Hindawi
Acta Neurologica Scandinavica
Volume 2023, Article ID 3864506, 8 pages
https://doi.org/10.1155/2023/3864506

Research Article

Verified Parental Cardiovascular Events for Young and Middle-Aged Ischaemic Stroke Patients and Controls

Solveig Boland,[1] **Beenish Nawaz**,[1,2] **Halvor Øygarden**,[3,4] **Annette Fromm**,[2] **Halvor Næss**,[1,2] **and Ulrike Waje-Andreassen**[2]

[1]*Department of Clinical Medicine, University of Bergen, Bergen, Norway*
[2]*Department of Neurology, Haukeland University Hospital, Bergen, Norway*
[3]*Department of Neurology, Sørlandet Hospital, Kristiansand, Norway*
[4]*Department of Health and Nursing Sciences, University of Agder, Kristiansand, Norway*

Correspondence should be addressed to Solveig Boland; solveig.boland@uib.no

Received 7 September 2022; Revised 23 October 2022; Accepted 15 November 2022; Published 8 February 2023

Academic Editor: Wen-Jun Tu

Introduction. Nonmodifiable cardiovascular risk factors, like age and sex, are easily quantifiable. Due to immense technical progress in diagnostics and medical data storage, the aim of this study was to quantify, verify, and to compare parental cardiovascular events (CVE) as an additional nonmodifiable risk factor for young and middle-aged ischaemic stroke patients and controls. *Methods.* Information about parental CVE was first obtained by standardized questionnaires answered by 385 acute ischaemic stroke patients (15-60 years of age) and 260 controls. After consent to contact living and include deceased parents, patients and controls provided necessary personal identification of their parents. Thereafter, CVE were verified by standardized questionnaires answered by parents or medical records in case of deceased parents. *Results.* One hundred-and-nine (14.2%) of 770 patient parents vs. 128 (24.6%) of 520 control parents were not available for verification. Active participation was obtained for 229 (73.9%) of 310 patient parents vs.113 (58.2%) of 194 control parents. Medical record verification was obtained for 192 (54.7%) of 351 deceased patient parents, vs.103 (52.0%) of 198 deceased control parents. This study showed highest death rates of fathers (65.3% patient fathers and 57.6% control fathers) and highest numbers of CVE, especially myocardial infarction among patient fathers of patients aged 50-60 years. *Discussion and Conclusion.* Obtaining verified parental CVE as a nonmodifiable risk factor is still challenging, despite widely available digital medical information. To attain more accurate information on parental CVE, we recommend active involvement of family members in addition to medical record verification, especially for patients aged <50 years. *Trial Registration.* This trial is registered with NCT01597453

1. Background

A family history of cardiovascular events (CVE) is a well-known risk factor for CVE in offspring [1]. CVE comprises cerebrovascular disease (ischaemic stroke (IS), transient ischaemic attack (TIA), intracerebral haemorrhage (ICH)), coronary artery disease (CAD), and peripheral artery disease (PAD). Most evident is the association between a family history of CVE and the development of CAD [2–4], and associations between family history of CVE and PAD in offspring are also supported [5]. However, the association between parental CVE and stroke is less evident and more challenging to establish as there are several nonatherosclerotic causes of stroke, whereas CAD and PAD are mainly caused by atherosclerosis.

The incidence of stroke at a young age has increased since the 1980s and now represents about 10% of all IS [6, 7]. Major modifiable risk factors for stroke and other CVE are hypertension, dyslipidaemia, smoking, and diabetes mellitus, and it has been suggested that the increased prevalence of these risk factors affects the incidence of stroke in the young [6]. Nonmodifiable risk factors, such as age, sex, and ethnicity, are easily quantifiable. However, detailed knowledge about parental CVE is highly reliant on the source of information, the extent of information exchange

between family members, and on the availability of diagnostic tools at the time of parental CVE.

Previous studies on family history depended on decade old information, usually provided by patients or controls themselves. One result was poor differentiation between IS and ICH [8]. Some studies registered missing information as "no CVE" for not overestimating CVE [9, 10]. Considering this, parental CVE ends up with a higher degree of uncertainty compared with other nonmodifiable risk factors.

Advances in imaging techniques have revolutionized diagnostics and treatment of stroke, with computed tomography (CT) and magnetic resonance imaging (MRI) becoming increasingly available since their sparse use in the 1980s and 1990s. Modern technologies make more detailed information on CVE available, and since digitalization of medical literature and databases have made information easily accessible at any time, we now expected parental CVE to be verifiable to a greater extent.

The aim of this study was to obtain and compare verifiable parental CVE for patients with IS and controls.

2. Methods

This study is a part of the Norwegian Stroke in the Young Study (NOR-SYS). NOR-SYS is a prospective, single centre, long term, observational 3-generation research program conducted at the Stroke Unit at the Department of Neurology at Haukeland University Hospital, Bergen, Norway [11].

