



Clinical Research

Computational Fluid-Dynamic Analysis after Carotid Endarterectomy: Patch Graft versus Direct Suture Closure

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Background: Closure technique after carotid endarterectomy (CEA) still remains an issue of debate. Routine use of patch graft (PG) has been advocated to reduce restenosis, stroke, and death, but its protective effect, particularly from late restenosis, is less evident and recent studies call into question this thesis.

Objective: This study aims to compare PG and direct suture (DS) by means of computational fluid dynamics (CFD). To identify carotid regions with flow recirculation more prone to restenosis development, we analyzed time-averaged oscillatory shear index (OSI) and relative residence time (RRT), that are well-known indices correlated with plaque formation.

Methods: CFD was performed in 12 patients (13 carotids) who underwent surgery for stenosis >70%, 9 with PG, and 4 with DS. Flow conditions were modeled using patient-specific boundary conditions derived from Doppler ultrasound and geometries from magnetic resonance angiography.

Results: Mean value of the spatial averaged OSI resulted 0.07 for PG group and 0.03 for DS group, the percentage of area with OSI above a threshold of 0.2 resulted 10.1% and 3.7%, respectively. The mean of averaged-in-space RRT values was 4.4 1/Pa for PG group and 1.6 1/Pa for DS group, the percentage of area with RRT values above a threshold of 4 1/Pa resulted 22.5% and 6.5%, respectively.

Conclusions: Both OSI and RRT values resulted higher when PG was preferred to DS and also areas with disturbed flow resulted wider. The absolute higher values computed by means of CFD were observed when PG was used indiscriminately regardless of carotid diameters. DS does not seem to create negative hemodynamic conditions with potential adverse effects on long-term outcomes, in particular when CEA is performed at the common carotid artery and/or the bulb or when ICA diameter is greater than 5.0 mm.

INTRODUCTION

Carotid bifurcation is a preferential site for the development of atherosclerotic plaque.¹ A major role in this

process is given by the blood fluid dynamics. In particular, low and oscillating wall shear stresses (WSS) promote the plaque formation² and myointimal

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Table I. Patient demographic characteristics and risk factors

	Patch graft = 9	%	Direct suture = 4	%
Age (years)	72.88 ± 6.33		70 ± 12.73	
Sex				
Males	3	37.5	2	50.0
Females	5	62.5	2	50.0
Weight (Kg)	58.75 ± 12.0		73.75 ± 17.1	
Height (cm)	162 ± 2.0		173 ± 17	
Body mass Index	22.33 ± 4.71		24.42 ± 2.6	
Risk factors				
Smoking	5	62.5	2	50.0
Hyperlipidemia	4	50.0	4	100
Hypertension	8	100	4	100
Diabetes	3	37.5	2	50.0
Coronary artery disease	1	12.5	2	50.0
Side				
Right	3		1	
Left	4		3	
Bilateral	1		0	

hyperplasia,^{3–5} which could lead to restenosis. Carotid endarterectomy (CEA) is the most commonly performed surgical treatment to restore the patency of extracranial district. Closure technique after CEA still remains a debated major issue. The values of WSS are dependent on individual anatomy.^{6,7} Thus, geometric changes, due to the removal of plaque and wall closure, could influence WSS and long-term biological behavior, such as restenosis.

Computational fluid dynamics (CFD), based on the finite element method, has been proved to be an effective tool to investigate blood flow quantities at the carotid bifurcation. Viscous forces, focused on WSS-derived parameters, cannot be measured in routine clinical examination but can be estimated with high grade of accuracy by CFD.⁸

The aim of the study was to provide CFD analysis based on patient-specific flow conditions and geometries to assess the effect of CEA on hemodynamics, by comparing WSS-based indices between different arteriotomy closure techniques, that is, direct suture (DS) and patch graft (PG).

METHODS

Ethics Statement

This study was approved by the ethics committee and was performed in accordance with institutional ethics committee guidelines. All patients gave consent for the publication of their data.

Clinical Data

We studied 13 consecutive carotids with a degree of stenosis greater than 70% in 12 patients who

underwent CEA. Demographic characteristics and risk factors are listed (Table I). Surgeon has followed the recommendations of Carotid Artery Stenosis Consensus for grading of stenosis (Table II).⁹ All cases were asymptomatic, 1 case (8.3%) had contralateral occlusion of the internal carotid artery (ICA), and 3 cases (25.0%) previously underwent contralateral CEA.

