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Abstract

Certain subgroups of patients are at higher risk for CAS. The identification of those patients could improve the decision-making and hence the outcome. This chapter covers factors that are associated with poor outcome during CAS based on the previously reported literature: (1) CAS in female patients, (2) CAS in octogenarians, (3) CAS in patients with difficult aortic arch configuration (type II, III, and bovine arch), (4) CAS in patients who have tortuous common carotid artery (CCA), angulated internal carotid artery (ICA) origin, and/or angulated distal ICA, (5) CAS in high-grade carotid stenosis, (6) CAS for long lesions (≥15 mm), (7) CAS for ostial-centered lesions, (8) CAS in the presence of calcified aortic arch and/or heavily calcified lesions, (9) CAS in the presence of contralateral carotid occlusion, (10) CAS in the presence of vertebral artery occlusion and/or stenosis, and (11) CAS in chronic kidney disease patients.

Keywords: carotid artery stenting, high-risk patients, female gender, octogenarian, difficult arch, tortuous common carotid, tortuous internal carotid, high-grade stenosis, long lesion, ostial stenosis, contralateral occlusion, vertebral artery occlusion, vertebral artery stenosis, chronic kidney

1. Introduction

The term “high-risk patients” was used extensively in the literature when talking about carotid intervention, unfortunately, with inconsistent meaning. Here, this term refers to patients at higher risk during carotid artery stenting (CAS).

The term high-risk carotid artery stenting raises an important question: is there any population at higher risk during carotid artery stenting? The identification of population at higher risk during
CAS could improve the decision-making, regarding patient selection and the used technique. Periprocedural risk of CAS is influenced by patient, device, technique, and operator-related factors. The outcome of CAS in those patients should be defined with respect to standard carotid endarterectomy (CEA), particularly in low-surgical risk patients and high-CAS risk patients.

2. CAS in subgroups at higher risk

2.1. CAS in female patients

The prevalence of carotid artery stenosis (>50%) in elderly females was 6% (8% for males), based on the data that were derived from the American Vascular Association screening program in 2002–2003 [1]. Many gender differences were reported in literature regarding the anatomy, physiology, and atherosclerotic pathology of carotid arteries. The carotid arteries in females have higher velocities in comparison to males [2], with higher outflow/inflow ratio. The atherosclerotic disease in females tends to affect the common carotid artery rather than the proximal internal carotid artery [3]. Meanwhile, the carotid atherosclerotic plaque in females carries more stable characteristics [4].

CEA is a valid option in preventing complications of carotid stenosis. However, the value of CEA in women with asymptomatic disease is questionable. CAS has emerged as an alternative to CEA in selected patients. Several trials [5–7] have compared CEA and CAS; unfortunately, they were not designed for subgroup analysis as regards gender effect on the outcome, especially in asymptomatic patients.

The large trials (the VA cooperative trial, the asymptomatic carotid atherosclerosis study (ACAS), and the asymptomatic carotid surgery trial (ACST)) approving CEA in asymptomatic patients either did not perform subgroup analysis for female patients or did not find significant effect in women. The VA cooperative trial studied males only.

The ACAS showed a 66% [95% confidence interval (CI), 36–82%] 5 years relative stroke risk reduction for males, on the other hand, statistically insignificant risk reduction for females 17% (95% CI, –96 to 65%) [8]. This difference was explained with higher perioperative rates of death or stroke seen in females than males (3.6 vs. 1.7%; P = 0.12), while the ACST showed 4.1% long-term nonperioperative risk reduction of stroke for females. The benefit was marginal when compared with perioperative risk of stroke or death (3.8%) [9].

The carotid revascularization endarterectomy versus stent trial (CREST) did not show sex difference as regards treatment effect [10, 11]. However, women had showed significantly higher perioperative stroke rate with CAS than CEA (5.5 vs. 1.7%; P = 0.01). The rates of myocardial infarction (MI) for women were equivalent for both CAS and CEA (1.5 vs. 1.7%, respectively; P = 0.81).