NOR-SYS is a population-based study, as our hospital is the only hospital providing stroke care to patients up to 60 years of age in a well-defined geographical region. Because the Western Norway Regional Health Authority has overall responsibility for the specialist health service in the counties of Vestland, digital medical records from all hospitals in Western Norway (hospitals in Bergen, Stavanger, Haugesund, Førde, Voss, Odda, and Stord) were accessible for verification. The methods of study inclusion have previously been published [11]. In brief, patients between 15 and 60 years with acute IS, documented by CT or MRI between 2010 and 2015, were included and gave as key-persons consent to contact their biological parents and partners or ex-partners in case of common adult offspring. Partners and ex-partners were included as controls. After consent to contact living and include deceased parents, patients, partners, and ex-partners provided necessary person identification information [11].

Patients and controls answered standardized questions about parental stroke, coronary, and peripheral arterial events by "yes", "no", or "do not know". By adding the option "do not know," we aspired to increase the precision on information about the prevalence, uncover uncertainty, and reduce the chance of under or overestimation.

Living parents participated by standardized questionnaires about their CVE. Questionnaire registration of CVE followed the same template as registration from medical records, with the exception that angina pectoris was registered as prevalent CAD when appropriate diagnostics and medication were reported. Also, TIA was an option for subtype of stroke in the questionnaire but was not verified when found in medical records. The questionnaires have previously been published [12] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5049640/.

Information about CVE in deceased parents was gathered from hospital and outpatient clinic records. In case of no documentation of any CVE in the medical record, we registered CVE as not prevalent. If medical records were unavailable, we could not be sure that this was equivalent to no CVE, rather more likely that parents were dead before the introduction of digital medical records, or that they had been to other hospitals outside Western Norway. Unavailable medical records and incomplete parental identification led to exclusion for verification.

2.1. Variable Definitions. Stroke was registered as IS, TIA, "brain bleeding", or unknown subtype. For verification, only IS and ICH were verified, and we registered if cerebral CT or MRI was taken. Interventions involving head or neck, like carotid endarterectomy were registered.

CAD was registered as myocardial infarction (MI) or angina pectoris. Acute and old MI were registered, along with performed interventions like coronary blocking, stenting, and aortocoronary bypass. Other cardiac diseases, such as arrhythmias or valve abnormalities were questionnaire options but not included in the verification.

Aorta pathology was registered if aortic aneurysm was found in medical records or if parents answered yes to aorta pathology without further specification.

PAD was registered if prevalent intermittent claudication was present, alongside therapeutic interventions, such as recommended training, thrombolysis, dilation, stenting, bypass surgery, and limb amputation.

2.2. Statistical Analysis. STATA (version 16.0) was used for statistical analysis. Descriptive statistics were given as proportions. Categorical variables were tested by Pearson's chi-square test or Fisher's exact test if values were less than five after categorization. Parents were dichotomized to a young group (patients or controls aged 15-49 years) and a middle-aged group (patients aged 50-60 years or controls ≥50 years). Groups were chosen to differentiate between young and middle-aged patients, since increasing age is also a risk factor for atherosclerosis and CVD.

2.3. Ethical Approval. NOR-SYS has been approved by the Regional Committee for Medical and Health Research Ethics, Western Norway (REK-VEST 2010/74) and is registered in ClinicalTrials.gov (identifier NCT01597453). Approval also included deceased parents when key persons gave their consent and necessary information for parental identification. Written informed consent was obtained from all active participants and for a few patients by their next of kin.

3. Results

3.1. Inclusion and Verification. Initially, 385 patients and 260 controls were included. After missing consent from key persons to contact parents, often due to serious illness such as advanced cancer or dementia, and after exclusion of adoptive parents and unknown parents, 14.2% of patient parents

