patients.

In the absence of any randomized evidence, we reinvestigated the effect of carotid stent cell design on acute and subacute neurologic events in an independent, contemporary, and large patient series treated in 10 centers across Europe.
Methods

Study Design
We included consecutive, previously unpublished patient series treated at 10 European centers in Austria, Belgium, Italy, and the United Kingdom from periods between 2002 and 2007. Symptomatic patients with ≥60% stenosis and asymptomatic patients with ≥80% stenosis by NASCET angiographic criteria treated with self-expanding carotid stents were eligible. Only patients treated for atherosclerotic disease were eligible. No other specific exclusion criteria were applied. Baseline and follow-up data in all centers were recorded prospectively according to standardized protocols. Pooling of the data and analyses were done retrospectively. Registries were approved by institutional ethics committees.

The study end point was the occurrence of neurologic events until 30 days after the procedure, including transient ischemic attack (TIA), minor and major stroke, and death. Frequencies (95% CIs) are reported separately for acute events on the day of the procedure and for subacute postprocedure events at days 1 to 30, as well as for symptomatic and asymptomatic patients. Occurrence of neurologic events until discharge was assessed by independent neurologists at all centers and confirmed by mandatory cerebral imaging (computed tomography or magnetic resonance imaging). Additional routine follow-up at 30 days was done by the treating physicians; neurologic exams were initiated in patients with suspected events.

Definition of End Points
Uniform definitions of end points were applied across all centers. TIA was defined as a focal neurologic deficit persisting for <24 hours. Minor stroke was defined as a neurologic deficit resulting in a permanent impairment equivalent to a modified Rankin Scale score of ≤2. Major stroke was defined as a permanent neurologic deficit rated on the modified Rankin Scale as ≥3.

Patient Data
Demographic and clinical data, including traditional cardiovascular risk factor profile, presence of cardiovascular comorbidities, and baseline characteristics of carotid disease including side, length, and degree of the lesion by angiography, were available in all registries. NASCET angiographic criteria were uniformly applied to assess the degree of stenosis. Preprocedure symptoms were assessed by independent neurologists in all centers to define a symptomatic or asymptomatic stenosis. Postprocedure neurologic evaluation before discharge also was done by neurologists. Data were recorded by 2 independent observers per center, of whom 1 could be the interventionist. Inconsistencies between observers were resolved by consensus.

CAS Procedures
Cerebral protection was available in all centers, and all centers had unrestricted access to closed- and open-cell carotid stents during the entire study period. Procedures were done uniformly via transfemoral access with either a long sheath (6F) or a guiding catheter (8F) with the use of rapid-exchange devices. Interventional strategies were closely comparable, including routine baseline and final carotid and intracranial angiograms in the same projections. Predilatation was done in patients with tight lesions according to the discretion of the interventionist; postdilatation was done routinely in all centers, usually with the postdilatation balloon slightly undersized compared with the distal nondiseased vessel diameter. Periprocedure medication included heparin in doses between 5000 and 10 000 IU, atropine, and fluids on demand. All patients were on dual antiplatelet therapy with aspirin 100 mg daily and clopidogrel 75 mg daily; the latter was started at least 3 days before the procedure. Otherwise, a loading dose of 300 mg was administered 1 day before CAS. Dual antiplatelet therapy was maintained in all centers for at least 1 month.

Statistical Methods
We used Fisher’s exact tests and Mann–Whitney U tests for univariate analyses, as appropriate. Multivariable propensity-score-adjusted logistic-regression models were applied to assess the association between carotid stent cell design and neurologic complications. Calculations were performed with Stata (release 8.0; Stata Corp, College Station, Tex).
Results

We included 1684 of 1782 consecutive patients; 98 patients (5%) had to be excluded owing to incomplete data. One thousand ten patients were asymptomatic and 674 were symptomatic. Cerebral protection was used in 88% (filter devices in 1403 patients, distal balloon occlusion in 9 patients, and proximal balloon occlusion in 62 patients). Closed-cell stents were implanted in 51% (n=859), including the Wallstent (n=830), XAct (n=18), and Nexstent (n=11), and open-cell stents in 49% (n=825), including the Acculink (n=616), Precise (n=164), Protégé (n=23), Sinus (n=10), and Vivexx (n=12; the Table).

Within 30 days after treatment, 49 TIAs (2.9%) and 34 subacute (2.0%), 12 major (0.7%), and 1 fatal (0.05%) strokes occurred. TIAs and minor, major, and fatal strokes after treatment with closed-cell design stents occurred in 35 patients (4.1%), 19 patients (2.2%), 7 patients (0.8%), and 1 patient (0.01%), respectively, and after treatment with open-cell design stents in 14 patients (1.7%), 15 patients (1.8%), 5 patients (0.6%), and 0 patients, respectively.

Combined acute and subacute TIA, stroke, or death rates, and stroke or death rates were 6.1% (95% CI, 5.0 to 7.2) and 3.1% (95% CI, 2.3 to 3.9) with closed-cell versus 4.1% (95% CI, 3.2 to 5.0) and 2.4% (95% CI, 1.7 to 3.1) with open-cell stents (P=0.077, P=0.38), respectively, without significant differences between asymptomatic and symptomatic patients. However, by univariate analysis, acute event rates on the day of the procedure were lower for open-cell design stents, whereas subacute events at days 1 to 30 occurred less frequently with closed-cell design stents (Figure 2).