The availability of comprehensive medical treatment and CAS as alternative options to CEA added to the complexity of the decision-making in asymptomatic females. Further research is needed in this area.
2.2. CAS in octogenarians

The studies, which have validated CEA for stroke prevention in symptomatic and asymptomatic carotid stenosis patients, have excluded high-risk patients for surgery (including octogenarians) [8, 12, 13]. On the other hand, other smaller studies have shown safety of CEA in octogenarians [14–19].

The CREST trial reported 12% 30-day rate of stroke and death among octogenarians [20]. Kastrup et al. reported 10% rate of stroke and death among symptomatic patients and 13% among asymptomatic patients >75 years [21]. Stanziale and his colleagues reported 8% 30-day stroke among octogenarians [22].

In a meta-analysis for three randomized controlled trials, the treatment effect was modified by age in the CAS group (12 vs. 5.8% in patients <70 years) [23].

The high rate of stroke in octogenarians is partially assumed to unfavorable anatomy which precludes safe navigation; this was reported in several studies [24–27]. This includes aortic arch elongation, aortic calcification, ostial stenosis, and vessel tortuosity. Lam and his colleagues [26] assessed 133 CAS patients for the anatomic characteristics that affect the feasibility of CAS. They found increased incidence of unfavorable anatomical characteristics among octogenarians in comparison with younger patients; arch elongation (82 vs. 56%, P = 0.008), arch calcification (59 vs. 30%, P = 0.003), common carotid artery origin stenosis (47 vs. 22%, P = 0.006), common carotid artery tortuosity (70 vs. 38%, P = 0.0009), and internal carotid artery tortuosity (74 vs. 50%, P = 0.019). It has been suggested that with correcting for complex anatomy, old age was no longer a predictor for poor outcome [26, 28–30]. Unfortunately, other age-related factors may increase the risk in such age group. Specific comorbidities such as congestive heart failure, aortic stenosis, and contralateral carotid stenosis are more common among octogenarians [20, 22, 27, 31, 32]. On the other hand, different mechanisms such as emboli, hypoperfusion, and neuronal susceptibility in elderly contribute to increased risk for CAS [33].

Werner and his colleagues reported a 10-fold increase in death among octogenarians compared to younger patients [27]; they attribute their finding to high incidence of symptomatic aortic stenosis among octogenarians. Three of 12 patients with this problem died before discharge; death occurred only in preoperatively decompensated patients. The safety of CAS in severe aortic stenosis patients was assessed in small cohort (52 patient); the 30-day death rate was 6%. Noteworthy, all patients in that cohort were hemodynamically stable prior to CAS [34].

Despite the higher CAS periprocedural risk, surprisingly, octogenarians have fewer comorbidities [35]. We think that good selection of octogenarian CAS candidates can minimize the perioperative risk. A more comprehensive preoperative assessment is needed in such group of patients.

2.3. CAS in patients with difficult aortic arch configuration (type II, III, and bovine arch)

Aortic arch type is a key in CAS success. Difficult aortic arch is associated with repeated aggressive manipulation, which may generate emboli. Nevertheless, unfavorable aortic arch
configuration may impede guiding catheter or long sheath insertion. Faggioli and his colleagues reported that the proximal tortuosity (difficult aortic arch due to arterial elongation) was associated with technical failure [36]. Type of arch was found to contribute to higher stroke rates in six of the seven studies. [21, 25, 27, 37–39]. Wimmer and his colleagues [37] reported that type II and III arches were predictors of stroke following carotid stenting, whereas Werner et al. [27] found the same with bovine arches. Dumont et al. [39] demonstrated that unfavorable arch anatomy, namely a target vessel taking an acute angle off the arch, was a predictor of perioperative stroke risk. In fact, in certain studies, type III aortic arch was contraindicated for CAS [40].

The carotid revascularization endarterectomy versus stenting trial 2 (CREST-2) study will compare outcomes in asymptomatic carotid stenosis patients randomized to best medical treatment (BMT) versus CEA plus BMT versus CAS plus BMT, and patients will be excluded from undergoing CAS if they have a type III arch, severely angled or tortuous innominate artery or CCA, or a severely calcified aortic arch [41].