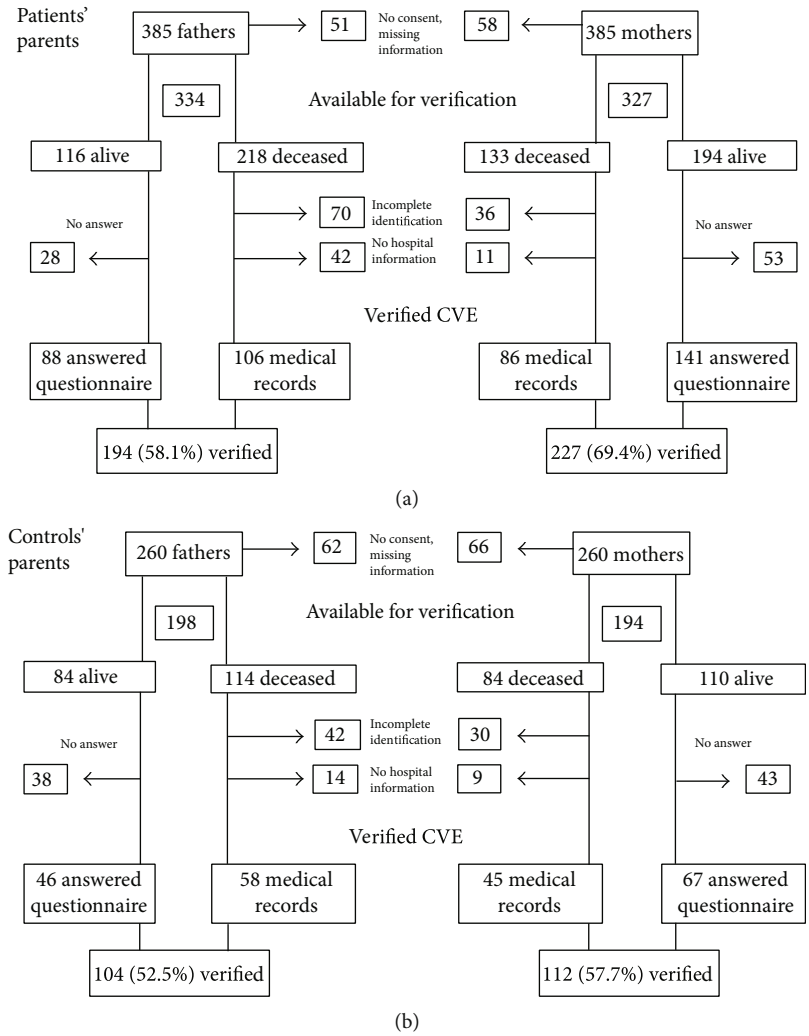

Figure 1: Verification of patients' parental (a) and controls' parental (b) cardiovascular events (CVE). Information was provided by parents' active study participation or by medical records in case of deceased parents.

vs. 24.6% of control parents were excluded. In total, 661 patient parents and 392 control parents were available for verification of CVE. Figure 1 shows detailed information, obstacles, and final numbers of successful verification.

Among parents available for verification, 81 (26.1%) of 310 patient parents and 81 (41.8%) of 194 control parents did not return the parental questionnaires and were therefore not included. Active participation was greater among patient parents than control parents (75.9% patient fathers vs. 54.8% control fathers and 72.7% patient mothers vs. 60.9% control mothers) and most relevant for parents of patients and controls <50 years. Of deceased parents, 106 (30.2%) of 351 patient parents and 72 (36.4%) of 198 control parents had insufficient information for definite identification provided by their key person. Incomplete identification was most prevalent among deceased patient fathers (32.1%) and deceased control fathers (36.8%). Medical records were the major source of parental CVE verification for patients and controls ≥50 years, especially for fathers with the highest number of deceased patient fathers (65.3%) and deceased control fathers (57.6%). Mean age of death was 75.5 years for patient fathers and 76.1 years for control fathers.

Figure 2 shows the distribution of source of verified information of parental CVE in total and for available parents. Figure 2 shows that patients were more likely to aid in inclusion of their parents, while controls were more reserved. Thereafter, the participation rate of all potentially available parents shows that the rates of the living parents who participated was higher among patients' parents than for parents of controls. Figure 3 shows source of information by age groups of patients and controls. This shows a similar distribution of information from questionnaires and medical records between gender of parent and the two age categories, thus suited for comparison. Figure 4 shows percentages of reported and verified types of parental CVE. Among the parents of the young patients, the differences between reported events and verified events were less evident than the differences between reported and verified events for the parents of middle-aged patients.

Table 1 shows reported and verified parental CVE. In total, 121 (31.4%) patients reported to have at least one

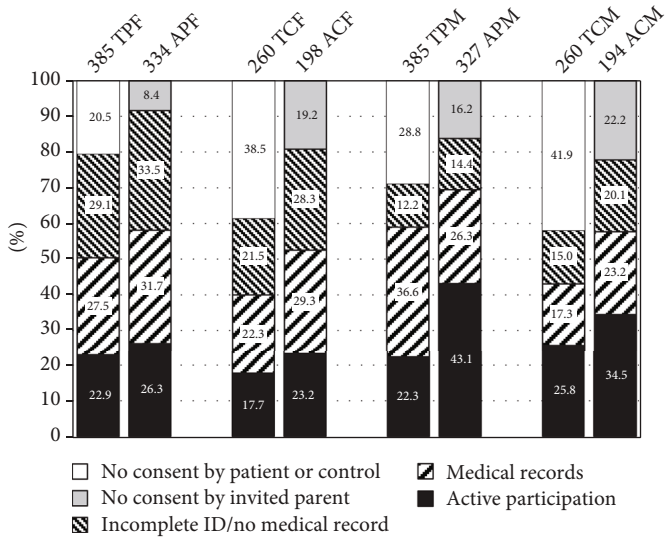

Figure 2: Source of verification of parental cardiovascular events (CVE) shown as percentages of the total number of parents and numbers of parents available for verification.

