Comparison of the Outcome and Efficacy of Single-Layer versus Dual-Layer Mesh Stent among Carotid Stenosis Patients Attending a Tertiary Care Setting—A Prospective Observational Study

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Abstract

Introduction The effect of stent design whether single-layer or double-layer on long-term durability of carotid artery stenting (CAS) is unknown. The aim of this article was to compare the clinical outcome and efficacy of single-layer versus dual-layer mesh stent for CAS among carotid stenosis patients.

Methods A prospective observational study was conducted among 41 consecutive patients, who underwent CAS procedures between November 2019 and November 2021. Procedural data and outcomes for patients treated with the single-layer stent ($n = 19$patients) and double-layer stent ($n = 22$) were compared. Procedural efficacy and complications were considered as primary outcome variable. SPSS version 22 was used for statistical analysis.

Results Mean age of study population in dual-layer stents group was 63.86 ± 11.08 years and it was 61.47 ± 8.26 years in single-layer stent group. There was no statistically significant difference between two groups with age, stenosis, side of stenosis, prestenting angioplasty, and poststenting angioplasty (p-value >0.05). Out of 22 participants with dual-layer stent, only one (4.5%) participant experienced five episodes of transient ischemic attack in last 1 month. Both clinical and associated complaints were more in dual-layer group compared with single layer. One (5.26%) participant in single-layer group had reclusion/restenosis at 30 days. Majority in single-(57.8%) and double-layer (63.64%) stents group showed modified Rankin Scale score of 0.

Conclusion Restenosis after CAS occurred less frequently in patients treated with double-layer mesh when compared with single-layer stent. However, both stents were equally effective at preventing peri procedural complications.

Keywords
- carotid artery
- ischemic
- stenosis
- stroke
- cardiovascular diseases

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Introduction

Worldwide, cardiovascular diseases (CVDs) are considered among the leading causes of mortality. Compared with Europeans, Indians are affected a decade earlier in their most productive midlife years. Nearly 52% of deaths in India before the age of 70 years are due to CVD, whereas 23% of deaths happen in Western countries.[1] Increased prevalence of CVD and its related risk factors had led to this epidemiological transition in India. In 2016, 54.5 million was the estimated prevalence of CVDs. Presently, more than 80% of deaths in India are because of CVDs with ischemic heart disease and stroke.[2]

Stroke is a major global public health problem and is a common among various CVDs. Global Burden of Diseases considers stroke as the second leading cause of death and major cause of disability worldwide.[3] Almost 20% of strokes across the globe are due to atherosclerotic stenosis of the extracranial carotid artery. The diagnosis and treatment of carotid artery disease have improved significantly over the past two decades with the emergence of medical treatment and carotid revascularization procedures. Both carotid artery endarterectomy (CEA) and carotid artery angioplasty with stenting (CAAS) are recommended for symptomatic patients with 50% or more stenosis or asymptomatic patients with 70% or more stenosis.[4]

For the past three decades, carotid artery stenting (CAS), an alternative to CEA, has been used for carotid artery stenosis revascularization. Interventionalists are experiencing increased technical developments in arterial stents and neuroprotection for CAS deployment. Comparative studies have reported varied patient outcomes, health status, major and minor complications, and health-related quality of life regarding the effectiveness of the CAS and CEA.[5]

Evidence shows that postprocedural plaque protrusion (PP) through the stent struts, which occurs in 30 to 100% of conventional carotid stents depending on the plaque type and imaging technique used, is not benign.[6] One fundamental difference between the open surgical and endovascular methods of carotid revascularization is that by removing the plaque, CEA eliminates the postprocedural problems of the plaque. In contrast, conventional CAS does not remove plaque but seeks to stabilize the potentially embolic lesion by covering it with a layer of the metallic stent and subsequent stable fibrous tissue layer (healing).[7]

