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ORIGINAL ARTICLE

Cardiac surgery in the presence of chronic internal carotid artery occlusion

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Abstract

The aim was to evaluate the incidence of stroke in the setting of cardiac surgery with or without hemodynamically relevant asymptomatic carotid stenosis contralateral to the occlusion. We designed a historical cohorts study, focused on patients with unilateral totally occluded internal carotid arteries who were referred for any cardiac surgery at our center. Isolated unilateral occlusions were assigned to group 1 ($n=60$), and those with a contralateral stenosis grade ≥ 60% were included in group 2 ($n=51$). A total of 111 patients operated in our center from 1997 to 2016 were included. Patients in group 2 had an asymptomatic contralateral internal carotid artery stenosis with a mean stenosis grade of 71 ± 20%. Simultaneous carotid endarterectomy (CEA) was performed in 22 patients from group 2. The overall mortality was 8/111 (7.2%). Carotid-associated mortality was not observed, whereas an overall stroke incidence of 8/111 (7.2%) was detected. The group-related outcome showed comparable results for mortality (group 1: 4/60 (6.7%) vs. group 2: 4/51 (7.8%); $p=1.0$). Regarding stroke incidence, group 2 had a higher incidence of overall strokes (2/60 (3.3%) vs. 6/51 (11.8%); $p=0.14$) with more contralateral (0/60 (0%) vs. 2/51 (3.9%); $p=0.209$) and ipsilateral strokes (2/60 (3.3%) vs. 4/51 (7.8%); $p=0.411$). Stroke rate peaked in patients with simultaneous carotid and cardiac surgery ($n=22$; 18.2%; $p=0.048$). Performing simultaneous CEA during cardiac surgery in the presence of a contralateral occlusion may promote stroke. Asymptomatic contralateral carotid stenosis is a risk factor for stroke in patients with carotid occlusion prior to cardiac surgery.

Keywords Endarterectomy · Carotid · Carotid stenosis · Stroke · Cardiac surgical procedures

Introduction

Carotid occlusion may lead to cerebrovascular insufficiency if compensatory collateral pathways do not adequately replace the anatomic blood supply.

In case of unfavorable hemodynamic situations which may occur perioperatively during cardiac surgery, those pathways may be insufficient to prevent stroke. Chronic total carotid occlusion increases the occurrence of perioperative stroke during isolated carotid endarterectomy (CEA) [1–3]. However, the risk of perioperative mortality and stroke in patients with total internal carotid artery occlusion referred for cardiac surgery is not that well established.

In the setting of cardiac surgery, the aim of our retrospective study was to evaluate the outcome in those high-risk patients. Regarding the neurological outcome, the impact of the CEA and the relevance of a carotid stenosis on the contralateral side to the occlusion were evaluated.

Materials and methods

This study was approved by our local ethics committee (No. 125/2017BO2). We designed a historical cohort study, focused on patients with unilateral totally occluded internal carotid arteries who were referred for any cardiac surgery at our center. All patients received a carotid ultrasound prior to the operation. Patients with isolated unilateral occlusions without contralateral carotid stenosis were assigned to group 1. Patients with contralateral internal carotid artery stenosis

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with a stenosis of 60% or greater were included in group 2, who were either referred for isolated cardiac surgery or for the synchronous carotid endarterectomy (CEA). Preoperative diagnostics for carotid stenosis were performed by duplex sonography, and the stenosis grade was assessed according to NASCET-based criteria [4].

We evaluated the postoperative outcomes such as death, stroke and myocardial infarction. All patients with postoperative stroke were isolated from the cohort. Subsequently, they were analyzed for the severity of stroke according to the NIHSS score in the acute phase as proposed by Kasner et al. and modified Rankin scale (mRS) at discharge based on medical records [5]. Subgroup analysis was performed to evaluate the risk of simultaneous operations in patients with a carotid occlusion. Myocardial infarction, shock or embolism-promoting disease, such as endocarditis, were defined as exclusion criteria.

Data acquisition

Data acquisition was performed based on medical records. Demographic data and the existence of morbidity predictors were included. Outcome parameters of the two groups were in-hospital mortality and morbidity variables, including any stroke, ipsilateral stroke, contralateral stroke, myocardial infarction, carotid-related mortality and delirium. Postoperative stroke was defined as an acute focal dysfunction of the brain lasting longer than 24 h with an evidence of infarction in the CT imaging [6]. Elevation of creatine kinase (CK) levels with concomitant significant elevation of CK-MB levels (both measured 24 h postoperatively) and ST-segment elevation in the ECG were indicative of postoperative myocardial infarction [7].