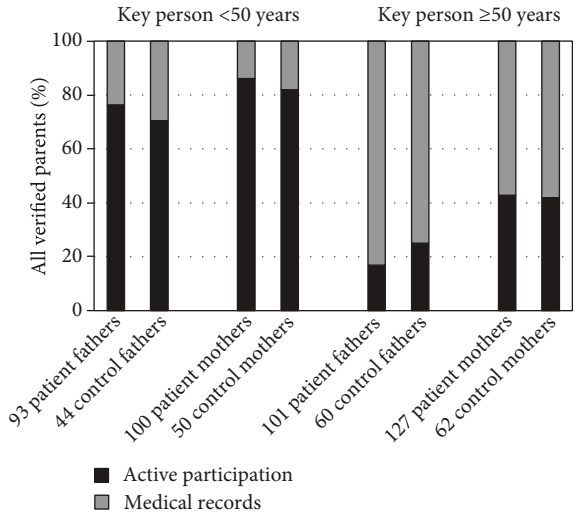

Figure 3: Distribution of the source of verified information of parental cardiovascular events (CVE) by age group of their key person (patient or control).

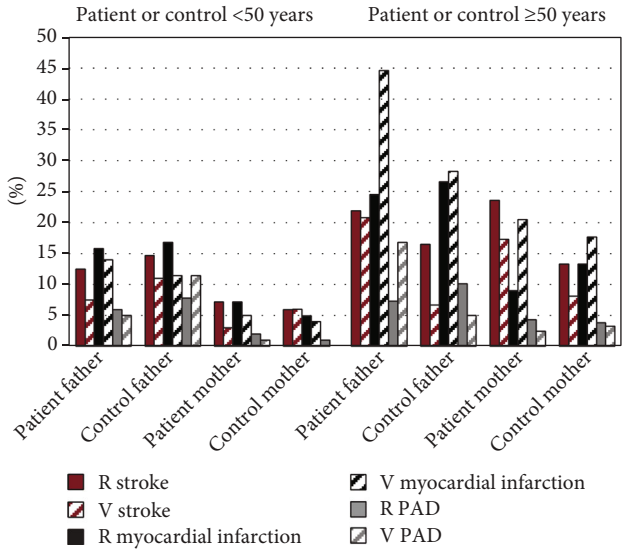

Figure 4: Parental cardiovascular events (CVE) reported (R) by ischaemic stroke patients and controls as key persons and parental CVE verified (V) by parents or medical record information. All data are given in percentages. Reported events in percentage of all possible parents and verified events in percentage of all parents available for verification. PAD = peripheral arterial disease.

parent suffering a stroke, 128 (33.2%) reported at least one parent with CAD, and 39 (10.1%) reported at least one parent with PAD. Sixteen patients reported stroke in both parents, and 17 patients reported CAD in both parents. Controls reporting stroke, CAD, and PAD in at least one parent were 67 (25.8%) for stroke, 98 (37.7%) for CAD, and 29 (11.2%) for PAD. One control reported stroke in both parents, 16 reported CAD in both parents, and 2 reported PAD in both parents. Aorta pathology was not included in the questionnaire for patients and controls to report about parental history; therefore, only verified aorta pathology is presented in Table 1.

Comparing verified CVE of all fathers with all mothers (Table 1) showed a higher burden among fathers for MI ($p < 0.001$) and PAD ($p < 0.001$), also when looking at the young (MI $p = 0.011$ and PAD $p = 0.008$) and the middle-aged group (MI $p < 0.001$ and PAD $p = 0.001$), separately.

Among all 385 young and middle-aged stroke patients, CVE information from both parents was verified for 149 patients (77 (51.7%) were <50 years old), while 78 and 45 had only maternal or paternal information available for verification.

Of the verified parents, 3 patient mothers, 6 patient fathers, 3 control mothers, and 5 control fathers reported "do not know" about their own stroke status. Some did suffer both an IS and a haemorrhagic stroke, and a few did not

Table 1: Parental cardiovascular events (CVE) reported by patient or control and parental CVE verified by active parental participation through questionnaire or medical records in case of deceased parents. Reported events are showed in numbers and percentages for answer alternatives "yes," "no," and "do not know" regarding analysed CVE variables. Verified events are shown as numbers and percentages. Comparisons between patients' parents and controls' parents were done separately for the reported information and for the verified information. *P* values are from Chi-square tests or from Fischer's exact test if one or more numbers in the categories were less than five. (a) Parents of patients and controls <50 years of age. (b) Parents of patients and controls ≥50 years of age.