Operative Management

In all cases, CEA was performed under regional block anesthesia. Standard surgical techniques, including longitudinal arteriotomy, 2.5× optical magnification, and systemic heparin, were used.

PG was generally used with the exception of stenosis mainly localized in the carotid bulb and with ICA diameter ≥5.0 mm, where DS was preferred (Table III). PG angioplasty was performed in 9 cases (01–09) (69.2%), using 6 × 75-mm polyester collagen-coated patch (Ultra-thin Intervascular®, Mahwah, NJ) properly tailored and distally trimmed to give a smoothly tapered transition. In particular, cases 01 and 02 were submitted to obliged patch according to guidelines.^{10,11} DS was performed in 4 cases (10–13; 30.8%), as first choice in 3 cases, and 1 case, initially scheduled for PG, was adopted for intraoperative onset of patient's discomfort and lack of collaboration in absence of major neurological concerns (case 10) (Fig. 1).

PG and DS were always performed with a 6-0 non absorbable, monofilament polypropylene suture line (Everpoint-M, Ethicon, Somerville, MA). No perioperative complications were observed, and no shunts

Table II. Closure technique, location of the stenosis

Patient	Closure technique	Location	Stenosis, PSV (cm/sec)
01	PG	CCA, B	375
02	PG	B	300
03	PG	B, ICA	280
04	PG	B, ICA	300
05	PG	ICA	372
06	PG	B	350
07	PG	B, ICA	200
08	PG	B	270
09	PG	B, ICA	240
10	DS	B, ICA	220
11	DS	B, ICA	280
12	DS	CCA, B, ICA	200
13	DS	B	200

(CCA, B [=bulb], ICA), and duplex scan values of the peak of systolic velocity (PSV).

were necessary. During the 2-year follow-up, no cases of restenosis were observed in both groups.

Acquisition of Doppler Ultrasound Signals

Carotid Doppler ultrasound (DUS) was performed with linear 8-MHz probe and iU22 ultrasound scanner (Philips Ultrasound, Bothwell, UT). After the morphological analysis of the plaque, in all the cases, the velocities were acquired at the center of the vessel and with a beam-to-flow angle less than or equal to 60°, to obtain measures along the longitudinal direction. The sample volume was positioned within the area of greatest stenosis for the preoperative evaluation of peak of systolic velocity. After CEA, all the 13 ICAs were completely sampled, and velocities were measured 2 cm retrograde from the bifurcation in the common carotid artery (CCA), and 2 cm downstream the bifurcation in the ICA. Velocity data have been used to prescribe patient-specific boundary conditions at the inlet (CCA) and outlet (ICA) in our numerical simulations. In particular, starting from these velocity values, we estimated the flow rates by means of the formula proposed in the study by Ponzini et al.,¹² that have been then prescribed by means of the Lagrange multiplier method.^{13,14} At ECA, a zero stress condition was imposed.

Acquisition of Radiological Images and Mesh Generation

Three-dimensional carotid reconstructions were derived from postoperative magnetic resonance

angiography (MRA), performed with a 1.5-T Avanto MR scanner (Siemens, Munich, Germany). MRA was performed for all the patients 1 month after CEA. Surface models of the boundary lumen were obtained using a level-set segmentation technique (VMTK<http://www.vmtk.org>) (Fig. 2A, B) and then were converted into volumetric meshes of tetrahedra in view of CFD simulations (Fig. 2C). We performed a refinement study with respect to time and space discretization parameters, by testing that the results on WSS remained the same, up to a tolerance of 2%, when reducing the time and space steps, separately.

Numerical Simulations and Fluid Dynamic Indices

Unsteady numerical simulations for blood fluid dynamics were performed by means of the academic software LifeV (<http://www.lifev.org>). Blood was assumed Newtonian and incompressible, the flow laminar and the wall rigid. These assumptions are well accepted for nonstenotic carotids, and the choice of rigid walls little influences the value of WSS but should not affect the results of our comparisons.