One of the major causes of ischemic complications after stent deployment in patients with unstable plaques is PP through stent struts. Open-cell stent devices have a higher risk of periprocedural stroke compared with closed-cell devices.[8] PP can be reduced by using recently developed new-generation double-layer, thin-strut nitinol stents with a mesh covering that traps and exclude thrombus and plaque debris.[9] The superiority of micromesh stents compared with conventional stents for CAS has been reported by clinical studies with good short- to medium-term follow-up results. In Japan, a clinical trial using the micromesh stent has been performed that reduced postprocedure ischemic complications.[10]

Literature related to mechanical properties of single-layer and double-layer stents, stent design, and their deployment causing procedural ipsilateral stroke risk after treatment is unclear. A better understanding of different stents deployment in facilitating clinical choice and further enhancing the productivity of life is needed in developing countries like India. Therefore, we aimed to compare the clinical outcome and efficacy of single-layer and dual-layer mesh stent for CAS among carotid stenosis patients.

Aims and Objectives

The aim of this article was to compare the clinical outcome and efficacy of single-layer versus dual-layer mesh stent for CAS among carotid stenosis patients.

Materials and Methods

Study Design

A prospective observational study was conducted among 41 patients undergoing CAS for carotid stenosis in the department of interventional radiology in a tertiary care setting. The study was conducted for a period of 2 years, from November 2019 to November 2021.

Sample Size

In our pilot study results with 10 cases in each group we found that the minimum clinical important difference in proportion of reclusion rate between single-layer and double-layer stent groups was 37%. Hence considering 80% power of the study and 5% α error 19 cases in each group was the our sample size. Based on availability of dual-layer group, three more cases were included and hence the sample size included in study was 41 participants. The formula used for sample size calculation was.[11]

$$N = \frac{\{u\sqrt{[\pi_1(1-\pi_1)+\pi_0(1-\pi_0)]} + v\sqrt{[2\bar{\pi}(1-\bar{\pi})]}\}^2}{(\pi_0-\pi_1)^2}$$

$$\bar{\pi} = \frac{\pi 0 + \pi 1}{2}$$

N: Sample Size
π_1, π_0: Proportion
U: One-sided percentage point of the normal distribution corresponding to 100%—the power
power is = 80%, u = 0.84
V: Percentage point of the normal distribution corresponding to the (two-sided) significance level, e.g., if significance level = 5%, v = 1.96
Single-layer stent group (N = 19)
Dual-layer stent group (N = 22)

Inclusion Criteria

- Symptomatic patients showing ≥50% stenosis of the internal carotid artery (ICA).
- Asymptomatic patients showing ≥80% stenosis of the ICA.

➢ Patients with more than 5 years life expectancy.

Exclusion Criteria

➢ Simultaneous contralateral stenosis or occlusion of the ICA.
➢ Uncorrectable bleeding diathesis.
➢ Allergy to antiplatelet medication and metals in-stent (nickel, titanium, cobalt, chromium).
➢ Recent intracranial hemorrhage.
➢ Intracranial aneurysm.
➢ Patients with acute stroke.

Data Collection

All procedures were performed under conscious sedation. A biplane angiography system (Allura Xper, Phillips, the Netherlands) was used for the endovascular procedures. All patients received DAPT with aspirin and clopidogrel at least 5 days prior to intervention and a loading dose of oral ticagrelor 90 mg on the day of the procedure. Using Seldinger's technique, retrograde common femoral arterial access was obtained, and diagnostic carotid and a cerebral angiogram were performed. The diagnostic catheter was exchanged for 6F Neuro Max guiding catheter (Penumbra Inc.), which was placed in mid-common carotid artery (CCA). An exchange length guidewire was navigated through the narrowed segments of distal CCA and carotid bulb into the petrous ICA. Whenever possible embolic protection device was navigated by over the wire technique and deployed 3 cm distal to the carotid bulb in distal cervical ICA. Prestenting angioplasty was performed in cases where the stent placement had difficulty in directly advancing over the lesion. Then, the carotid stent system was tracked over the bare wire of the embolic protection device and deployed from the proximal cervical ICA up to the proximal CCA to completely cover the plaque. If necessary, poststenting angioplasty was done.

