Atherosclerosis 237 (2014) 521–527

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

The impact of female sex on long-term survival of patients with severe atherosclerosis undergoing endarterectomy

Joyce E.P. Vrijenhoek [a, b, c, *], Saskia Haitjema [a], Gert Jan de Borst [c], Jean-Paul P.M. de Vries [d], Ilonca Vaartjes [e], Frans L. Moll [c], Gerard Pasterkamp [a], Hester M. den Ruijter [a]

[a] Experimental Cardiology Laboratory, University Medical Center Utrecht, Utrecht, The Netherlands
[b] Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands
[c] Department of Vascular Surgery, University Medical Center Utrecht, Utrecht, The Netherlands
[d] Department of Vascular Surgery, St. Antonius Hospital Nieuwegein, The Netherlands
[e] Julius Center of Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

ARTICLE INFO

Article history:
Received 30 June 2014
Received in revised form
15 September 2014
Accepted 2 October 2014
Available online 18 October 2014

Keywords:
Atherosclerosis
Endarterectomy
Mortality
Prognosis
Sex-specific

ABSTRACT

Objectives. Long-term age- and sex-specific mortality data in patients undergoing carotid endarterectomy (CEA) and iliac/femoral endarterectomy (FEA) are scarce. We examined long-term mortality in these patient groups, stratified by age and sex. **Methods**. Between 2002 and 2012, 1771 patients (1200 men, 571 women) treated by CEA, and 685 patients (495 men, 190 women) who underwent FEA, were included and linked to the national mortality registry of the Netherlands. Absolute mortality risks during follow-up were analyzed by life-table and Kaplan Meier survival analyses in two age groups and stratified by sex, and compared to a matched sample from the general population. In addition, multivariable Cox regression analyses were performed. **Results**. After CEA, with a median follow-up duration of 4.3 years (interquartile range 2.0–7.1), 298 all-cause deaths had occurred in men (25%) and 105 (18%) in women. As in the general population, cumulative survival after CEA was significantly better in women compared to men ($P = 0.002$) and absolute CEA-associated mortality risk in women was similar to that of the general population. For FEA patients, mortality risk was worse than for CEA patients and the general population in both sexes and surprisingly, female sex did not have a favorable effect on survival. Following FEA, 130 men (26%) and 51 women (27%) died after a median follow-up time of 3.0 years (interquartile range 1.5–5.9). Stratifying by age, and adjusting for cardiovascular risk factors did not change these trends. **Conclusions**. Long-term mortality after CEA is higher in men than in women, and in women mortality risk is similar to the general population. After FEA, the benefit of women as seen after CEA is lost.

1. Introduction

Any vascular procedure for obstructive atherosclerosis could have an effect on survival. Carotid and iliac or femoral endarterectomy (CEA/FEA) are procedures that are widely performed by vascular surgeons throughout the world to improve prognosis and/or relieve (ischemic) symptoms in patients with severe atherosclerosis. CEA has shown a benefit in patients with symptomatic carotid artery stenosis and subgroups of asymptomatic patients compared to medical treatment alone [1,2]. FEA is performed in patients with iliac and/or femoral arterial occlusive disease and intermittent claudication or critical limb ischemia. Yet, there is limited information on the short- and mid-term survival of patients undergoing CEA or FEA and noticeably, long-term prognostic data are even rarer (Supplemental material, Tables 1 and 2). In addition, the available data ignore age and sex as important determinants of mortality. Therefore the aim of the present study is to describe absolute mortality risks after CEA or FEA procedures up to 10 years of follow-up, stratified by age and sex.

* Corresponding author. University Medical Center Utrecht, P.O. Box 85500, 3508 GA Utrecht, The Netherlands.
E-mail address: j.e.p.vrijenhoek@umcutrecht.nl (J.E.P. Vrijenhoek).

http://dx.doi.org/10.1016/j.atherosclerosis.2014.10.010
0021-9150/

Table 1
Patient characteristics.