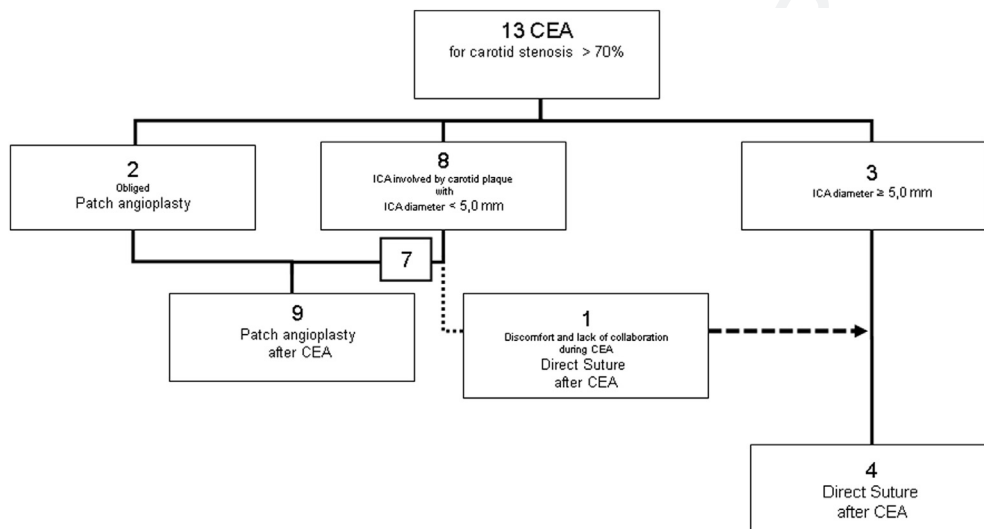
The analyzed CFD quantities were the oscillatory shear index (OSI) and the relative residence time (RRT). OSI is a dimensionless parameter that provides a measure of the oscillating nature of WSS. RRT is an emerging fluid dynamics index that combines the time average of WSS and OSI. Its distribution is proportional to the residence time of blood near the wall, and it is considered a robust indicator to identify regions where WSS is contemporary low and oscillating. OSI and RRT were here used to provide an indication about the risk of restenosis. Indeed, regions with elevated values of OSI and RRT have been recognized at risk of plaque formation^{2,15–18} and myointimal hyperplasia development.^{3–5} Statistical analysis was performed using GNU PSPP (<https://www.gnu.org/software/pspp/>) for descriptive statistics and *t*-test for 2 independent means of sampled data.

RESULTS

In Table IV, we reported the systolic maximum velocities at CCA, ICA, and ECA sections after CEA. We observe that in our simulations, we have prescribed the flow rate at these sections (see above) so that these velocity values are in fact computed by the CFD.

Table III. Carotid blockage location and diameters of common carotid artery (CCA), bulb, internal carotid artery (ICA), and external carotid artery (ECA)

Case	Closure	Plaque localization	CCA ϕ (mm)	Bulb ϕ (mm)	ICA ϕ (mm)	ECA ϕ (mm)
01	PG	CCA, B	6.00	6.00	5.00	3.80
02	PG	B	6.00	5.90	5.40	4.00
03	PG	B, ICA	6.80	5.40	4.20	3.50
04	PG	B, ICA	6.60	5.40	4.00	3.80
05	PG	ICA	6.69	4.83	4.50	3.97
06	PG	B	5.82	5.04	4.50	4.10
07	PG	B, ICA	6.00	6.00	4.90	3.26
08	PG	B	7.00	5.15	4.00	3.86
09	PG	B, ICA	6.33	6.20	4.80	2.40
10	DS	B, ICA	7.48	7.52	4.74	4.00
11	DS	B, ICA	6.17	7.00	5.00	3.25
12	DS	CCA, B, ICA	8.00	8.80	7.00	5.00
13	DS	B	6.88	7.62	6.60	5.40

**Fig. 1.** Flowchart of the CEA included in CFD analysis.

OSI

In Table V, we reported spatial average of OSI distributions that showed higher values when PG was chosen (mean: 0.07 ± 0.02 ; range: 0.02–0.09) than for DS cases (mean: 0.04 ± 0.02 ; range: 0.02–0.06) (t -value: 2.58149; $P = 0.02$). This is qualitatively confirmed by the spatial OSI distribution reported for all the cases (Fig. 3). We notice that PG cases showed different spatial OSI distribution depending on CEA location. For example, case 05 (PG inserted in distal ICA) highlighted uniform low OSI distribution, whereas case 06 (PG inserted in the carotid bulb) featured higher OSI values. We computed the

percentage of area with OSI values above a threshold of 0.2, which has been identified as a reliable value which discriminates between disturbed and nondisturbed flow (Table V).¹⁹ Also these values resulted higher for PG group (mean: $10.17\% \pm 4.55$; range: 2.0–16.0) compared to DS group (mean: $3.78\% \pm 3.15$; range 0.9–7.6) (t -value: 2.522217; $P = 0.02$).