(a)

Patients and controls <50 years of age		Patient fathers *n* (%)	Control fathers *n* (%)	P	Patient mothers *n* (%)	Control mothers *n* (%)	*P*
Parental cardiovascular events reported by patients and controls							
Reported parents		152 (100%)	102 (100%)	—	152 (100%)	102 (100%)	—
Stroke	Yes	19 (12.5%)	15 (14.7%)	0.809	11 (7.2%)	6 (5.9%)	0.861
	No	125 (82.2%)	83 (81.4%)		139 (91.4%)	94 (92.2%)	
	Do not know	8 (5.3%)	4 (3.9%)		2 (1.3%)	2 (2.0%)	
	Ischaemic	7 (4.6%)	6 (5.9%)	0.670	2 (1.3%)	1 (1.0%)	0.222
	Haemorrhagic	1 (0.7%)	2 (2.0%)		1 (0.7%)	1 (1.0%)	
	Unknown type	10 (6.6%)	5 (4.9%)		5 (3.3%)	0 (0.0%)	
	TIA	1 (0.7%)	2 (2.0%)		3 (2.0%)	4 (3.9%)	
Heart disease	Yes	46 (30.3%)	30 (29.4%)	0.549	23 (15.1%)	10 (9.8%)	0.271
	No	95 (62.5%)	68 (66.7%)		120 (78.9%)	89 (87.3%)	
	Do not know	11 (7.2%)	4 (3.9%)		9 (5.9%)	3 (2.9%)	
	Angina	5 (3.3%)	4 (3.9%)	0.952	2 (1.3%)	1 (1.0%)	1.000
	MI	24 (15.8%)	17 (16.7%)		11 (7.2%)	5 (4.9%)	
	Insuff/arrhyt	10 (6.6%)	5 (4.9%)		8 (5.3%)	4 (3.9%)	
	Unknown type	7 (4.6%)	4 (3.9%)		2 (1.3%)	0 (0.0%)	
PAD	Yes	9 (5.9%)	8 (7.8%)	0.557	3 (2.0%)	1 (1.0%)	0.810
	No	130 (85.5%)	82 (80.4%)		138 (90.8%)	92 (90.2%)	
	Do not know	13 (8.6%)	12 (11.8%)		11 (7.2%)	9 (8.8%)	
Parental cardiovascular events verified by active parental participation or medical record information							
Verified parents		93 (100%)	44 (100%)	—	100 (100%)	50 (100%)	—
Stroke	Yes	7 (7.5%)	5 (11.4%)	0.522	3 (3.0%)	3 (6.0%)	0.401
	Ischaemic	5 (5.4%)	3 (6.8%)	0.711	3 (3.0%)	2 (4.0%)	1.000
	Haemorrhagic	2 (2.2%)	1 (2.3%)	1.000	0 (0.0%)	1 (2.0%)	0.333
Heart disease	Angina	16 (17.2%)	7 (15.9%)	0.850	7 (7.0%)	2 (4.0%)	0.718
	MI	13 (14.0%)	5 (11.4%)	0.672	5 (5.0%)	2 (4.0%)	1.000
Aorta pathology	Yes	2 (2.2%)	2 (4.5%)	0.593	1 (1.0%)	0 (0.0%)	1.000
PAD	Yes	4 (4.3%)	5 (11.4%)	0.146	1 (1.0%)	0 (0.0%)	1.000
Cardiovascular intervention	Head/neck	1 (1.1%)	1 (2.3%)	0.541	1 (1.0%)	0 (0.0%)	1.000
	Heart disease	12 (12.9%)	4 (9.1%)	0.584	4 (4.0%)	3 (6.0%)	0.686
	PAD	0 (0.0%)	3 (6.8%)	0.032	1 (1.0%)	0 (0.0%)	1.000

(b)

Patients and controls ≥50 years of age		Patient fathers *n* (%)	Control fathers *n* (%)	*P*	Patient mothers *n* (%)	Control mothers *n* (%)	*P*
Parental cardiovascular events reported by patients and controls							
Reported parents		233 (100%)	158 (100%)	—	233 (100%)	158 (100%)	—
Stroke	Yes	51 (21.9%)	26 (16.5%)	0.036	55 (23.6%)	21 (13.3%)	0.003

Table 1: Continued.