	CEA			FEA			
	Male patients ($n = 1200$)	Female patients ($n = 571$)	P-value[a]	Male patients ($n = 495$)	Female patients ($n = 190$)	P-value[a]	
Age (mean) (SD)	68.8 (8.9)	69.2 (9.9)	0.46	67.4 (8.7)	67.6 (10.7)	0.83	
Current smoking	388/1176 (33)	208/548 (38)	0.044	188/482 (39)	87/187 (47)	0.076	
Diabetic mellitus	278/1200 (23)	115/570 (20)	0.16	149/495 (30)	52/190 (27)	0.48	
Hypertension	815/1162 (70)	441/557 (79)	<0.001	345/479 (72)	135/186 (73)	0.89	
Body Mass Index (BMI) (mean) (SD)	26.3 (3.6)	26.3 (4.7)	0.91	26.8 (10.2)	25.1 (4.4)	0.027	
Alcohol use							
No	379/1111 (34)	334/520 (64)		74/163 (45)	108/458 (24)		
1 to 10 units/week	417/1111 (38)	131/520 (25)		57/163 (35)	162/458 (35)		
≥10 units/week	315/1111 (28)	55/520 (11)	<0.001	32/163 (20)	188/458 (41)	0.003	
Hypercholesterolemia	736/1108 (66)	353/516 (68)	0.43	302/445 (68)	117/166 (71)	0.54	
History of coronary artery disease	428/1199 (36)	137/569 (24)	<0.001	221/495 (45)	55/190 (29)	<0.001	
History of peripheral intervention	204/1195 (17)	112/568 (20)	0.18	231/493 (47)	91/190 (48)	0.81	
Bilateral carotid stenosis	510/1074 (48)	217/508 (43)	0.076	NA	NA		
Preoperative acetylsalicyl acid use	998/1197 (83)	500/569 (88)	0.014	389/494 (79)	145/190 (76)	0.49	
Preoperative statin use	909/1199 (76)	446/569 (78)	0.23	362/495 (73)	138/190 (73)	0.90	
Osteoporosis therapy	28/1199 (2.3)	36/568 (6.3)	<0.001	15/494 (3.0)	22/190 (11)	<0.001	
Total cholesterol (mean) (SD)	4.6 (1.2)	5.0 (1.3)	<0.001	4.7 (1.2)	4.9 (1.3)	0.31	
HDL (mean) (SD)	1.1 (0.45)	1.3 (0.70)	<0.001	1.1 (0.35)	1.4 (0.47)	<0.001	
LDL (mean) (SD)	2.9 (2.4)	3.0 (1.1)	0.43	2.7 (0.95)	2.6 (1.1)	0.76	
Glomerular filtration rate, CG (mean) (SD)	76.4 (26.5)	67.9 (24.4)	<0.001	86.4 (56.4)	70.5 (33.4)	0.001	
Clinical presentation							
Asymptomatic	179/1196 (15)	64/567 (11)		242/428 (57)	70/153 (46)		Fontaine IIb
Ocular symptoms	174/1196 (15)	100/567 (18)		101/428 (24)	47/153 (31)		Fontaine III
Transient ischemic attack	521/1196 (44)	244/567 (43)		85/428 (20)	36/153 (24)	0.067	Fontaine IV
Stroke	322/1196 (27)	159/567 (28)	0.096				
Event to operation time, (median) (IQR)	35 (15–85)	35 (14–79)	0.47	NA			
							Operated artery
				53/177 (30)	116/461 (25)		SFA/DFA
				96/177 (54)	260/461 (56)		CFA
				14/177 (7.9)	40/461 (8.7)		Iliac
				14/177 (7.9)	45/461 (9.8)	0.62	Combination femoral and/or iliac segments

CEA: carotid endarterectomy; FEA: femoral endarterectomy; SD: standard deviation; HDL: High Density Lipoprotein; CG: Cockroft–Gauld; IQR: interquartile range; SFA: superficial femoral artery; CFA: common femoral artery; DFA: deep femoral artery; NA: not applicable.
[a] Comparing men and women.