RRT

Spatial average distribution of RRT was greater than 2.0 1/Pa in all the cases of PG group (mean: 4.39 ± 3.24 1/Pa; range: 0.5–11.3) except for case

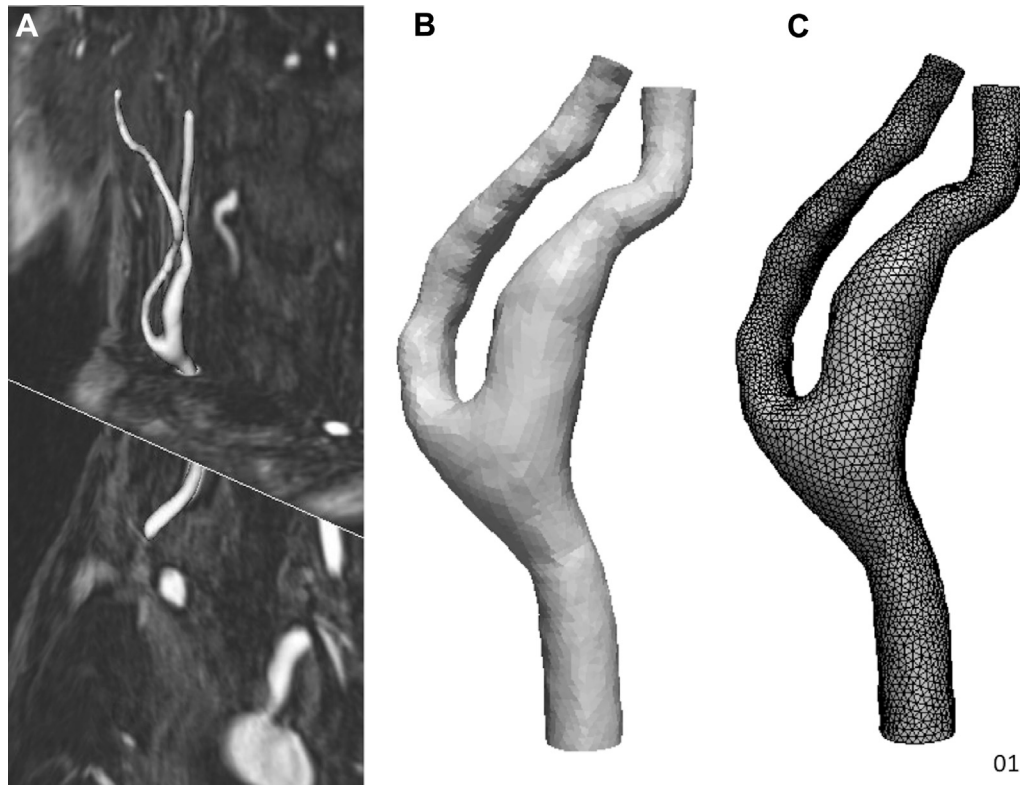


Fig. 2. (A) Segmentation of a representative carotid bifurcation after CEA (case 01) provided by VMTK; (B) surface models of the carotid bifurcation; (C) Volumetric mesh of linear tetrahedral.

05, whereas in DS group, we observed lower values (mean 1.65 ± 0.44 1/Pa; range: 1.0–1.8 1/Pa) (t -value 1.64583; $P = 0.06$) (Table IV).

The percentage of area with RRT values greater than 4.0 1/Pa resulted higher in PG group (mean: $22.48\% \pm 13.46$, 0.1–43.6%) compared to DS group (mean: $6.58\% \pm 3.48$, range: 1.7–9.8%; t -value 2.27749; $P = 0.04$; Table IV). We notice that this threshold value is smaller than the one reported in the study by Gallo et al.¹⁹ (6 1/Pa); however, the qualitative conclusions were comparable.

The values of percentage area with RRT above the selected threshold resulted greater in the PG group than for DS group. In particular, we observed values lower than 10% in all the DS cases, values ranging from 10–20% in 3 cases with PG, and values greater than 20% in 5 cases with PG with the only exception of case 05 (Table V).

An overview of the distribution of RRT values shown in Figure 4 demonstrated that in PG group, they resulted particularly concentrated at the CCA and/or carotid bulb in 8 cases (01–04 and 06–09) and at ICA level only in case 02, while low RRT values were observed just in case 05. In DS group,

we detected higher values of RRT prevalently localized at the CCA and/or bulb in 3 cases (10–12) and both at bulb and ICA only in 1 case (13).