Surgery

All surgical procedures were performed under general anesthesia either in cardioplegic cardiac arrest on cardiopulmonary bypass (CABG, aortic valve repair and aortic valve repair + CABG) or as off-pump coronary artery bypass (OPCAB) procedures. Synchronous CEA was accomplished before sternotomy in 22 patients from group 2. Routine carotid shunting was employed to avoid clamping ischemia during CEA. Neuromonitoring was assessed by near-infrared spectrometry (INVOS™, Medtronic, Minneapolis, USA) in all procedures. Postoperatively, patients were transferred to the intensive care unit, where neurological examination occurred after extubation. Patients with neurological symptoms were additively evaluated by neurologists. Native CT scans were performed directly after the neurological diagnosis and 24 h after symptom onset.

Statistical analysis

The statistical analysis was performed using the SPSS 23 software (IBM Corporation, Somer, NY, USA). All variables were tested for normality using the Kolmogorov–Smirnov test. After Gaussian distribution was proven, two tailed t-tests were used for further evaluation of the metric data. In terms of nominal variables, the statistical significance between the groups was assessed by Fisher's exact test. In this work, metric variables are presented as the mean with the standard deviation in parentheses, whereas ordinal variables are shown as percentages. p values < 0.05 were regarded as statistically significant.

Results

From January 1997 to December 2016, a total of 113 patients with a completely occluded internal carotid artery were scheduled for cardiac surgery. One patient with endocarditis and another patient in cardiogenic shock were excluded accordingly to the exclusion criteria. Two study groups were formed: group 1 ($n = 60$) with intact contralateral carotid arteries, including patients with contralateral stenosis grade 0–60% and group 2 ($n = 51$) with an asymptomatic contralateral stenosis greater than 60%. The follow-up time was defined by the duration of the mean hospital stay (in-hospital outcome), which was 15.6 ± 7.8 days in the overall study population (group 1: 16 ± 9 d; group 2: 15 ± 5 d; $p = 0.445$).

Baseline characteristics

Table 1 shows the characteristics of patients from both study groups. The group profiles were similar regarding comorbidities. Demographically, patients in group 2 were 3.3 years older ($p < 0.05$) than in group 1 (Table 1). At the same time, there were more combination procedures in group 2, whereas aortic valve replacement was performed more frequently in group 1. Isolated CABG was the most common operation (80% of all surgical procedures). CABG without cardiopulmonary bypass (OPCAB) was accomplished in 10% of all cases. The OPCAB revascularization rate was higher in group 2 (8.3 vs. 12.3%). The mean contralateral carotid stenosis level in group 2 was $71 \pm 20\%$.

Overall outcome

We report an overall mortality of 7.2%; however, carotid-associated mortality was not observed. Table 2 gives an overview of the causes of death observed in this study. Stroke occurred in 8.1% of the cases in the entire study

Table 1 Baseline characteristics of study groups 1 and 2

Characteristic	Group 1 $n=60$	Group 2 $n=51$	p
Female sex (%)	16.7	17.6	1.000
Age (years ± SD[a])	67.5 (±8.6)	70.8 (±7.7)	0.039*
Ejection fraction (% ± SD)	48.6 (±12.7)	52.2 (±11.8)	0.125
Grade of contralateral carotid stenosis (%)	–	71 (±20)	–
Vertebrobasilar stenosis (%)	13.3	17.6	0.409
Left main disease > 50% (%)	26.6	35.3	0.602
Coronary 3-vessel disease (%)	75	80.4	0.649
Aortic stenosis (%)	18.3	17.6	1.000
CABG[b] (%)	80	80.4	1.000
AVR[c] (%)	6.7	2	3.72
AVR + CABG (%)	13.3	17.6	0.602
Renal replacement therapy (%)	1.7	2.0	1.000

*Statistically significant ($p < 0.05$)