Radial, brachial, or direct carotid access may be used as alternative for femoral in this subgroup of patients. Alternative access may increase the technical success rate and decrease the perioperative risk of complication.

2.4. CAS in patients who have tortuous common carotid artery (CCA), angulated internal carotid artery (ICA) origin, and/or angulated distal ICA

Tortuous carotid is found on ~16% of cerebral angiograms [42]. Carotid tortuosity represents a challenge in patients undergoing CAS. Wimmer et al. [37], Faggioli et al. [36], and Fanous et al. [43] found that tortuosity of the CCA and proximal ICA were correlated with both technical failure and increased risk of complications. The periprocedural risk significantly increased in a study of 262 patients with symptomatic carotid artery stenosis when the angulation between the ICA and the CCA exceeded 60° [44]. Similarly, the stroke risk was correlated with severe tortuosity of the CCA and significant angulation of the ICA origin in an unselected population of 751 patients who underwent 833 CAS procedures [27]. In fact, several authors were forced to abort CAS procedures secondary to severe ICA tortuosity [26, 45, 46]. Myouchin reported that among 31 symptomatic and asymptomatic carotid artery stenosis patients, successful stenting was not possible in two (6.5%) patients because of severe carotid tortuosity (angles of 60° and 73°) [47].

An anatomically difficult distal landing zone not only makes deployment of protection devices more difficult but also makes the retrieval of these devices more challenging [43, 48, 49]. Reimers et al. [50] reported that the distal EPD could not be advanced beyond the lesion in 10 patients owing to high degree of distal ICA tortuosity and lesion severity in a series of 753 patients who underwent 808 CAS procedures. Fanous et al. [43] reported that despite the successful deployment and retrieval of distal EPD in all cases, the presence of hostile anatomy for the deployment of distal EPD was correlated with increased periprocedural risk among 221 symptomatic patients who underwent CAS.
2.5. CAS in high-grade carotid stenosis

Critical stenosis (>85%) was previously considered by some authors as a contraindication for CAS [40, 42]. Earlier, critical stenosis was technically challenging, as it impeded the safe advancement of distal EPD [43, 44]. With improvement of the available endovascular devices, stenting of such lesion is no more challenging except for subtotal occlusion (99% stenosis). Subtotal occlusion was associated with increased perioperative risk [43, 52].

2.6. CAS for long lesions (≥15 mm)

The American Heart Association/American College of Cardiology defines lesion length as the distance from the definite proximal to distal shoulder of the lesion in the projection of the best elongation of the stenosis. Only the portion of stenosis that was ≥50% was quantified [42].

Long lesions (≥15 mm) carry higher risk of poor outcome, even in the presence of cerebral protection [37]. The periprocedural stroke rate in those patients group was 17 versus 2.1% in other patients. Also, they were more prone to 30-day adverse events (19.1 vs. 3.4% in other patients) [25].

It seems that proximal protection devices may be more suitable in those patients with long lesions. Saini and his colleagues reported that patients with carotid lesions >10 mm length who underwent CAS with proximal protection devices showed a trend of better safety outcomes including perioperative stroke than patients with distal protection devices [53].

2.7. CAS for ostial-centered lesions

The definition of ostial lesions should be limited to those lesions with maximum stenosis at the ostium of the ICA.

Difficult wire engagement and hemodynamic instability are more common to occur with ostial lesions [43]. They are associated with higher rate of stroke and cardiac complications [44–46].

Sayeed and his colleagues reported that patients with ostial lesions have higher incidence of periprocedural stroke (7.1 vs. 1.8% in patients without ostial lesions). The rates of 30-day adverse events were also higher in those patients (9.1 vs. 2.9%) [25].

2.8. CAS in the presence of calcified aortic arch and/or heavily calcified lesions

Extensive calcification either concentric carotid calcification or aortic arch calcification was associated with increased perioperative risk [47–49]. They were considered a contraindication for CAS in certain studies [50, 51].