DISCUSSION

Background

Since its introduction, PG has been advocated by many authors to avoid restenosis^{20–22} both in early postoperative period, when closure with DS could allow technical defect narrowing the lumen and reproducing stenosis, and in late postoperative period, when PG should minimize the effects of recurrences. The latter is intended as development of myointimal hyperplasia within 2 years from the intervention, or recurrent atherosclerosis thereafter.²² PG should not be used to enlarge the site of CEA but rather to recreate the original shape of carotid bifurcation.²²

Instead, PG is undoubtedly associated with some perioperative risks strictly linked to the need of double suture line, longer times of cross-clamp, and increased risk of cerebral ischemia or discomfort for

Table IV. Values of peak systolic velocities (in cm/s) computed by CFD at inlet and outlet section after CEA

Case	CCA	ICA	ECA
01	56.9	68.9	63.7
02	30.8	41.8	34.9
03	54.3	91.9	37.5
04	86.6	105.0	109.0
05	81.6	163.0	69.6
06	96.5	135.0	51.2
07	60.5	54.1	69.7
08	39.7	59.7	20.7
09	84.0	114.0	150.0
10	97.3	117.0	81.4
11	50.6	80.0	58.9
12	119.0	176.0	119.0
13	66.2	79.3	56.9

the patient when locoregional anesthesia is used. Moreover, the insertion of alloplastic material increases blood losses and is subjected to possible severe complications, like infections or pseudoaneurysms.²³

After a long and heated debate between supporters of the 2 motions,^{24–26} in 2004, a meta-analysis of the outcomes of randomized clinical trials, conducted before 1986, was published.²⁷ PG showed reduced 30-day and long-term risk of stroke, deaths, and lower rates of return to surgery, thus supporting its standard use in the guidelines of the European, as well as the American Society of Vascular Surgery^{10,11} and in many textbook of vascular surgery.

A later update, still endorsing routinary use of PG, declared less robust results than in the past maintaining “just a borderline significant benefit” for PG.²⁸ Recent studies reported no higher complication rates nor worst long-term clinical outcomes when PG was used.^{29,30} Despite recommendations supporting routinary use of PG, the individual preferences of surgeons still vary widely. The fact that this recommendation is primarily based on earlier data has raised doubts in some authors that suggest selective use of PG, in particular when smaller arteries are submitted to CEA or in case of associated repair of a distal ICA with kinking or coiling.^{25,26,31,32}

CFD Analysis

An interesting way to study the effects of closure techniques is provided by CFD. Hemodynamics plays a crucial role in plaque growth. Biologic and molecular changes are mediated by endothelial cells, and low and oscillating WSS are associated to monocyte activation, increased vasoconstriction, oxidative

stress, higher cellular turnover, and apoptosis. This leads to an inflammatory process.¹⁵ Myointimal hyperplasia, the leading cause of restenosis in vascular surgery, is thought to be a reaction of the arterial wall to this mechanical injury.³³ Computational studies in human carotids have been performed since 2 decades, and more recently, many works have focused on this issue using patient-specific data^{34,35} because these are considered necessary to obtain accurate numerical results.^{8,36}

Archie et al. reported relatively mild WSS after CEA with venous PG.²¹ Kamenskiy et al., using CFD in 16 patients submitted to CEA or carotid eversion, observed that PG considerably modified bifurcation geometries increasing the cross-sectional area and bulb's length.³⁷ This leads to wide areas of high OSI as a consequence of abrupt diameter's transition from PG level to the native artery. Harloff et al., investigating carotid bifurcation with 4D MRA in healthy patients, found that WSS was influenced by individual carotid geometries.³⁸ The presence of a severe stenosis changes WSS, whereas eversion CEA of previously high-grade ICA stenosis tends to resume WSS distribution similar to the physiological values observed in healthy patients.³⁸ Harrison et al. compared DS versus 2 different PG sizes (5 and 8 mm), performing a CFD study on silicone carotid bifurcation models; they reported that PG did not generate any favorable flow dynamic condition but the tighter one offered better hemodynamic behavior than the wider one.³⁹

In our study, as well as in Harrison et al.,³⁹ we did not address a comparison between the effects of the different mechanical properties of the patch and of the native artery in terms of disturbed flow. We have assumed rigid walls in our computations, so that the only factor which in fact drives the results is the geometry. Since after CEA, this is heavily influenced by the closure technique, this could be considered in fact a comparison between PG and DS techniques. In particular, together with OSI, which is suitable to forecast the risk of plaque and restenosis formation, we have analyzed RRT, a robust WSS-derived marker of disturbed flow that quantifies transport of atherogenic substances to wall, able to increase platelets and macrophages' deposition. This index has been used to investigate the role of disturbed flow at carotid bifurcation in the development of atheromatic plaque.⁴⁰