[a]Standard deviation

[b]Coronary artery bypass graft

[c]Aortic valve replacement

Table 2 Analysis of the cause of death among the study population

No.	Age	Group	CEA[a]	Cardiac surgery	Cause of death
1	58	1	No	CABG[b]	Respiratory failure
2	78	1	No	CABG	Pneumonia, sepsis
3	77	1	No	CABG	Pneumonia, sepsis
4	77	1	No	AVR[c]	Low cardiac output syndrome
5	75	2	No	AVR	Mediastinitis, sepsis
6	74	2	No	CABG (OPCAB)[d]	Hyperkalemia
7	72	2	No	CABG + AVR	Myocardial infarction, cardiogenic shock
8	70	2	Yes	CABG	Bowel ischemia, sepsis

[a]Carotid endarterectomy

[b]Coronary artery bypass graft

[c]Aortic valve replacement

[d]Off-pump coronary artery bypass

population. A total of six (6.3%) ipsilateral and two (1.8%) contralateral strokes were observed: two mild, five moderate and one severe stroke according to the NIHSS score. At discharge, six patients with mild-to-moderate strokes had a mRS of 3, whereas one patient with moderate stroke and a patient with severe stroke had a mRS of 4 and 5, respectively. Postoperative cardiac morbidity detected by the occurrence of postoperative myocardial infarction was low, with only two cases 2/111 (1.8%). Postoperative delirium was found in 21.6% of the study population.

Group-related outcomes

There were more postoperative strokes in the group 2 with contralateral carotid stenosis (Fig. 1). Regarding all types of strokes, group 1 showed a superior outcome (3.3% vs. 11.8%; $p=0.140$). There were more contralateral and ipsilateral strokes in group 2 (group 1: 0/3.3%; group 2: 3.9/7.8%; $p=0.209$/$p=0.411$). Mortality was non-significantly higher in group 2 (7.1% vs. 8.5%; $p=0.547$). Carotid-associated mortality was not observed. Other indicators of postoperative morbidity (myocardial infarction and postoperative delirium) were comparable in both groups.

Considering only the results for CABG procedures ($n=89$), the results are reported in Table 3. The incidence of any stroke (group 1: 1/48 (2.1%) vs. group 2: 5/41 (12.2%); $p=0.091$), ipsilateral stroke (group 1: 2.1%; vs. group 2: 7.3%; $p=0.331$) and contralateral stroke (group 1: 0% vs. group 2: 4.9%; $p=0.209$) was higher in group 2.

The incidence of stroke peaked in patients with synchronous CEA. The stroke rate in those patients was 4/22 (18.2%) and thus significantly higher compared to the

Fig. 1 Incidence of the in-hospital mortality and morbidity parameters in study groups 1 and 2 as a percentage; * statistically significant ($p < 0.05$)

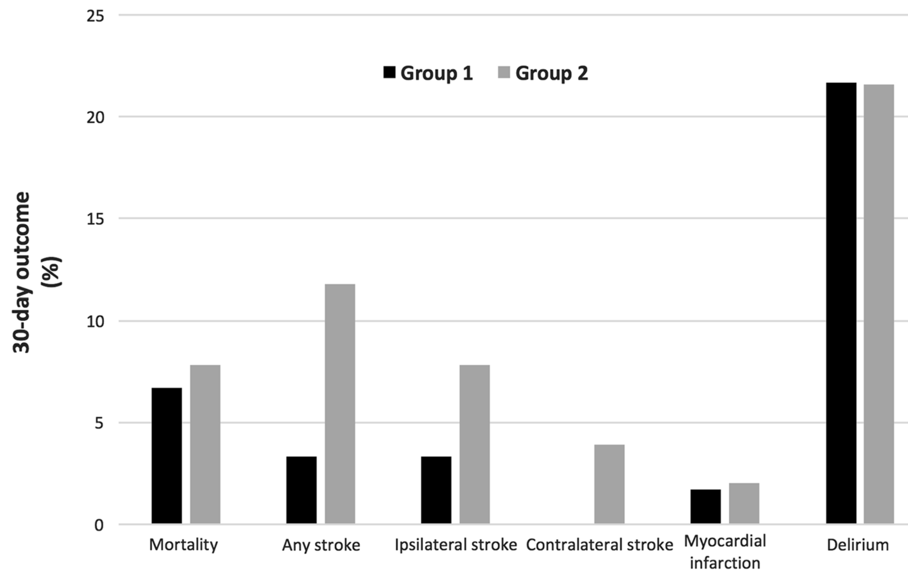

Table 3 Stroke incidence in the CABG subgroups

	Group 1 $n=48$	Group 2 $n=41$	p
Any stroke (%)	1/48 (2.1%)	5/41 (12.2%)	0.091
Ipsilateral (%)	1/48 (2.1%)	3/41 (7.3%)	0.331
Contralateral (%)	0/48 (0%)	2/41 (4.9%)	0.209