2. Methods

2.1. Patient population and selection

All studied patients were included in the Athero-Express, a prospective observational longitudinal study in patients undergoing CEA or FEA at the University Medical Center Utrecht, Utrecht, and the St. Antonius Hospital Nieuwegein, the Netherlands, as described in detail previously [3]. Indications for CEA were reviewed in a multidisciplinary meeting and based on recommended criteria by NASCET/ECST/ACST [2,4,5] Patients were treated by FEA if they had at least Fontaine IIb peripheral arterial disease (PAD) and unsuccessful supervised exercise therapy with an indication for iliac or femoral endarterectomy according to guidelines and multidisciplinary consensus [6,7]. All patients scheduled for these procedures were asked to participate, without applying any exclusion criteria. The Institutional Review boards of the hospitals approved the study and all patients provided written

Table 2
Cumulative 10-year mortality risks for men and women after carotid endarterectomy. Italics indicate control groups.

Follow-up years	1	2	3	4	5	6	7	8	9	10
Men	4 (0.6)	8 (0.8)	13 (1.1)	17 (1.2)	22 (1.4)	28 (1.6)	34 (1.8)	37 (1.9)	42 (2.2)	46 (2.8)
Control group men	*4 (0.3)*	*8 (0.4)*	*12 (0.5)*	*16 (0.5)*	*19 (0.6)*	*24 (0.6)*	*27 (0.6)*	*31 (0.7)*	*34 (0.7)*	*38 (0.7)*
Women	4 (0.9)	8 (1.2)	10 (1.3)	13 (1.5)	17 (1.8)	19 (2.0)	22 (2.2)	26 (2.6)	33 (3.3)	35 (3.7)
Control group women	*3 (0.4)*	*6 (0.5)*	*8 (0.6)*	*11 (0.7)*	*15 (0.7)*	*18 (0.8)*	*21 (0.8)*	*23 (0.9)*	*27 (0.9)*	*30 (1.0)*
Age stratified										
Men ≤ 70	2 (0.6)	4 (0.8)	7 (1.1)	10 (1.3)	13 (1.5)	18 (1.8)	21 (2.1)	24 (2.2)	28 (2.7)	32 (3.5)
Control group men ≤ 70	*2 (0.2)*	*3 (0.3)*	*5 (0.4)*	*6 (0.5)*	*8 (0.5)*	*10 (0.6)*	*12 (0.6)*	*14 (0.7)*	*17 (0.7)*	*19 (0.8)*
Men >70	7 (1.1)	13 (1.5)	20 (1.9)	26 (2.2)	34 (2.5)	41 (2.7)	50 (3.0)	56 (3.2)	62 (3.6)	66 (4.2)
Control group men >70	*6 (0.5)*	*13 (0.7)*	*20 (0.9)*	*27 (1.0)*	*34 (1.0)*	*40 (1.1)*	*45 (1.1)*	*51 (1.1)*	*56 (1.1)*	*60 (1.1)*
Women ≤ 70	3 (1.0)	4 (1.1)	4 (1.3)	6 (1.6)	8 (1.8)	9 (2.0)	9 (2.0)	12 (2.5)	18 (3.5)	20 (4.3)
Control group women ≤ 70	*1 (0.2)*	*2 (0.4)*	*2 (0.4)*	*3 (0.5)*	*5 (0.6)*	*6 (0.7)*	*7 (0.7)*	*9 (0.8)*	*10 (0.9)*	*12 (0.9)*
Women >70	6 (1.5)	13 (2.1)	15 (2.3)	20 (2.7)	26 (3.1)	31 (3.5)	38 (4.0)	43 (4.5)	55 (6.3)	NA
Control group women >70	*6 (0.7)*	*11 (0.9)*	*15 (1.1)*	*20 (1.2)*	*26 (1.3)*	*31 (1.4)*	*36 (1.5)*	*40 (1.5)*	*45 (1.5)*	*50 (1.5)*

Numbers are percentages representing absolute mortality rates at different years of follow-up. NA: not available due to low numbers at risk during interval.
Numbers in parentheses indicate standard error of survival risks at each timepoint.