On the other hand, Tsutsumi and his colleagues reported the feasibility of CAS in near-total circumferential calcified lesions, with no reported morbidity or mortality [54].
Bazan and his colleagues studied 94 patients. They found that the patient ≥75-years old have significantly more aortic arch calcification than younger patients. They advised for preprocedural assessment of arch calcification as method for CAS risk stratification [28].

Kastrup and his colleagues studied 62 symptomatic patients (49 aged <80 years; 13 aged >80 years) who underwent CAS. They found that octogenarians had a significantly higher incidence of severe aortic arch calcification (54 vs. 14%, P < 0.01). A severe aortic arch calcification was found to be a predictor for new DWI lesions inside and outside the treated territory (OR, 1.8; 95% CI, 0.99–3.335; P = 0.05) [55].

2.9. CAS in the presence of contralateral carotid occlusion

Patients with CCO have bilateral carotid disease and therefore may have increased cardiovascular risk. The impaired collateral system and the perioperative hemodynamic changes may contribute in increased risk during carotid intervention in those patients.

The range of incidence of contralateral carotid occlusion (CCO) among CEA patients was 6–10% [56].

The North American symptomatic carotid endarterectomy trial (NASCET) [57, 58] and two meta-analysis [59, 60] showed that the contralateral carotid occlusion was a predictor of poor outcome after ipsilateral CEA. The presence of contralateral carotid artery occlusion was considered as high-risk criteria for CEA in many trials [5, 37]. On the other hand, Rockman and his colleagues reviewed previous studies and concluded that the presence of CCO does not increase the CEA perioperative risk [61]. Kretz and his colleagues identified one study in their meta-analysis that reported different outcome for patients with and without CCO after CEA [62]. Many large center trials have reported excellent outcome after CEA in patients with CCO [63–66]. A retrospective analysis of CEA operative data in patients with CCO and/or vertebral artery occlusion (VAO) revealed that the presence of CCO increases the need for carotid shunt during CEA but did not increase the perioperative risk. [67] Worth to know, among CEA patients who had CCO, the procedural outcome was not affected using shunts [56].

Halm and his colleagues reported that contralateral carotid stenosis >50% was independent predictor for stroke after CEA [68].

Yang and his colleagues retrospectively analyzed the data of 698 CEA patients and 455 CAS patients. They reported that the CCO was associated with higher rate of early symptomatic neurological complication (ESNC) but not stroke alone in CEA patients only. Vertebral artery occlusion either unilateral or bilateral was not associated with increased risk of ESNC or stroke in CEA or CAS patients [69].

The posterior part of circle of Willis provides collateral supply to contralateral hemisphere during carotid clamping in patients with CCO. The CCO patients with incomplete posterior part of circle of Willis are at higher risk of cerebral ischemia during carotid clamping [70].
Elective CAS in patients with contralateral high-grade carotid stenosis or occlusion was not associated with poor neurological outcome [71–73]. On the other side, based on the carotid artery revascularization and endarterectomy (CARE) registry, Mercado and his colleagues reported increased risk of early post CAS stroke, myocardial infarction, or death in CCO patients [74].

Ricotta and his colleagues evaluated 1128 CAS and 666 CEA patients with CCO. They concluded that the benefit of lower periprocedural risk CEA is lost in patients with CCO because of increased stroke rates in those patients. CAS periprocedural risk was not affected by the presence of CCO regardless of the symptomatic state [56].

In patients with CCO, CAS has theoretical advantages over CEA, of short carotid occlusion duration and the lack of general anesthesia. It is important to know that CCO is one of the factors that identify patients at high risk for CEA and qualify them for reimbursement of CAS according to the Centers for Medicare & Medicaid Services (CMS). We think that in the presence of CCO or contralateral high-grade carotid stenosis, CAS should be encouraged over CEA.

2.10. CAS in the presence of vertebral artery occlusion or stenosis

In patients with unilateral carotid occlusion, Nicolau and his colleagues observed increase in the peak systolic velocity and blood volume in vertebral artery [75]. Severe vertebral artery stenosis (>80%) was associated with increased 30 days risk of stroke or death in CEA patients [76]. On the other hand, Yang and his colleagues found that unilateral or bilateral vertebral artery occlusion (VAO) was not a risk factor for early symptomatic neurological complication or postoperative stroke in CEA or CAS patients [69].