The whole series of WSS-based descriptors, obtained by our computations, resulted higher when PG was preferred to DS. This has been confirmed by the statistical tests performed over the values of OSI and percentage area with OSI and RRT greater

Table V. Values of OSI and RRT computed by CFD after CEA

Case	Closure technique	Averaged in space OSI	Area above threshold OSI >0.2 (%)	Averaged in space RRT (1/Pa)	Area above, threshold RRT > 4, 1/Pa (%)
01	PG	0.09	11.6	5.7	34.6
02	PG	0.09	15.7	11.3	43.6
03	PG	0.07	10.4	7.2	35.8
04	PG	0.06	9.0	3.6	16.2
05	PG	0.02	2.0	0.5	0.1
06	PG	0.09	16.0	2.2	13.0
07	PG	0.07	7.8	2.9	16.0
08	PG	0.06	6.0	2.9	20.0
09	PG	0.09	13.0	3.2	23.0
10	DS	0.02	0.9	1.0	1.7
11	DS	0.06	5.1	1.8	6.8
12	DS	0.03	1.5	1.8	8.0
13	DS	0.04	7.6	2.0	9.8

than a suitable threshold. As for RRT values, the trends in PG group resulted higher, but statistically nonsignificant.

Our results showed that, among the PG group, cases 01 and 02, submitted to obliged PG, and cases 03 and 09 highlighted the worst results in terms of both RRT and OSI, whereas cases 04, 06, 07, and 08 showed more scattered or intermediate values; only in case 05, OSI and RRT resulted low (Table IV). Referring to Table II, it is interesting to notice that, for almost all the cases reported, CEA was performed chiefly in the bulb region, whereas case 05 was the only 1 where CEA was performed exclusively at the ICA. This supports the thesis of a selective use of PG; in particular, it would seem to be highly recommended for those cases of plaque localization chiefly confined at the distal ICA, whereas it could be avoided when CEA is performed at the CCA and/or the bulb or when ICA diameter is greater than 5.0 mm.²⁴ Among the DS group (cases 10–13), OSI and RRT values resulted low, and distribution patterns of high OSI and RRT values were found in a narrower area. One case (10), initially intended for PG but then submitted to DS, showed just slightly higher values of OSI and RRT but still in the range of the other DS cases, without any other particular adverse hemodynamic effect. In this case, although the diameter of the ICA was less than 5.0 mm, the diameter at the bulb level resulted >7.5 mm, the greatest of all those initially scheduled for PG.

The present study neither proves nor disproves the notion that one closure technique is superior to the other one in the immediate postoperative period. PG still maintains its fundamental clinical role mainly in selected cases, for example, to

overcome specific technical problems occurring during CEA, in presence of smaller diameter of the bulb and carotid artery or for lesions confined to the ICA. PG use has been proposed to reproduce a sort of “normal” bifurcation’s anatomy, and it should be correctly tailored to reach such a goal providing a nonnarrowing and, at the same time, nonenlarging graft.

More unexpected were the results considering the potential late effects of the choice of closure technique. The cross section area’s increase created by PG in the bulb region, even in a “not enlarging way”, could equally create recirculation phenomena, thus not providing protection against myointimal hyperplasia development or, at worst, even generating possible adverse consequences on long-term outcomes. On the contrary, not-complicated CEA in the bulb region with a diameter >7 mm and with ICA diameter >4.5 mm could be closed with DS without any significant deleterious hemodynamic effects as demonstrated by our results. Therefore, CFD analysis seems to highlight that, from a strictly hemodynamic point of view, PG does not seem to offer indiscriminately protective conditions from late restenosis.

We observe that in all the cases studied in this work, no restenosis has been observed during the first 2 years of follow-up. The percentage of restenosis occurring during the first 2 years is of about 0–33% depending on the method of evaluation, definition of restenosis, and time of follow-up.⁴¹ Considering that, it is possible that restenosis could not occur in our cohort. On the other hand, this percentage is not negligible, and the corresponding clinical problem deserves much attention in terms of study of the possible causes.