Analysis of isolated CABG surgery in study groups 1 and 2

Table 4 Stroke incidence in patients with carotid occlusion and simultaneous CEA or isolated cardiac surgery

	Simultaneous CEA[a] $n=22$	Isolated cardiac surgery $n=89$	p
Any stroke (%)	4/22 (18.2%)	4/89 (4.5%)	0.048
Ipsilateral (%)	2/22 (9.1%)	4/89 (4.5%)	0.34
Contralateral (%)	2/22 (9.1%)	0/89 (0%)	0.038

[a]Carotid endarterectomy

Table 5 Stroke incidence in patients with contralateral carotid stenosis and simultaneous CEA + CABG or isolated CABG

	Simultaneous CEA[a] + CABG[b] $n=20$	Isolated CABG $n=21$	p
Any stroke (%)	4/20 (20%)	1/21 (4.8%)	0.184
Ipsilateral (%)	2/20 (10%)	1/21 (4.8%)	0.606
Contralateral (%)	2/20 (10%)	0/21 (0%)	0.232

[a]Carotid endarterectomy

[b]Coronary artery bypass graft

isolated cardiac surgery 4/89 (4.5%; $p=0.048$; Table 4). Table 5 shows the same trend for CABG patients with contralateral carotid stenosis. Synchronous CEA was associated with a stroke rate of 20% (4/20), whereas isolated CABG in the presence of a contralateral stenosis > 60% had a stroke incidence of 4.8% (1/21; $p=0.184$).

Stroke rate among patients with concomitant vertebral artery stenosis and carotid occlusion was not elevated (5.9%; 1/17; $p=1.0$) compared to those with patent vertebral arteries, and none of the overall strokes were observed in the vertebrobasilar supply area.

Discussion

The management of patients with carotid occlusion undergoing cardiac surgery is not well established. Smaller studies that predominantly included CABG patients showed controversial results: either a higher incidence of stroke or similar neurological outcomes compared to patients without relevant cerebrovascular diseases (Table 6) [8–12]. Prospective studies have not been reported in the literature. Moreover, the reported data fail to prove the optimum treatment of patients with stenosis contralateral to the occlusion.

Study design

This work is of retrospective character. Consequently, the interpretation of the findings aims to give insights into the topic and to determine the statistical trends. A greater reliability can be achieved by prospective randomized trials, even though the realization of such trials is difficult. In our high-volume center, we identified 111 patients in the last 20 years based on our inclusion criteria. In particular, patients with

Table 6 Literature overview

Author	*n*	Mortality *n* (%)	Stroke *n* (%)	Stroke (CEA)[a] *n* (%)	Cardiac surgery	cl-CEA[b]
Illuminati et al. [16]	61	5 (8.6)	4 (6.5)	2 (100)	CABG[c]	Yes
Brener et al. [18]	49	Not reported	1 (2.0)	Not reported	CABG	Yes
Dashe et al. [19]	44	Not reported	9 (20.5)	3 (42.9)	CABG, valve	Yes
Mickleborough et al. [20]	25	Not reported	2 (8.0)	–	CABG	No
Schwartz et al. [21]	22	0 (0)	6 (27.3)	3 (33.3)	CABG	Yes
Furlan and Craciun [17]	22	2 (9.1)	3 (13.6)	3 (13.6)	CABG	Yes
Rizzo et al. [22]	21	Not reported	1 (4.8)	–	CABG, valve	No
Abbasi et al. [23]	20	Not reported	3 (20)	3 (15)	CABG	Yes
Perler et al. [24]	15	1 (6.7)	1 (6.7)	–	CABG, valve	No
Suematsu et al. [25]	13	3 (23.1)	0 (0)	0 (0)	CABG, valve	Yes
Thanvi and Robinson [26]	11	0 (0)	1 (9.1)	0 (0)	CABG	Yes
Total	303	11/144 (7.6%)	31/303 (10.2%)	14/74 (18.9%)		

Studies including more than ten patients with a total carotid occlusion who were undergoing cardiac surgery