By propensity-score–adjusted multivariable analysis, the open-cell carotid stent design was not associated with a differential risk for combined acute and subacute neurologic complications compared with closed-cell stents (odds ratio [OR]=0.84; 95% CI, 0.48 to 1.46, P=0.53). Consistently, when analyzed separately, the risk for acute events (OR=0.83; 95% CI, 0.43 to 1.59, P=0.57) and the risk for subacute events (OR=1.61; 95% CI, 0.40 to 6.48, P=0.51) were not significantly different between the 2 groups. Final models were adjusted for age, sex, smoking, hyperlipidemia, diabetes, center and year of treatment, degree of stenosis, symptoms, de novo versus restenotic lesion, use of cerebral protection, predilatation before stenting, and for the propensity to receive an open- versus closed-cell design stent.

We then performed 2 sets of sensitivity analyses. First, we excluded patients with restenotic lesions (n=129) to account for the fact that treatment of neointimal hyperplasia due to a previous stent or an endarterectomy might be associated with a differential risk for complications than treatment of de novo atherosclerotic lesions. Effect sizes and 95% CIs for open-versus closed-cell stents of the fully adjusted propensity score models for combined acute and subacute neurologic complications (OR=0.86; 95% CI, 0.44 to 1.58, P=0.65), acute events (OR=0.85; 95% CI, 0.40 to 1.68, P=0.66), and subacute events (OR=1.57; 95% CI, 0.37 to 7.08, P=0.72) remained almost unchanged when we analyzed the 1555 patients with de novo lesions.

Table. Baseline and Interventional Data for 1674 Patients Undergoing CAS With Either Closed- or Open-Cell Design Stents

<table>
<thead>
<tr>
<th></th>
<th>Closed-Cell Design (n=859, 51%)</th>
<th>Open-Cell Design (n=825, 49%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>72 (64 to 77)</td>
<td>71 (64 to 78)</td>
<td>0.34</td>
</tr>
<tr>
<td>Male sex</td>
<td>599 (70)</td>
<td>524 (64)</td>
<td>0.007</td>
</tr>
<tr>
<td>Current smokers</td>
<td>211 (25)</td>
<td>310 (38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>682 (79)</td>
<td>516 (63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>678 (79)</td>
<td>673 (82)</td>
<td>0.21</td>
</tr>
<tr>
<td>Diabetes</td>
<td>269 (31)</td>
<td>263 (32)</td>
<td>0.84</td>
</tr>
<tr>
<td>Symptomatic stenosis</td>
<td>293 (34)</td>
<td>381 (46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ipsilateral degree of stenosis</td>
<td>85 (80 to 90)</td>
<td>85 (80 to 90)</td>
<td>0.63</td>
</tr>
<tr>
<td>Contralateral degree of stenosis</td>
<td>30 (20 to 60)</td>
<td>30 (20 to 50)</td>
<td>0.23</td>
</tr>
<tr>
<td>Restenosis after</td>
<td></td>
<td></td>
<td>0.081</td>
</tr>
<tr>
<td>Endarterectomy</td>
<td>40 (5)</td>
<td>70 (9)</td>
<td></td>
</tr>
<tr>
<td>Stent</td>
<td>12 (1)</td>
<td>7 (1)</td>
<td></td>
</tr>
<tr>
<td>Cerebral protection</td>
<td>744 (84)</td>
<td>730 (89)</td>
<td>0.27</td>
</tr>
<tr>
<td>Predilatation before stenting</td>
<td>674 (79)</td>
<td>432 (52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postdilatation after stenting</td>
<td>854 (99)</td>
<td>814 (99)</td>
<td>0.14</td>
</tr>
<tr>
<td>No. of stents</td>
<td></td>
<td></td>
<td>0.69</td>
</tr>
<tr>
<td>1</td>
<td>812 (95)</td>
<td>806 (98)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>31 (4)</td>
<td>15 (2)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Nominal diameter of stents, mm</td>
<td>8 (7 to 9)</td>
<td>8 (6 to 10)</td>
<td>0.18</td>
</tr>
<tr>
<td>Nominal length of stents, mm</td>
<td>30 (30 to 40)</td>
<td>30 (30 to 40)</td>
<td>0.87</td>
</tr>
<tr>
<td>Technical success (residual stenosis &lt;30%)</td>
<td>838 (98)</td>
<td>815 (99)</td>
<td>0.070</td>
</tr>
</tbody>
</table>

Data are given as median (interquartile range) or counts (%).
Second, to account for the fact that different subtypes of stents were grouped within the open- and closed-cell groups, we compared the 2 most frequently used products, the Wallstent (830 of 859 of closed-cell stents) versus the Acculink (616 of 825 of open-cell stents). Similarly, effect sizes and 95% CIs for the comparison of Acculink versus Wallstents by the fully adjusted propensity score models for combined acute and subacute neurologic complications (OR = 0.89; 95% CI, 0.40 to 1.88, \( P = 0.84 \)), acute events (OR = 0.88; 0.36 to 1.91, \( P = 0.69 \)), and subacute events (OR = 1.48; 95% CI, 0.31 to 8.65, \( P = 0.61 \)) were not significantly different from the entire patient sample.