Currently, no special recommendation regarding cases with vertebra-basilar occlusive disease, yet in some cases, the author may prefer CAS to avoid the effect of general anesthesia and temporal carotid clamping, which may be dangerous.

2.11. CAS in chronic kidney disease patients

Patient is defined to have chronic kidney disease (CKD) once the estimated glomerular filtration rate (eGFR) is less than 60 mL/min/1.73 m². Once the patient has renal failure that necessitates dialysis, he is considered to have end-stage renal disease (ESRD). CKD patients are at higher risk for ischemic stroke than general population [77]. Extracranial carotid artery disease is a common comorbidity in CKD patients [78].

The available data on the outcome of CEA or CAS in those patients are scarce. All CKD patients are at high surgical risk [79]. AbuRahma and his colleagues studied the effect of CKD of CEA outcome and concluded that the patients with moderate to severe CKD (GFR <60) had increased risk of stroke or death and, that CEA should not be used as alternative for CAS in CKD patients [80]. Tarakji and his colleagues retrospectively reviewed the outcomes of CEA in CKD patients including hemodialysis patients. They classified
CKD patients into three groups according to serum creatinine level into: normal renal function, 121 patients with mild renal impairment (serum creatinine 1.6–2.9 mg/dL), and 23 patients with severe renal impairment (serum creatinine >2.9 mg/dL or requiring hemodialysis). In patients with mild renal impairment, the incidence of stroke, MI, and death were 2.4, 9.0, and 4.9%, respectively. The figures were higher in patient with severe renal impairment; incidence of stroke, MI, and death was 9.5, 4.7, and 9.5%, respectively [81]. Rigdon and his colleagues assessed the outcome of CEA in CKD patients (21 patient with mild renal impairment and 7 patients with severe renal impairment). Patients with mild renal impairment had the same perioperative outcome of patients with normal kidney function. Patients with severe renal impairment had higher rate of stroke and death (43%) [82].

Donahue and his colleagues studied 126 CKD patients who underwent CAS for the risk of acute kidney injury (AKI) and 30 days major adverse events. AKI occurred in 26 patients (21%) and mostly caused by hemodynamic depression (mainly hypotension). AKI was associated with a higher rate of 30 days major adverse events [83].

Chronic kidney disease (CKD) was an independent predictor of CAS periprocedural complications and long-term disability [35, 37, 84]. On the other hand, a care registry analysis showed that CKD was not an independent predictor for early outcome [85].

Saw et al. studied the outcome of CAS in CKD patients. They reported that the presence of CKD was associated with higher combined endpoints of MI, stroke, and mortality at 7 days (4.1%) and 6 months (8.8%) [84].

Adil and his colleagues retrospectively reviewed the United States nationwide inpatient sample data files from 2005 to 2011 for the outcome of end-stage renal disease (ESRD) and CKD patients who underwent CAS or CEA. They reported that 43,875 CEA were performed in CKD patients, 3888 (8.8%) of them were ESRD patients. ESRD patients were associated with higher rates of in-hospital mortality (odds ratio (OR) 4.3, 95% confidence interval (CI) 2.1–9.0; P ≤ 0.0001) and moderate to severe disability (OR 1.4, 95% CI 1.1–1.8; P = 0.009). On the other side, 8148 CKD patients underwent CAS, 693 (8.5%) of them were ESRD patients. ESRD patients were associated with higher rates of in-hospital mortality (OR 3.7, 95% CI 1.0–13.9; P = 0.04) and moderate to severe disability (OR 1.7, 95% CI 1.0–3.3; P = 0.05). No significant difference was found between both the procedures in ESRD patients [86].

Unfortunately, the result of these studies cannot be generalized due to lack of power, patient selection bias, and retrospective nature of these studies. CKD patients are high-risk surgical candidates, and CAS may be advised in the author opinion.

Conflict of interest

There are no conflicts of interests.
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