Patients and controls ≥50 years of age		Patient fathers *n* (%)	Control fathers *n* (%)	*P*	Patient mothers *n* (%)	Control mothers *n* (%)	*P*
	No	155 (66.5%)	123 (77.8%)		164 (70.4%)	134 (84.8%)	
	Do not know	27 (11.6%)	9 (5.7%)		14 (6.0%)	3 (1.9%)	
	Ischaemic	8 (3.4%)	7 (4.4%)		19 (8.2%)	2 (1.3%)	
	Haemorrhagic	6 (2.6%)	5 (3.2%)	0.141	6 (2.6%)	2 (1.3%)	0.065
	Unknown type	28 (12.0%)	7 (4.4%)		18 (7.7%)	7 (4.4%)	
	TIA	9 (3.9%)	7 (4.4%)		12 (5.2%)	10 (6.3%)	
	Yes	103 (44.2%)	67 (42.4%)		62 (26.6%)	49 (31.0%)	
	No	115 (49.4%)	81 (51.3%)	0.932	159 (68.2%)	102 (64.6%)	0.627
	Do not know	15 (6.4%)	10 (6.3%)		12 (5.2%)	7 (4.4%)	
Heart disease	Angina	12 (5.2%)	10 (6.3%)		12 (9.0%)	14 (8.9%)	
	MI	57 (24.5%)	42 (26.6%)	0.511	21 (9.0%)	21 (13.3%)	0.283
	Insuff/arrhyt	20 (8.6%)	9 (5.7%)		21 (9.0%)	10 (6.3%)	
	Unknown type	14 (6.0%)	6 (3.8%)		8 (3.4%)	4 (2.5%)	
	Yes	17 (7.3%)	16 (10.1%)		10 (4.3%)	6 (3.8%)	
PAD	No	191 (82.2%)	116 (73.4%)	0.126	206 (88.4%)	132 (83.5%)	0.204
	Do not know	25 (10.7%)	26 (16.5%)		17 (7.3%)	20 (12.7%)	
Parental cardiovascular events verified by active parental participation or medical record information							
Verified parents		101 (100%)	60(100%)	—	127 (100%)	62 (100%)	—
	Yes	21 (20.8%)	4 (6.7%)	0.023	22 (17.3%)	5 (8.1%)	0.088
Stroke	Ischaemic	18 (17.8%)	2 (3.3%)	0.006	18 (14.2%)	3 (4.8%)	0.082
	Haemorrhagic	4 (4.0%)	3 (5.0%)	0.712	6 (4.7%)	1 (1.6%)	0.429
Heart disease	Angina	32 (31.7%)	17 (28.3%)	0.655	24 (18.9%)	15 (24.2%)	0.398
	MI	45 (44.6%)	17 (28.3%)	0.041	26 (20.5%)	11 (17.7%)	0.657
Aorta pathology	Yes	11 (10.9%)	5 (8.3%)	0.600	3 (2.4%)	0 (0.0%)	0.552
PAD	Yes	17 (16.8%)	3 (5.0%)	0.028	3 (2.4%)	2 (3.2%)	0.664
Cardiovascular intervention	Head/neck	1 (1.0%)	1 (1.7%)	1.000	1 (0.8%)	0 (0.0%)	1.000
	Heart disease	16 (15.8%)	10 (16.7%)	0.891	7 (5.5%)	7 (11.3%)	0.154
	PAD	8 (7.9%)	2 (3.3%)	0.324	3 (2.4%)	2 (3.2%)	0.664

n = number of subjects; TIA = transient ischaemic attack; MI = myocardial infarction; Insuff/arrhyt = aortic insufficiency or arrhythmia; PAD = peripheral artery disease.

report the stroke subtype. There was no reporting of "do not know" regarding own history of CAD or PAD.

As presented in Table 1, neither of the verified CVE showed a significant difference when comparing total numbers among verified patient fathers vs. control fathers and patient mothers with control mothers. However, among fathers of the middle-aged group, patient fathers did have a significantly higher burden of stroke ($p = 0.023$), MI ($p = 0.041$), and PAD ($p = 0.028$) compared with control fathers. Reported stroke was higher for patient fathers ($p = 0.036$) and patient mothers ($p = 0.003$) in the middle-aged groups compared with stroke of respective parents of controls in their corresponding age group.

4. Discussion

In this descriptive study of parental CVE in young and middle-aged IS patients and controls, our reported prevalence of parental CVE was somewhat lower than previously presented in a Swedish study, where patients and controls reported their family history of stroke in 41% vs. 27% and MI in 38% vs. 34%, respectively [10]. Their patient group was older with a mean age of 56 years (range 18-69 years), and siblings were additionally included, which probably contributes to the difference [10]. In the European multicentre study of stroke in young Fabry patients, patients reported a family history of stroke in 37.1% and CVE in 41.0%, slightly higher than in our study; however, we could not find how the study defined family history of CVE [13]. Methodological differences in collection and definition of family history make comparison between studies difficult. A previously published systematic review of the genetic epidemiology of IS concluded that the interpretation of family studies was undermined by major heterogeneity and insufficient detail [8], problems we also met regarding our comparisons with existing literature.

A previous NOR-SYS publication has shown good concordance between reported family history of CVE by

patients and information provided by their actively participating parents, especially for stroke and CAD, though increasing age was associated with impairment of concordance [12]. In addition, gender impacts the knowledge of family history, and females as traditional caregivers have better knowledge of family history than males. We also found that knowledge about parental CVE was more accurate with female linkage [14]. Similar gender differences have been shown for self-reported family history of cancer in several studies [15, 16]. A study of communication about family health history showed that women, with their traditional role as health gatekeepers in families, were more likely to share family health history than males, and that young generations were more likely to talk about family history than old generations [17], resulting in better knowledge about own family history for younger individuals.