[a]Stroke after contralateral carotid endarterectomy

[b]Endarterectomy of the carotid artery contralateral to the occlusion

[c]Coronary artery bypass graft

pronounced morbidities, including ongoing myocardial infarction, shock or embolism-promoting disease, such as endocarditis, were excluded from the analysis to avoid bias. The number of included patients was respectable in both groups. However, the analysis of synchronous CEA patients with contralateral occlusion has to be interpreted critically due to the small subgroup size ($n = 22$). Furthermore, the present study is a retrospective analysis, and thus, the use of the NIHSS score and the mRS to determine the stroke severity must be seen as a limitation, although Kasner et al. reported high reliability and validity of this method [5]. The NIHSS score was calculated only in those patients, who were isolated from the cohort due to focal neurological deficits and pathological imaging. Thus, the conservative stroke definition including the imaging and neurological symptoms may lead to an underestimation of the stroke incidence.

Baseline characteristics

The study groups were comparable in terms of their demographic data and, particularly, their cardiac and neurologic comorbidities. A relevant difference between the study groups was found regarding the age. Higher age was reported to have a negative impact on postoperative morbidity and mortality after cardiac surgery and could have influenced the results of our study [13].

CABG procedures were reported to have better outcomes regarding stroke incidence rates compared to valve replacement or combination procedures [8–10]. In this study, group 1 underwent more combination procedures, whereas group 2 underwent more isolated aortic valve repair procedures. Only one stroke in each study group was observed in the setting of a combination procedure. Furthermore, aortic stenosis with an opening area < 1.0 cm^2 was present in 20 patients (17.4%). Aortic stenosis and preoperative hemodynamic instability are regarded as risk factors for stroke in the presence of carotid stenosis. In our study, one stroke in each study group was observed in patients with aortic valve stenosis.

Mortality

Cardiac surgery patients without concomitant cerebrovascular disease were reported to have a mortality rate of 1.4–2.7% for CABG procedures and 2.8% for aortic valve surgery [8–10]. Carotid stenosis had no impact on perioperative mortality in patients who were referred for cardiac procedures. Illuminati et al. showed a mortality rate of 1% in their prospective study of patients with unilateral carotid stenosis who were scheduled for CABG. In the presence of a carotid occlusion, the reported mortality rates were higher. Tunio et al. reported a mortality rate of 8.6%, whereas Kougias et al. found an increase in mortality to 9.1%. In our study, we observed an overall mortality rate of 7.2%, which was comparable to the previous reports, but the difference between the study groups was not statistically significant [14, 15]. The elevated mortality rate was induced by other complications that arose from cardiac surgery rather than by carotid-related complications (Table 2). The explanation for higher mortality among patients with carotid occlusion may be due to the advanced atherosclerosis and comorbidities in these patients. The apparent increased mortality in patients with carotid occlusion observed in our study should be considered when selecting patients for surgery that may be elective in some circumstances.

Stroke

The overall stroke rate in this study was 7.2%, with a better neurological outcome in the study group without contralateral stenosis. The overall stroke rate in our study was considerably higher than that in CABG procedures without carotid stenosis or occlusion [8–10]. Illuminati et al. described a tendency toward a higher stroke risk of 8.8% in patients who were referred for cardiac surgery with isolated unilateral carotid stenosis > 70% [16]. In terms of occlusion, the largest retrospective study so far by Tunio et al. included 61 patients with carotid occlusion who were scheduled for CABG.[16] This report found a considerable low stroke incidence of 6.5% when compared to a wide range of reported stroke rates in the literature from 0 to 27.3% (Table 6) [14, 15, 17–25]. Considering series from the literature, that included more than ten patients, we found 303 patients with carotid occlusions who were referred for cardiac surgery. Among them, 31 cases of postoperative stroke (10.2%) were reported. CEA was performed in 74 out of 303 included patients because of a contralateral hemodynamically relevant stenosis, resulting in an incidence of stroke in 18.9% of this subgroup. Encouraged by these findings, our subgroup analysis of patients with hemodynamically relevant stenosis contralateral to carotid occlusion is shown in Table 4. We found a stroke incidence of 18.2% among CEA patients compared to 4.5% among isolated cardiac surgery in the presence of carotid occlusion ($p=0.048$). Among CEA patients with contralateral carotid occlusion, these results are comparable to the stroke rates reported by Mickleborough et al. (33.3%), Rizzo et al. (15%) and Kougias et al. (13.6%) [15, 16, 20, 22]. To summarize, stenosis contralateral to the occlusion increased the risk of stroke in our study, but contralateral CEA had rather negative effects on neurological outcome.

