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Long-Term Outcome of Symptomatic Patients Undergoing Hybrid Revascularisation for Extracranial Carotid Artery Tandem Stenosis

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WHAT THIS PAPER ADDS

This study shows that hybrid revascularisation is feasible and safe in symptomatic patients with an extracranial carotid artery tandem stenosis. This study provides data on purely symptomatic patients including a long-term clinical and imaging follow up period of more than six years. In the future, these surgical outcomes need to be offset against the natural course in patients with a symptomatic carotid tandem lesion.

Objectives: Carotid tandem lesions are a multilevel significant (>50%) atherosclerotic disease involving both the internal carotid artery (ICA) and either the ipsilateral common carotid artery (CCA) or the innominate artery (IA). These lesions may be challenging to treat. Current guidelines offer no definitive recommendation on the optimal treatment algorithm. The aim of this analysis was to assess the long-term outcome of patients undergoing surgical revascularisation for tandem lesions.

Methods: In two centres, consecutive patients who underwent carotid endarterectomy (CEA) for a symptomatic carotid artery stenosis between 2003 and 2017 were screened retrospectively for the presence of a carotid artery tandem lesion. All eligible patients were treated by a hybrid approach, consisting of retrograde stenting of the proximal CCA or IA followed by CEA. All patients had a yearly clinical check up including duplex ultrasound. The primary outcome was occurrence of any stroke, death, myocardial infarction (MI), or transient ischaemic attack (TIA) within 30 days. Secondary outcomes were any stroke, death, MI, or TIA and occurrence of restenosis ≥50% during follow up.

Results: Sixteen of 2368 symptomatic patients were included. Besides a high grade ICA stenosis, patients had a significant ipsilateral stenosis of the CCA ($n = 13$) or IA ($n = 3$). Within 30 days there were no deaths, strokes, or TIAs. Two patients had a clinical MI. During a median follow up of 73 (interquartile range 22–85) months, three patients died. One patient developed a symptomatic restenosis of the ICA (ipsilateral TIA). Two patients (without restenosis) developed an ipsilateral stroke and a MI.

Conclusions: In this small case series, hybrid revascularisation of carotid tandem lesions in symptomatic patients seems feasible and safe. Long-term data show a relatively high number of any adverse events. These surgical outcomes need to be offset against the natural course in patients with a symptomatic carotid tandem lesion.

Keywords: Tandem stenosis, Hybrid revascularisation, Carotid, Symptomatic, Stroke
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INTRODUCTION

Proximal carotid tandem lesions are defined as a multilevel significant (>50%) atherosclerotic disease involving the internal carotid artery (ICA) in combination with the proximal ipsilateral common carotid artery (CCA), or the innominate artery (IA). It is a relatively uncommon condition, with an incidence of less than 5% among all patients with a significant carotid stenosis at the level of the bifurcation on cerebral angiogram.[1] Nevertheless these patients have been considered as high surgical risk and have therefore been excluded from recent randomised controlled trials. In the longer term, this condition has been associated with high death rates.[2]

Although the effectiveness of carotid endarterectomy (CEA) for stroke prevention has been established for patients with a significant symptomatic carotid artery stenosis, the optimal treatment approach for the subset of patients with a proximal tandem lesion is still a matter of debate.[3] Over recent years, several small retrospective cohort studies have published their treatment approach and results with variations in outcome.[2,4–10] In 2011, a meta-analysis of

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13 observational studies was performed, of which only 79 of the 129 included patients underwent revascularisation by a hybrid technique.[11] This hybrid technique was first described in 1996[12] and includes surgical exposure of the carotid bifurcation, followed by retrograde stenting of the proximal CCA or IA with subsequent CEA of the ICA. The authors reported a relatively low 30 day stroke/death rate of 1.5%. The largest study within this meta-analysis was published in 2004 on 34 patients with a follow up of 34 months. No distinction between symptomatic and asymptomatic patients was made in this study. Based on the results of the meta-analysis, cohort studies, and the expert opinion panel of the European Society of Vascular Surgery (ESVS), a recommendation on the treatment approach for this high risk subgroup was made in the recent ESVS guideline on treatment of carotid artery disease.[13] Based on Level C and Class IIA evidence, a hybrid technique should be considered as a treatment approach in these patients. However, no definitive recommendation could be made based on the available and published literature.

Owing to this marginal available evidence on the effectiveness of the hybrid treatment approach in symptomatic patients with a carotid tandem lesion, the aim was to assess the outcome of the hybrid approach and results of a series of patients in two vascular centres.

METHODS

Ethical approval was obtained from the local Research Ethics Committee.