Since we now additionally assessed parents who were deceased at the time of inclusion of patient and control, and since the largest proportion of deceased parents were fathers, we can assume that the information about CVE reported by their key person was less accurate, mostly due to a higher age in both key person and parent.

Patient fathers were most highly represented among deceased parents, and they had more often insufficient identification information provided by their key person. This may be explained by a higher age among fathers, death a long time ago, or even less knowledge about fathers, as previously suggested [14]. The individuals where we could not access medical records, despite successful identification, were also a problem, most likely due to high age and death before digital medical records became the standard. Digital medical records were established in Vestland between 2000 and 2002.

Most reported CVE were observed in parents of patients and controls ≥50 years, which was expected since these parents were older and since CVE increases with age. Fathers had higher rates of reported and verified CVE than mothers, which can be explained by atherosclerosis emerging earlier in life for males than females [18].

Interestingly, despite the known accuracy of reported family history of CAD, among our middle-aged group, verified events of MI exceeded reported events. This was mostly evident for patient fathers but also present in patient mothers and control parents. Since this was not found in the young group, one reason could be differences in the level of detail in parental questionnaires and medical records, as most parents in the middle-aged group were verified through medical records, and most parents in the young group answered questionnaires. It also shows increasing errors in reports with higher age but may also point toward more CAD than families were aware of. Discrepancies in reported and verified stroke in parents of middle-aged patients were also observed, though there were more reported than verified events. This was also seen in the young group and shows that stroke might be a more difficult topic for families to report, and that it is difficult to know if the reported parental stroke really was a stroke or if it was a TIA or even a stroke mimic.

4.1. Strengths and Limitations. Our study is strengthened by the well-defined study population and the inclusion of deceased parents. Limitations were the number of parents that we could not verify, and that we limited our verification of family members to parents. Categorization by age of patients and controls led to smaller numbers, and more missing information among parents of controls contributed to more uncertain results. Due to our study design, patients were mostly men (68.8%), and controls were mostly women [19], which may also have influenced our results. Identification of deceased parents during patients' hospital stay would probably have contributed to a higher proportion of parents with complete identification. Participation from parents of partners and ex-partners was lower than parents of patients; however, the proportion of nonresponders to study invitations tends to be about 20-40% [20], meaning our participation rate might actually be quite good.

5. Conclusion

The process of verification showed us that obtaining verified parental CVE still is challenging, despite widely available digital medical records.

To gain more accurate information about the role of familial CVE in stroke patients and for future targeted genetic analysis, we recommend active involvement of actual family members by written consent to permit verification by assessment of their medical records and images, especially when patients are at age <50 years.

Data Availability

All data are stored on the research server of Haukeland University Hospital and are available on request.

Additional Points

Guarantor. The guarantors are the Department of Neurology, the Bergen Stroke Research Group, Bergen, Norway, and the Faculty of Medicine, University of Bergen, Bergen, Norway.

Ethical Approval

Ethical approval for this study was obtained from the Regional Committee for Medical and Health Research Ethics, Western Norway (REK-VEST 2010/74). The Regional Committee for Medical and Health Research Ethics, Western Norway approved inclusion of deceased parents if patients and controls as key persons agreed and provided the study doctors with necessary identifying information. The ethical principles in the Declaration of Helsinki conducted to protect human research subjects have been followed. This study did not change any medical treatment and did not involve any risk or burden for the subjects.

Consent

Written informed consent was obtained from all active participating subjects.

Disclosure

This study was presented as a poster at the 7th European Stroke Organisation Conference (https://cslide.ctimeetingtech.com/esoc21/attendee/eposter/poster/1462).

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

Authors' Contributions

UWA conceived the study and gained ethical approval. UWA, AF, BN, and HN were involved with development of the study protocol. Data collection was done by AF, HØ, and UWA. SB verified the parental cardiovascular events in collaboration with UWA, performed data analysis and literature search, and wrote the manuscript. All authors reviewed and edited the manuscript and approved the final version for submission.

Acknowledgments

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article. This research was funded by the Medical Student Research Programme at the Faculty of Medicine, University of Bergen (SB), which had no influence on the study design, data collection, and presentation or the conclusions made.

We would like to thank the study nurse Maria Sætveit Stokkan and the secretary Jeanette Haveland Antoniazzi for their valuable assistance in this research.

References

[1] D. M. Lloyd-Jones, B.-H. Nam, R. B. D'Agostino Sr. et al., "Parental cardiovascular disease as a risk factor for cardiovascular disease in middle-aged adults," *JAMA*, vol. 291, no. 18, pp. 2204–2211, 2004.