**Discussion**

Based on the study by Bosiers et al., an ongoing discussion on the potential superiority of the closed-cell carotid stent design has been initiated. Undoubtedly, the hypothesis that increased wall coverage by a closed-cell design may yield additional stabilization of the plaque and thus increase the procedure’s safety seems appealing. Unfortunately, this hypothesis can be proven scientifically only by a large-scale, randomized trial, as selection bias for specific stents in specific clinical settings otherwise certainly plays a major role: Closed-cell stents are known to be more rigid and are therefore more likely to be used in straight morphologies. In contrast, open-cell design stents are flexible; kinked lesions are ideally treated with these devices. By the nature of carotid morphology, treatment of straight and kinked lesions may have a differential complication risk, thus potentially introducing relevant bias. Accordingly, in the present study, several baseline imbalances between the treatment groups have to be acknowledged. Most important, the proportion of symptomatic patients was lower in favor of closed-cell design stents. Nevertheless, we did not observe a clear advantage of closed-cell stents.

In contrast to Bosiers et al., we included data from a larger number of centers across Europe, and only recently treated patients (starting in 2002) were eligible. This may have partly eliminated the impact of a center-specific treatment strategy and problems of a learning curve. In a further comparison of the

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**Figure 2.** Rates of TIA, stroke, and death in patients undergoing CAS with closed-cell or open-cell design stents. Event rates are given separately for asymptomatic and symptomatic patients; for the day of the procedure (day 0); and for days 1 to 30 after the procedure.
dataset of Bosiers et al and the current findings, a substantially lower rate of overall neurologic complications was observed in the study of Bosiers et al (2.8%), mainly consisting of TIA’s, and two thirds of the events occurred subacutely after the procedure. In contrast, we recorded a 5.7% overall TIA, stroke, or death rate with only <1% of the events occurring in the subacute phase. This may reflect differences in treatment strategies between centers and countries; eg, whether aggressive postdilatation was done, whether stents were oversized to a certain proportion, and which patients were selected for the procedures, or otherwise these differences may have arisen from the retrospective nature of the 2 studies and their limitations, making a direct comparison difficult to interpret.

If one examines the findings of the sensitivity analysis by directly comparing the Wallstent (as the prototype of the closed-cell design concept) with the smallest free cell area (1.08 mm²) versus the Acculink stent system, which has the largest free cell area (11.48 mm²) of all open-cell design stents, the observed differences became even smaller than in the entire patient sample. This suggests that other stent-related factors in addition to wall coverage may be relevant determinants for procedural and postprocedural complications; eg, for the Wallstent, a “scissor effect” during stent deployment has been described. This refers to the fact that the angle between the stent struts changes during expansion and foreshortening of the stent, thereby potentially cutting off parts of the atherosclerotic plaque and potentially mobilizing embolic material.

Although our current data do not support the view that currently available closed-cell design stents improve the safety of CAS by providing increased wall coverage, the concept of optimized plaque stabilization remains promising. In this context, it has been speculated that covered stents may achieve an immediate and complete mechanical stabilization of the carotid plaque, thus minimizing the risk for dislodging debris and distal embolization. Experimentally, covered stents have proved to be efficient in ex vivo flow models, and an initial clinical experience in atherosclerotic carotid stenosis also seemed promising. Consistently, in a previous randomized trial, we demonstrated a significantly reduced rate of microembolic signals during CAS by transcranial Doppler with the covered Symbiot stentgraft compared with Wallstents. Unfortunately, the stentgraft revealed an excessively high restenosis rate of ~40% at 6 months and the trial had to be stopped. The favorable procedural data and transcranial Doppler findings with the stentgraft still seem a proof of concept worth further investigation.

Limitations

Several limitations of the present study have to be recognized. First, data were taken from nonrandomized registry datasets. Registries imply the likelihood that not all adverse outcomes were recorded. Lack of an external audit of data completeness and accuracy also has to be acknowledged. Nevertheless, the latter biases should be equally balanced regardless of which type of stent was used and may have been minimized by the thorough data-acquisition processes within the registries (2 observers entering the data, routine neurologic examinations). Addressing the lack of randomization, we tried to account for baseline imbalances between the 2 groups by multivariable analysis and calculation of a propensity score. Selection bias still may have influenced our findings.

Second, different devices are grouped within the categories of closed-cell and open-cell design stents. However, no substantial differences between these crude categories were observed, and the sensitivity analysis that directly compared Wallstents versus Acculink stents also showed no significant differences; device-specific complication risks still may exist but likely can only be detected in very large, randomized, head-to-head comparisons of different devices.

Conclusions

Current data do not support the superiority of a specific carotid stent cell design with respect to neurologic complications, stroke, and mortality risk.

Disclosures

None.

References

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