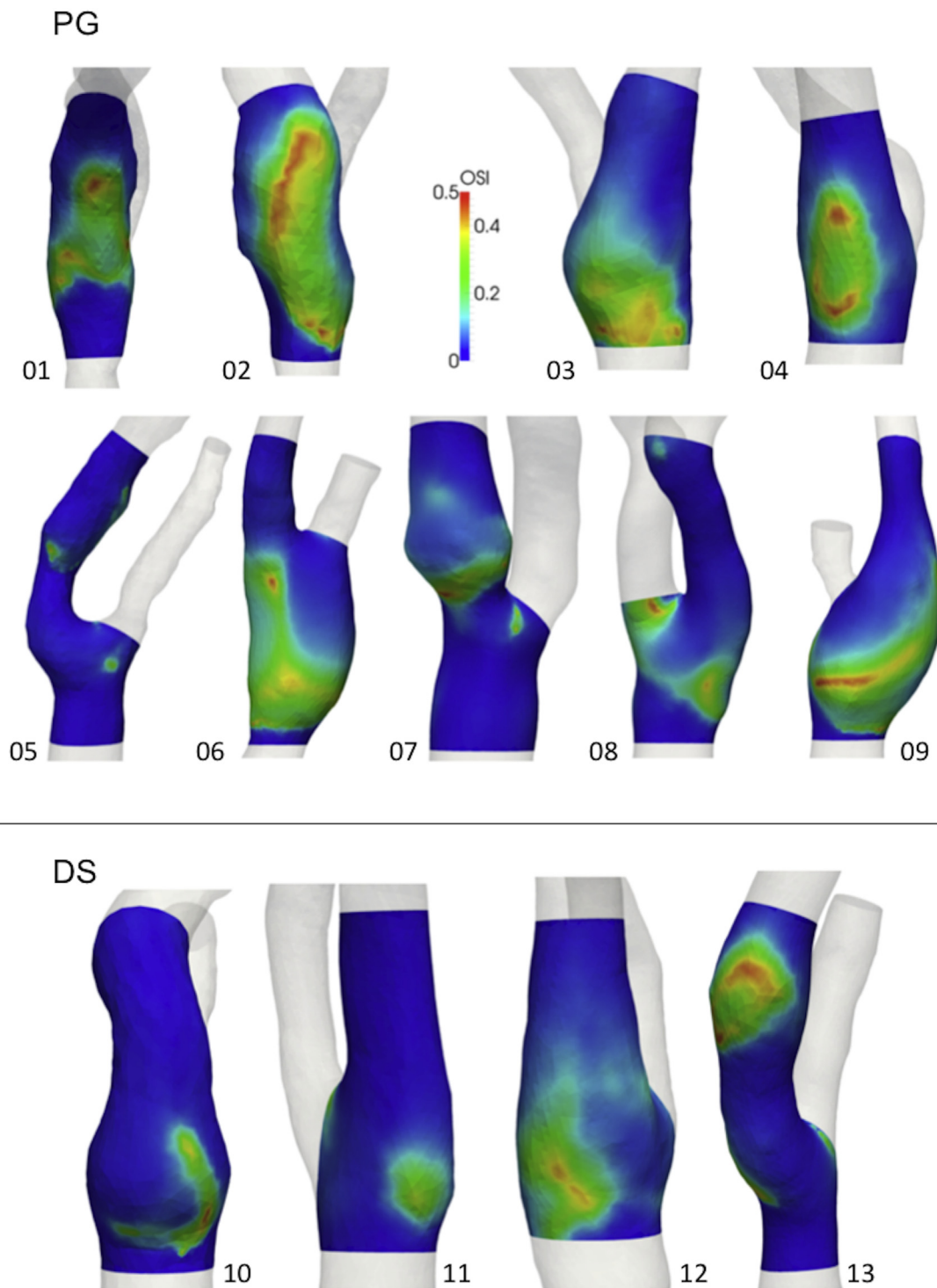


Fig. 3. Plot of OSI distribution computed in the PG group (cases 01–09) and DS group (cases 10–13).