Patient selection

The Athero-Express is an ongoing, prospective biobank study collecting atherosclerotic plaques, patient baseline characteristics and outcomes from patients undergoing CEA in two Dutch tertiary referral hospitals: University Medical Centre Utrecht and St. Antonius Hospital Nieuwegein. All patients recorded in the Athero-Express biobank between 2003 and 2017 were included for analysis in the present study. All patients were screened retrospectively for the presence of a carotid artery tandem lesion.

All patients with a carotid artery tandem lesion underwent a hybrid procedure, which is the standard multidisciplinary treatment approach. Furthermore, all patients were treated with adequate medical therapy, including standard antiplatelet therapy and lipid lowering medication, and if necessary antihypertensive or antidiabetic medication.[14]

The following baseline patient characteristics were collected in a dedicated database: (1) patient demographics (age, gender), (2) clinical characteristics (medical history: hypertension, diabetes mellitus, hypercholesterolemia, peripheral artery disease, smoking, previous ipsilateral CEA, type of index event), (3) use of medication, (4) imaging characteristics.

Definition of a carotid artery tandem lesion

Routine pre-operative imaging was performed in all patients, and included a carotid duplex in combination with either a magnetic resonance angiography (MRA) or computerised tomography angiography (CTA) scan. All patients were evaluated according to the stenosis criteria by the North American Symptomatic Carotid Endarterectomy Trial (NASCET).[15] According to these criteria, a significant stenosis of the ICA was defined as 50% or more in men and 70% or more in woman. A significant stenosis of the CCA or IA was defined as 50% or more, regardless of patient sex.

Treatment

The hybrid revascularisation technique as applied in the secondary and tertiary referral centres is a modification of the original technique as suggested by Dietrich et al.,[12] and has been reported previously in detail.[16] In short, the procedure was performed under general anaesthesia with cerebral monitoring (electroencephalography and transcranial Doppler), which is similar to the treatment approach in patients who undergo a CEA for high grade symptomatic carotid artery stenosis. A standardised longitudinal skin incision is used. After exposure of the carotid bifurcation, the CCA, ECA, and ICA are clamped. If tolerated, the CCA clamp is removed and retrograde puncture of the CCA is performed. If clamping is not tolerated (flattening on electroencephalography), the CCA and ECA clamps are removed, and the ICA is intermittently clamped during retrograde puncture of the CCA and during angioplasty. After placing the balloon expandable stent (length 30 mm, diameter 8 or 9 mm; Scuba, Medtronic, Minneapolis, MN, USA), the arteriotomy is extended distally over the carotid bulb and standard longitudinal CEA is performed. If clamping was not tolerated a shunt was placed before starting the CEA procedure. Before re-establishing cerebral blood flow, the vessel was flushed to provide protection from cerebral embolisation. Closure was performed with a (bovine) patch angioplasty.

Standard post-operative care was performed according to the hospital protocol, which includes neuromonitoring by transcranial Doppler 2 h after the procedure.[17]

Outcome

The primary outcome was defined as the occurrence of any stroke, death, myocardial infarction (MI) (defined as ischaemic changes on electrocardiogram or elevated troponin levels), or transient ischaemic attack (TIA) within the first 30 days of treatment. Secondary outcomes were (1) occurrence of stroke, death, MI, or TIA after 30 days, and (2) occurrence of restenosis of the ICA, CCA, or IA (which includes a stenosis of >50% according to the North American Symptomatic Carotid Endarterectomy Trial criteria for carotid stenosis).

All patients were seen at the outpatient clinic six weeks to three months after the procedure. A duplex ultrasound was performed before the appointment. Afterwards, patients were seen on a yearly basis at the outpatient clinic with duplex. An additional CTA was performed in those patients who developed an event, who had upper extremity effort fatigue with lowered asymmetric blood pressure on

the affected arm considered for brachiocephalic stents, or in patients with an abnormal duplex.

Statistical analysis

Data were entered and analysed in SPSS (IBM SPSS Statistics for Windows, Version 23.0. Released 2015; IBM Corp, Armonk, NY, USA). Categorical variables are presented as frequencies. Continuous variables are presented as medians with interquartile ranges (IQR). No formal statistical analysis could be conducted because of the limited sample size.

RESULTS

Patient population

During the inclusion period, 2368 CEAs were performed. Sixteen patients were identified in whom a hybrid revascularisation was performed because of a carotid artery tandem stenosis (Table 1). The median age was 68 years (IQR 62—71 years) and 13 patients (81%) were female. Thirteen patients (81%) presented with a TIA or amaurosis fugax and three patients (19%) with a stroke. Three patients had a significant stenosis of the innominate artery and 13 patients had a significant stenosis of the CCA. Four patients experienced symptoms because of an ipsilateral restenosis of the ICA after previous CEA. The median time between the last cerebral event and treatment was 17 days (IQR 12—29 days).