Patients were kept under DAPT with aspirin (75 mg once daily) and ticagrelor (90 mg twice daily) for the 6-month postinterventional period. They received a lipid-lowering medication, and cerebrovascular risk factors such as hypertension and diabetes were controlled and medically treated.

Stents used in single-layer stent group were X Act, Wall, and Acculink stents.

C Guard stent is used in all patients of dual-layer stent group.

Imaging

Preprocedure all patients underwent computed tomographic neck and cerebral angiography for the exact assessment of the carotid stenosis according to the North American symptomatic carotid endarterectomy trail (NASCET) criteria.

Operational Definitions

Patients with amaurosis fugax, hemispheric transient ischemic attack (TIA), or ipsilateral ischemic stroke without major disability (National Institutes of Health Stroke Scale] score <15, modified Rankin Scale [mRS] score >3) were considered symptomatic if these events occurred in the 6 months before intervention. The mRS is used for assessing general daily life functionality and independence (with ≤ 2 defined as independence).

Patients were classified as high risk if they met at least 1 of the below criteria:

- Clinically (age >80 years, Canadian Cardiovascular Society class III or IV angina or unstable angina, congestive heart failure [New York Heart Association functional class III or IV]),
- Left ventricular ejection fraction less than 30%,
- Severe stenosis of the common coronary artery of the left or 2 or more epicardial coronary arteries,
- Need for cardiac surgery in less than 30 days,
- Recent myocardial infarction and severe chronic lung disease,
- Anatomic abnormalities (high cervical lesions, sub clavicular lesions, previous radical neck surgery or radiotherapy treatment, restenosis after CEA, obstruction of the carotid contra-lateral, tracheostomy, and paralysis of the larynx and the contralateral nerve).[12]

Study Variables

Procedural efficacy and complication were considered as the primary outcome variable. Mortality rate and favorable clinical outcome—defined as mRS score less than or equal to 2 within 30 days—were secondary outcome variables.

Statistical Analysis

All quantitative variables were presented as mean and standard deviation and categorical variables as frequency and proportions. Categorical outcomes were compared between study groups using the chi-squared test. *p*-Value less than 0.05 was considered statistically significant. SPSS version 22 was used for statistical analysis.[13]

Results

A total of 41 subjects were included in the final analysis with a follow-up of 30 days.

Mean age of study population in dual-layer stents group was 63.86 ± 11.08 years and it was 61.47 ± 8.26 years in single-layer stent group. Present angioplasty was performed in eight (42.11%) participants of in single-layer group and only four (18.18%) participants in dual-layer stent group where poststenting angioplasty was done in almost equal participants in both groups (94.74% in single layer and 95.45% in double layer). There was no statistically significant difference between two groups in other baseline parameters like age, stenosis, side of stenosis, prestenting angioplasty and poststenting angioplasty (p-value >0.05) (►**Table 1**).

Out of 22 participants with dual-layer stent, only 1 participant experienced five episodes of TIA in last one (4.55%) month with free floating thrombus. Both clinical and associated complaints were more in dual-layer group compared with single layer (►**Table 2**).

In single- and dual-layer stents group, all 100% were with good wall apposition. One (5.26%) participant in single-layer group had reclusion/restenosis at 30 days. In single-layer stents group, majority (57.89%; 11 out of 19) showed MRS score of 0 and 31.58% reported MRS score as 1. In dual-layer

Table 1 Comparison of baseline parameter between study group ($n = 41$)