[2] J. Putaala, N. Yesilot, U. Waje-Andreassen et al., "Demographic and geographic vascular risk factor differences in European young adults with ischemic stroke: the 15 cities young stroke study," *Stroke*, vol. 43, no. 10, pp. 2624–2630, 2012.

[3] N. I. Parikh, S. J. Hwang, M. G. Larson et al., "Parental occurrence of premature cardiovascular disease predicts increased coronary artery and abdominal aortic calcification in the Framingham offspring and third generation cohorts," *Circulation*, vol. 116, no. 13, pp. 1473–1481, 2007.

[4] J. M. Bachmann, B. L. Willis, C. R. Ayers, A. Khera, and J. D. Berry, "Association between family history and coronary heart disease death across long-term follow-up in men: the Cooper center longitudinal study," *Circulation*, vol. 125, no. 25, pp. 3092–3098, 2012.

[5] R. J. Valentine, R. Guerra, P. Stephan, E. Scoggins, G. P. Clagett, and J. Cohen, "Family history is a major determinant of subclinical peripheral arterial disease in young adults," *Journal of Vascular Surgery*, vol. 39, no. 2, pp. 351–356, 2004.

[6] J. Putaala, "Ischemic stroke in the young: current perspectives on incidence, risk factors, and cardiovascular prognosis," *European Stroke Journal*, vol. 1, no. 1, pp. 28–40, 2016.

[7] B. von Sarnowski, J. Putaala, U. Grittner et al., "Lifestyle risk factors for ischemic stroke and transient ischemic attack in young adults in the stroke in young Fabry patients study," *Stroke*, vol. 44, no. 1, pp. 119–125, 2013.

[8] E. Flossmann, U. G. Schulz, and P. M. Rothwell, "Systematic review of methods and results of studies of the genetic epidemiology of ischemic stroke," *Stroke*, vol. 35, pp. 212–227, 2004.

[9] P. Jousilahti, D. Rastenyte, J. Tuomilehto, C. Sarti, and E. Vartiainen, "Parental history of cardiovascular disease and risk of Stroke," *Stroke*, vol. 28, no. 7, pp. 1361–1366, 1997.

[10] K. Jood, C. Ladenvall, A. Rosengren, C. Blomstrand, and C. Jern, "Family history in ischemic stroke before 70 years of Age," *Stroke*, vol. 36, no. 7, pp. 1383–1387, 2005.

[11] A. Fromm, L. Thomassen, H. Naess et al., "The Norwegian stroke in the young study (NOR-SYS): rationale and design," *BMC Neurology*, vol. 13, no. 1, pp. 89–89, 2013.

[12] H. Øygarden, A. Fromm, K. M. Sand et al., "Can the cardiovascular family history reported by our patients be trusted? The Norwegian stroke in the young study," *European Journal of Neurology*, vol. 23, no. 1, pp. 154–159, 2016.

[13] A. Rolfs, F. Fazekas, U. Grittner et al., "Acute cerebrovascular disease in the young: the stroke in young Fabry patients study," *Stroke*, vol. 44, no. 2, pp. 340–349, 2013.

[14] H. Øygarden, A. Fromm, K. M. Sand et al., "Stroke patients' knowledge about cardiovascular family history - the Norwegian stroke in the young study (NOR-SYS)," *BMC Neurology*, vol. 15, no. 1, p. 30, 2015.

[15] M. Krakow, C. J. Rising, N. Trivedi, D. C. Yoon, and R. C. Vanderpool, "Prevalence and correlates of family cancer history knowledge and communication among US adults," *Preventing Chronic Disease*, vol. 17, article E146, 2020.

[16] M. Sieverding, A. L. Arbogast, S. Zintel, and C. Wagner, "Gender differences in self-reported family history of cancer: a review and secondary data analysis," *Cancer Medicine*, vol. 9, no. 20, pp. 7772–7780, 2020.

[17] G. Campbell-Salome, E. A. Rauscher, and J. Freytag, "Patterns of communicating about family health history: exploring differences in family types, age, and sex," *Health Education & Behavior*, vol. 46, no. 5, pp. 809–817, 2019.

[18] G. Mercuro, M. Deidda, A. Piras, C. C. Dessalvi, S. Maffei, and G. M. C. Rosano, "Gender determinants of cardiovascular risk factors and diseases," *Journal of Cardiovascular Medicine (Hagerstown, Md.)*, vol. 11, no. 3, pp. 207–220, 2010.

[19] B. Nawaz, G. E. Eide, A. Fromm et al., "Young ischaemic stroke incidence and demographic characteristics – the Norwegian stroke in the young study – a three-generation research program," *European Stroke Journal*, vol. 4, no. 4, pp. 347–354, 2019.

[20] A. Stang, "EDITORIAL: nonresponse research – an underdeveloped field in epidemiology," *European Journal of Epidemiology*, vol. 18, no. 10, pp. 929–931, 2003.