Table 1. Patient and procedural characteristics

Characteristic	Total (n = 16 patients)
Median age (IQR), years	68 (62—71)
Male: Female, *n*	3:13
Symptoms, n	
TIA or amaurosis fugax	13
Stroke	3
Asymptomatic	0
Hypertension, *n* (%)	13 (81)
Diabetes mellitus, *n* (%)	1 (6)
Hypercholesterolaemia, *n* (%)	12 (75)
Current smoker, *n* (%)	9 (56)
Use of antiplatelet therapy, n (%)	14 (88)
Acetylsalicylic acid	4 (25)
Acetylsalicylic acid + clopidogrel	3 (19)
Acetylsalicylic acid + dipyridamole	6 (38)
Clopidogre	1 (6)
Use of anticoagulant therapy, *n* (%)	2 (13)
Use of lipid lowering therapy, *n* (%)	14 (88)
Use of antihypertensive medication, *n* (%)	13 (81)
Peripheral artery disease, *n* (%)	7 (44)
Previous ipsilateral CEA, *n* (%)	4 (25)
Site of proximal lesion, n (%)	
Common carotid artery	13 (81)
Innominate artery	3 (19)
Operated artery, right, *n* (%)	5 (31)
Days between event and intervention, median (IQR)	17 (12—29)

n = number; IQR = interquartile range; TIA = transient ischaemic attack; CEA = carotid endarterectomy.

Clinical outcome and follow up

Clinical outcome and follow up are shown in Table 2. Within 30 post-operative days, two patients developed a clinical MI of which one presented as an in hospital cardiac arrest with successful resuscitation. No strokes, TIAs, or deaths were reported in the remaining patients. This resulted in a 30 day stroke or death rate of 0%, and a 30 day any adverse event rate of 12.5%.

Clinical follow up was performed in all patients, with a median follow up duration of 73 (IQR 22—85) months. One patient developed an ipsilateral TIA (significant restenosis), one patient an ipsilateral stroke (no restenosis), and one patient a MI. This resulted in a stroke incidence rate of 15 of 1000 patients yearly. Furthermore, three patients died after 1.5, 5, and 47 months, of whom one died of a cardiovascular cause. In this patient coronary artery bypass grafting (CABG) was performed six weeks after the carotid revascularisation. The patient developed a MI and mesenteric ischaemia after CABG and died. One patient developed a symptomatic restenosis of the ICA (ipsilateral TIA) of more than 50%, treated by a switch in antiplatelet therapy.

DISCUSSION

In this small case series it was revealed that in patients with a combined high degree stenosis of the carotid bifurcation and inflow track, a hybrid revascularisation is a technically feasible and, in terms of stroke or death, a safe revascularisation technique. However long-term data shows a relatively high number of adverse events.

A limited number of studies have published results of their preferred treatment approach. The stroke/death rates varied from zero to 9% within 30 days and from 0% to 54% in the long term.[2,4—9] These stroke/death rates are generally higher than the group of patients without a tandem

Table 2. Outcome after hybrid revascularisation for symptomatic extracranial carotid artery tandem stenosis in 16 patients

Outcome	Number (%)
Primary outcome <30 days	
TIA	0
Stroke	0
Cranial nerve injury	0
Myocardial infarction	2 (12.5)
Death	0
Secondary outcome >30 days	
Median follow-up (IQR), months	73 (IQR 22—85)
Ipsilateral TIA	1 (6.3)
Ipsilateral stroke	1 (6.3)
Myocardial infarction	1 (6.3)
Death	3 (18.8)
Cardiovascular death	1 (6.3)
Non-cardiovascular death	2 (12.5)
Restenosis	
Symptomatic > 50% ICA	1 (6.3)
Symptomatic > 50% CCA or IA	0

TIA = transient ischaemic attack; IQR = interquartile range; ICA = internal carotid artery; CCA = common carotid artery; IA = innominate artery.

lesion who underwent a CEA for a single symptomatic significant carotid artery stenosis. Over recent years a limited number of small observational studies have published results of this specific hybrid technique, with between five and 62 patients with a maximum clinical follow up of six years[4,6,8,10,18–24] (Table 3). The most recently published study reported a clinical follow up of six years and an imaging (only duplex) follow up of three years.[10] The current study is the first reporting imaging follow up data for as long as six years after hybrid revascularisation. In addition, this most recently published study performed the original hybrid approach in only 15% of the patients ($n = 9$).[10] The other patients were treated by CEA followed by the endovascular procedure. The largest observational study, in which the original hybrid approach was first performed, was published in 2004[4] after which the current study is the largest study in purely symptomatic patients.