Parameter	Study group		*p*-Value
	Single-layer stents ($n = 19$)	Dual-layer stents ($n = 22$)	
Age (in years)	61.47 ± 8.26	63.86 ± 11.08	0.445[a]
Stenosis	0.8 (0.8,0.9)	0.8 (0.7,0.9)	0.733[b]
Side of stenosis			
Left	14 (73.68%)	14 (63.64%)	0.491[c]
Right	5 (26.32%)	8 (36.36%)	
Used stent			
Acculink	1 (5.26%)	0 (0%)	[d]
C Guard	0 (0%)	22 (100%)	
Wall	9 (47.37%)	0 (0%)	
X Act	9 (47.37%)	0 (0%)	
Filter			
Emboshield	4 (21.05%)	0 (0%)	[d]
Filter Wire EZ	7 (36.84%)	2 (9.09%)	
Spider FX	7 (36.84%)	5 (22.73%)	
No	1 (5.26%)	15 (68.18%)	
Prestenting angioplasty	8 (42.11%)	4 (18.18%)	0.093[c]
Poststenting angioplasty	18 (94.74%)	21 (95.45%)	1.000[e]

Abbreviations: FW, Filter Wire.
[a]Independent sample *t*-test.
[b]Mann–Whitney U test.
[c]Chi-squared test.
[d]No statistical test was applied due to 0 subjects in the cells.
[e]Fisher's exact test.

stents group, majority (63.64%; 14 out of 22) showed MRS score 0 and 22.73% (5 out of 19) showed score 1 (►**Table 3**).

Discussion

According to the author's knowledge, this is the first study to compare clinical outcome and efficacy of single-layer and dual-layer mesh stent for carotid artery stenting among carotid stenosis patients in Indian scenario. In accordance with our study, sample size of 41 patients, restenosis in single-layer stenting group, 5.26%, is in agreement with the results published by Sýkora et al, as 3.4% population of single-layer stenting had restenosis. However, the same study concluded the restenosis rates are higher in dual-layer stenting group than in single-layer stenting group.[14] The same is contradicted by a meta-analysis published recently by Stabile et al, which concluded that dual-layer mesh-covered carotid stent systems (the Roadsaver/Casper or CGuard) can be safely used for CAS and their use minimizes the incremental risk related to symptomatic status and other risk factors.[15] A comparison study conducted by Kahlberg et al reported almost similar results in both the groups in terms of postprocedural adverse events, namely, TIA/stroke/mortality with 3% in dual-layer stenting group and 1% in single-layer stenting group.[16] This result is in same line with our study results of similar percentage population in both the groups presented postprocedural adverse events (26.32% in single-layer stenting group and 27.27% in dual-layer stenting group presented TIA). Lal et al found several stents used, lesion characteristics (length, ulceration), and procedural related risk factors of CAS playing a major role in CAS outcomes.[17]

However, there is contrast in the opinions that dual-layer stent had a higher rate of occlusion/restenosis in comparison to single-layer stents[18] and dual-layer stents has a lower incidence of embolic events/ restenosis.[19] To confirm either of the statement, further studies on large group of population or larger sample size are required.[20] Even the current study has a limitation of smaller sample size.

Findings from this study indicate dual-layer micromesh stent designs minimize embolism of particle release during stent deployment. For experienced operators attempting to minimize embolic events with currently available stents, the use of these double-layer stents is an appropriate strategy to exclude particle extravasation through stent struts. However, awareness about this approach should be reported and should be cited as an explanation by any of the interventionists using it.

Limitations

The major limitation is the single-center study with smaller sample size and hence the results cannot be generalized to overall population. Nonrandomized design and the potential of

Table 2 Comparison of clinical complaints between study group ($n = 41$)