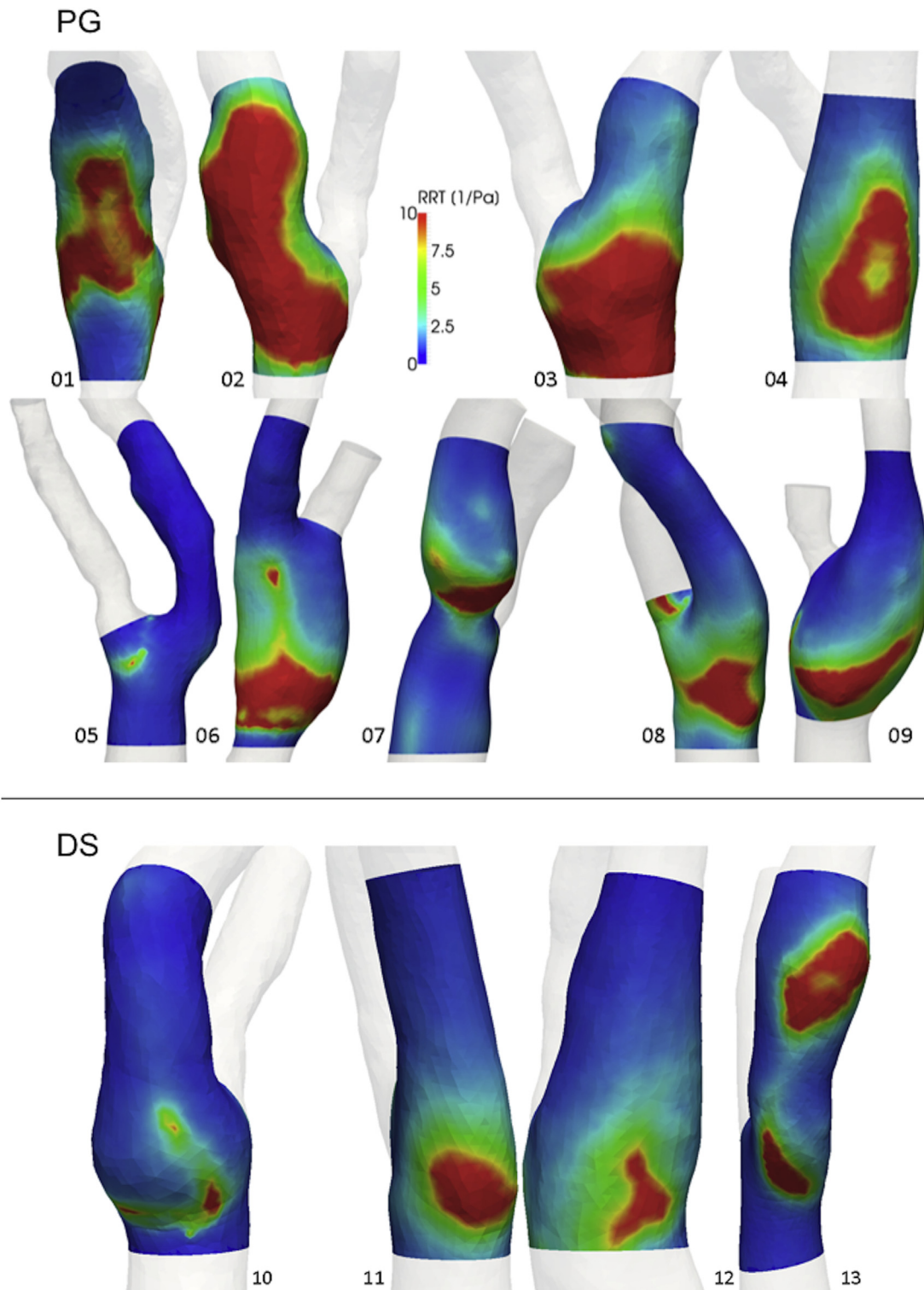


Fig. 4. Plot of RRT distribution computed in the PG group (cases 01–09) and DS group (cases 10–13).

CONCLUSIONS

CFD analysis allowed us to obtain accurate quantifications of WSS and related indices after CEA, neither available with standard ultrasonographic nor with radiological investigations, and to identify disturbed flow conditions prone to restenosis development.

By using patient-specific geometries and velocity data and creating models of carotid hemodynamics, we have observed that PG placement, if performed indiscriminately, could create potentially adverse hemodynamic effects less detected after DS.

PG maintains its prime importance in the management of irregular or complex arteriotomies, small arteries, and/or distal ICA lesions, increasing immediate patency and decreasing acute complications (notably carotid occlusion), but it seems to create (at least for the cases studied in this work) protective hemodynamic conditions from long-term restenosis only when CEA is made distally from the bulb region. On the contrary, DS would not seem to create unfair blood flow patterns, potentially promoting myointimal hyperplasia and/or atheromatous progression, even when CEA is performed at the bulb level.

A limitation of this study is related to the absence of any biological evaluation of factors able to influence the physiopathologic mechanism of restenosis, to the lack of randomization of the treatment, and to the small sample of cases reported. Another limitation is related to the absence of patients with restenosis in our group of patients. To assess the validity of our conclusions, it will be crucial to include in future work cases, when available, who will have encountered restenosis.

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