Over recent years, a variety of treatment approaches for this high risk subgroup have been published, including an endovascular approach (simultaneous stent placement), open surgical approach (extra-anatomic or in line reconstruction plus CEA), and the hybrid approach.[3] In particular, the continuous improvement in imaging techniques and endovascular devices is vital for the endovascular and hybrid approaches. Another reasonable explanation for the high event rate could be the relatively long 73 month follow up period.

A remarkable finding is the large number of women included in this study population (13 of 16). This could be due to bias by the limited sample size of this study. Alternatively, it could also imply that there is a different underlying atherosclerotic process, especially if compared with the symptomatic significant carotid artery stenosis group, the majority of whom are men.

The data support the statement that patients with a tandem lesion are a high risk subgroup mostly related to myocardial injury in two of the 16 patients. The cerebrovascular outcome within 30 days however was favourable. The cerebrovascular outcome during follow up seems acceptable with only one stroke within a median of 73 months. However, the cardiovascular event rate during follow up was high, and warrants intensified follow up of this high risk patient group. If these results are compared with the results of a recently published study, it must be reaffirmed that only 15% of the patients in the study by Clouse et al.[10] were treated with this original hybrid approach. Remarkably, all peri-procedural strokes (9.6%) were observed in patients who were treated by the non-original hybrid approach.[10] Only in 77% of the patients was cerebral protection by clamping the distal carotid artery during stent placement performed.[10] As such, the present series is the largest series with long-term follow up of the true hybrid intervention for extracranial carotid tandem stenoses. Besides this, the authors stated that flushing manoeuvres are less favourable in clearing the carotid by performing the non-original hybrid approach. These could be reasons for the higher peri-procedural stroke rate than the current study.

Optimal patient selection is the key to success in this high risk subgroup. Asymptomatic patients should be treated solely by best medical therapy. Only symptomatic patients with a haemodynamically relevant stenosis of the proximal lesion in combination with a high grade (>70%) stenosis of the internal carotid artery should be considered for treatment by this original hybrid approach. Additional imaging of the circle of Willis could be performed for better patient selection as this subgroup are likely to have a more diffuse and aggressive form of vascular disease (intracranial disease).

Limitations of the current study are its retrospective nature and the small sample size. These patients have been considered to be at high risk of surgery and therefore have been excluded from recent randomised controlled trials. Therefore, it is important to keep publishing results from observational studies, as they are the best available evidence at this moment. Besides this, the routine imaging follow up protocol consisted of a duplex ultrasound. Only in cases with an abnormal duplex was an additional CTA

Table 3. Overview of published reports on patients with extracranial carotid artery tandem stenosis treated by hybrid revascularisation

First author	Year of publication	Treated by hybrid technique (*n*)	Symptomatic patients (*n*)	Follow up (months)	Any stroke/death rate[a] (%)
Allie[4]	2004	34	NR	Median 34 (6–84)	0
Arko[20]	2000	6	2	Median 23.6 (6–43)	17
Bozzay[18]	2017	6	5	Median 7.8 (1–36)	0
Clouse[10]	2018	62[b]	26	Mean 72 (48)	19
Grego[6]	2003	16	8	Mean 1	0
Macierewicz[24]	2000	8	8	Median 20 (6–31)	0
Radak[8]	2017	12	NS	Median 22 (6–36)	0[c]
Starodubtsev[19]	2015	12	3	Median 33.5 (6–48)	17
Sullivan[21]	1998	14	5	Mean 14.3	NS
Vermeulen[23]	2011	11	NR	Median 33 (11–60)	0

Values are reported as mean (standard deviation) or median (range). NR = not reported; NS = not specified for this subgroup who were treated by hybrid revascularisation.

[a] Any stroke/death rate based on symptomatic and asymptomatic patients.

[b] Only nine patients were treated by the original hybrid technique.

[c] Only information on stroke rate available.

performed. The restenosis rate of the most proximal lesion treated by stenting could not be investigated reliably with this imaging protocol. Therefore, strictly taken, no definitive conclusions could be drawn on the durability of this hybrid treatment approach. Although there is no suspicion of a significant proximal restenosis in this series, a restenosis rate of 15% has been observed in a recently published study.[10] Although, no information on the exact type of treatment (original vs. non-original hybrid approach) compared with the restenosis rate have been reported. Lastly, no parallel cohort was available which described solely the conservative treatment of these patients. Therefore, no definitive conclusions on optimal efficacy and long term safety could be made.

In conclusion, in this small case series, hybrid revascularisation of proximal carotid tandem lesions in symptomatic patients seems feasible and safe in terms of stroke or death. Data for the long term show a relatively high number of any adverse events. These surgical outcomes need to be offset against the natural course in patients with a symptomatic carotid tandem lesion.

CONFLICT OF INTEREST

None.

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