Clinical complaints	Study group[a]	
	Single-layer stents ($n = 19$)	Dual-layer stents ($n = 22$)
Five episodes of transient ischemic attack in last 1 month with free floating thrombus	0 (0%)	1 (4.55%)
Acute left watershed infarcts	1 (5.26%)	1 (4.55%)
Right limb weakness	0 (0%)	1 (4.55%)
Blurring of vision	1 (5.26%)	2 (9.09%)
CVA with giddiness and slurring of speech	0 (0%)	2 (9.09%)
Left upper limb weakness	0 (0%)	1 (4.55%)
Multiple episodes of giddiness	1 (5.26%)	3 (13.64%)
Right stroke with carotid stenosis	2 (10.53%)	0 (0%)
Slurring of speech and imbalance	4 (21.05%)	0 (0%)
Syncopal attack	1 (5.26%)	0 (0%)
TIA	5 (26.32%)	6 (27.27%)
Treated for acute stroke—came after 3 weeks for carotid stenting	0 (0%)	1 (4.55%)
Unsteady gait with impaired vision	2 (10.53%)	0 (0%)
Weakness in upper and lower limbs	2 (10.53%)	4 (18.18%)
Associated findings/complaints ($n = 6$)		
Associated stroke	0 (0%)	1 (20%)
Cerebral hyperperfusion syndrome	0 (0%)	1 (20%)
Free floating thrombus in distal CCA extending into ICA	0 (0%)	1 (20%)
Left intracranial stenting also done for petrous and lacerum segments by Xience and Biomine stents	0 (0%)	1 (20%)
Recanalization by drug-eluting balloon (Lutonix) For neointimal hyperplasia	1 (100%)	0 (0%)

Abbreviations: CCA, common carotid artery; CVA, cerebrovascular accident; ICA, internal carotid artery; TIA, transient ischemic attack.
[a]No statistical test was applied due to 0 subjects in the cells.

Table 3 Comparison of clinical outcomes between study group ($n = 41$)

Parameter	Study group[a]	
	Single-layer stents ($n = 19$)	Dual-layer stents ($n = 22$)
Symptomatic Ischemic events	0 (0%)	0 (0%)
Reclusion rate at 30 days	1 (5.26%)	0 (0%)
Good wall apposition	19(100%)	22(100%)
Follow-up MRS score at 30 days		
0	11 (57.89%)	14 (63.64%)
1	6 (31.58%)	5 (22.73%)
2	2 (10.53%)	2 (9.09%)
6	0 (0%)	1 (4.55%)
Periprocedural complications	0 (0%)	0 (0%)

Abbreviation: MRS, modified Rankin Scale.
[a]No statistical test was applied due to 0 subjects in the cells.

selection bias. It was not possible to build multivariable models to confirm the independent effect of single- and double-layer stents. This study is not powered for any clinical outcome comparisons, and thus the respective findings must be treated as hypothesis-generating. Postprocedural antiplatelet medication and missing follow-up imaging are another limitation. Criteria used by individual practitioners to choose single-layer and double-layer were unknown. Information on vessel diameter was not recorded. Other comorbidities associated were not evaluated that could affect the findings of study. Patients were

followed for a period of 1 month only. Despite the limitations, the study provided real-world cohort data of patients undergoing CAS. Future multicentric longitudinal studies are recommended to validate the findings of present study. In asymptomatic carotid stenosis patients, large-scale evidence for the efficacy of carotid stent systems is highly desirable,

Conclusion

The results of the above study conclude that the both the stents are equally effective. Even more, both the stents had similar clinical complications and were equally effective in preventing periprocedural complications. Technical steps should be taken care during stent placement by avoiding movement of delivery system. This technical proficiency depends on the stent operator, who also modifies and reduces procedure-related risk factor during CAS.

Ethical Approval

The study was approved by the institutional ethics committee. The participants were informed in detail about the procedures involved, and they provided written informed consent in accordance with the guidelines of the Helsinki Declaration, 2008.

Authors' Contribution

V.P.K.R. has conceptualized the study and played primary role in compiling, analysis, and interpretation of the data. All the drafts were prepared, reviewed, and final draft was approved by V.P.K.R. and N.M.M. V.P.K.R. and N.M.M. have contributed in fine tuning of the proposal, data collection, and entry. They reviewed the results and contributed to preparation and review of drafts. All the authors have read and approved final version of the manuscript. All the authors take complete responsibility for the content of the manuscript.

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Conflict of Interest

None declared.

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