Thanvi et al. described pathogenetic factors for stroke in the aftermath of carotid occlusion: embolism from the proximal and distal ends of the stumps, hemodynamic factors and combined factors [26]. Contralateral carotid circulation via the posterior and anterior communicating artery, leptomeningeal collaterals and retrograde flow via the ophthalmic artery are natural pathways of collateralization and may compensate for the chronic carotid occlusion [27]. However, hemodynamic compromise may frequently lead to border-zone cerebral ischemia. Considering the poor hemodynamic situations that may occur on cardiopulmonary bypass, due to postoperative arrhythmias or intraoperative exposure during OPCAB procedures, the balance of collateralization may be affected by cardiac surgery. Additional collateral blood flow imbalance may be induced by clamping for contralateral CEA. Subgroup analyses of the NASCET and ECST trials and a study by Antoniou et al. [1–3] reported a higher stroke occurrence in patients with contralateral carotid occlusion who were referred for isolated CEA. Those findings support the higher overall stroke incidence observed in our study and the poorest outcome in the subgroup of CEA patients.

Cardiac surgery is frequently associated with the risk of embolization [28]. The main limitation of our study is the lack of evidence to prove that all of the reported strokes were due to carotid occlusion and not induced by atheroembolism, e.g., from the aorta. To limit that bias, intraoperative epiaortic ultrasound, transesophageal echocardiography or CT scans of the aorta may be useful [16, 29]. However, a total exclusion of that variable is impossible. As an argument in favor of carotid-associated strokes, we found that strokes in patients without CEA always occurred ipsilateral to the occlusion.

Bilateral strokes were not observed in our study. In the CEA subgroup, two strokes occurred on the surgical side and two strokes that were ipsilateral to the occlusion. As an explanation, ischemia on the operated side may be induced by embolism from the CEA site. The absence of concomitant stroke on the side of the occlusion in those two patients may be explained by well-established leptomeningeal and ophthalmic artery pathways with additional cerebral blood flow reserve. Ischemia on the side of the occluded carotid artery may be due to impaired collateralization during the clamping for CEA.

Alternative

The European Society for Vascular Surgery (ESVS) guidelines recommend staged or synchronous carotid revascularization prior to CABG in asymptomatic carotid stenosis ≥ 70% with contralateral occlusion [30]. Since simultaneous contralateral CEA showed a poor neurological outcome in patients with carotid occlusion prior to cardiac surgery in our study, staged CEA combined with local anesthesia or previous carotid artery stenting (CAS) may be alternatives in the treatment of those patients. However, at least in the context of carotid stenosis, Gopaldas et al. found no significant difference between "staged" and "synchronous" carotid and cardiac surgery in terms of mortality and neurological events. The authors reported a stroke rate of 3.9% for more than 16,000 synchronously operated patients and a stroke rate of 3.5% for 6000 patients with "staged" procedure [31]. A recent analysis by Nejim et al. found no risk reduction by CAS compared to CEA in more than 4000 patients with carotid occlusion and contralateral stenosis outside the context of cardiac surgery [32]. The ESVS guidelines recommend the CAS as an alternative to surgical revascularization, whereby the decision process should be based on patient characteristics, symptoms, and center's experience and perioperative platelet strategy [30]. The major challenge of CAS before cardiac surgery is shown in the analysis by Paraskevas et al., who recently reported an overall stroke rate of 8% in a meta-analysis of CAS patients with unilateral carotid stenosis scheduled for cardiac surgery [33]. In the studies included in the meta-analysis, bleeding complications after cardiac surgery were insufficiently reported: The highest reported rate of major bleeding with chest reopening was 5.9%. The meta-analysis revealed that the antiplatelet therapy strategy in this special setting is still not standardized on the one hand but seems to play an important role for the major events and bleeding complications on the other hand.

Conclusions

Combined CEA and cardiac surgery in the presence of a carotid occlusion had a significantly higher stroke rate compared to isolated cardiac surgery in this setting. Thus, concomitant CEA and cardiac surgery should be avoided. If carotid revascularization is required, a staged procedure or CAS should be rather considered given the lower risk of myocardial infarction. We emphasize the need for more evidence regarding this severe pathologic state in the context of cardiac surgery in order to initiate a meta-analysis with a higher number of patients.

Compliance with ethical standards

Conflict of interest The authors certify that they do not have any conflict of interest.

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