Cardiovascular risk reduction in referrals to outpatient vascular clinics

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ABSTRACT

INTRODUCTION Patients with peripheral arterial disease (PAD), aneurysmal disease (AD) or carotid atherosclerosis are at high cardiovascular risk, necessitating secondary cardiovascular protection. The aim of this study was to determine compliance with cardiovascular risk reduction guidelines in new patients referred to vascular clinics.

METHODS A multicentre collaborative national observational audit of new patients referred to eight tertiary general vascular clinics over a three-month period in England and Wales was conducted by the Vascular and Endovascular Research Network (VERN). Referral letters, case notes and investigations were reviewed by local investigators, and data analysed by VERN.

RESULTS A total of 656 patients were included in the study: 73.2% had PAD, 23.2% had AD and 3.7% had carotid atherosclerosis. A third (37.5%) were current smokers, two-thirds (61.7%) were on antiplatelet therapy and two-thirds (61.5%) were on statin therapy. Smoking was more prevalent in the PAD cohort (PAD 41.4%, AD 27.5%, $p=0.003$). However, more PAD patients were on antiplatelet therapy (PAD 63.9%, AD 53.3%, $p=0.024$). Both antiplatelet and statin prescription significantly increased with the number of cardiovascular risk factors. Patients with a previous cardiac or cerebrovascular history were more likely to have stopped smoking, and to be on antiplatelet and statin therapy ($p<0.0001$ for each). Overall, 47.3% of patients were on both antiplatelet and statin therapy, and 28.9% were on antiplatelet and statin therapy and not smoking.

CONCLUSIONS This study highlights deficiencies in cardiovascular risk minimisation in patients with established vascular disease. Patients with concomitant cardiac or cerebrovascular disease were more likely to be on best medical therapy.

KEYWORDS

Peripheral arterial disease – Aneurysm – Atherosclerosis – Statin therapy – Antiplatelet therapy

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Cardiovascular disease is the most common cause of mortality in the world,¹ accounting for 17.7 million deaths annually.² Although patients with established atherosclerotic disease under the care of vascular surgeons (ie those with peripheral arterial disease [PAD], aneurysmal disease [AD] and carotid atherosclerosis) are at high cardiovascular risk, their cardiovascular risk is often poorly treated.

National Institute for Health and Care Excellence (NICE) guidelines recommend the use of the QRISK[®]2 score to determine which patients require cardiovascular risk reduction.³ Other scoring systems used include the Framingham risk score,⁴ the Reynolds risk score^{5,6} and SCORE (Systematic COronary Risk Evaluation)⁷ but these scoring systems do not take account of stroke, PAD or AD as risk factors. Alternative cardiovascular risk scoring systems do include

history of stroke or ankle–brachial pressure index.^{8,9} However, these are not in common use and PAD is generally included under the umbrella of atherosclerotic cardiovascular disease, therefore requiring secondary cardiovascular risk reduction (although this is often not made clear).

Currently, guidelines exist from NICE,³ the Scottish Intercollegiate Guidelines Network,¹⁰ the European Society for Vascular Surgery,¹¹ the American Heart Association,¹² the European Society of Cardiology¹³ and the national abdominal aortic aneurysm screening programme¹⁴ on reducing cardiovascular mortality (including lifestyle modification such as exercise and diet, smoking cessation, antiplatelet therapy, blood pressure control and statin therapy). Despite these guidelines, optimisation of cardiovascular risk for vascular patients remains poor.^{15,16} The aim of this study was to

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determine compliance with best medical therapy guidelines in new patients referred to vascular outpatient clinics with evidence of arterial disease.

Methods

A multicentre collaborative national observational audit was conducted through the Vascular and Endovascular Research Network (VERN). VERN is a multidisciplinary collaborative for those involved or interested in the care of individuals with vascular conditions in the UK.¹⁷ The network consists of vascular surgical trainees, vascular scientists, vascular nurses, students and cardiovascular researchers, with mentorship from senior vascular surgeons. It aims to facilitate multicentre cross-specialty research and audit. VERN coordinated the recording of contemporary data relating to new arterial referrals to vascular clinics from various tertiary vascular centres in the UK.

Recruitment and data capture

Members of VERN recorded data (using a purpose built electronic database) from eight tertiary vascular units in England and Wales. VERN members (UK wide) were encouraged to participate in this study through electronic advertising, with participation being entirely voluntary. Unfortunately, there was no uptake from Scotland or Northern Ireland.

Consecutive new patients referred to vascular outpatient clinics with arterial disease (PAD, AD or carotid atherosclerosis) between 1 January and 31 March 2015 were identified through a retrospective review of case notes, primary care referral letters, clinic letters and imaging. Patients later found to not have arterial disease at clinic consultation or on imaging and those with venous disease were excluded based on clinic letter review and subsequent investigations.

Clinic letters, electronic patient records and physical notes were assessed for data completeness and quality. Data were captured between 1 January and 1 May 2016, to ensure that any resultant investigations had been completed and that any arterial diagnosis had been confirmed or excluded. Demographic details, medical history for standard cardiovascular risk factors (myocardial infarction, stroke, transient ischaemic attack [TIA], hypertension, diabetes and chronic obstructive pulmonary disease), current cardiovascular medications and smoking status were recorded. Institutional approval was granted for audit and service evaluation by each participating trust.

Definitions and outcomes

The primary outcome was the proportion of patients with arterial disease receiving antiplatelet and statin therapy, as per current guidance relating to cardiovascular secondary prevention. Secondary outcomes included rates of smoking habits, and antiplatelet and statin therapy in patients with differing co-morbidities and numbers of cardiovascular risk factors (CRFs), and in different age groups.

Statistical analysis

The chi-squared test was used for categorical variables. Continuous data were assessed with the t-test. All statistical analysis was performed using SPSS® version 22.0 (IBM, New York, US). A *p*-value of <0.05 was considered statistically significant.

Results

A total of 8 tertiary vascular units were included, totalling 656 patients (Table 1). The mean age was 70.9 years (standard deviation: 12.2 years). The majority (73.2%) of patients were referred with PAD, 23.2% with AD (142 abdominal aortic aneurysms, 3 iliac aneurysms, 2 thoracic aneurysms, 2 popliteal aneurysms, 2 mesenteric aneurysms, 1 femoral aneurysm) and 3.7% with carotid atherosclerosis. (Subgroup analysis was undertaken comparing AD and PAD only owing to the small sample size in the carotid cohort.)

Antiplatelet agents

Antiplatelet data were available for 627 patients. Overall, 61.7% were on either aspirin (46.3%), clopidogrel (15.5%), warfarin (7.1%), another anticoagulant (1.8%) or a combination of these. There was a significant difference in antiplatelet prescription between PAD and AD patients (PAD 63.9%, AD 53.3%, *p*=0.024). Only 17.3% of the PAD cohort were prescribed clopidogrel, which is the current recommended treatment.¹⁸

Patients with no additional CRFs were less likely to be on antiplatelet therapy than those with an additional risk factor (no CRFs 49.3%, 1 CRF 58.1%, 2 CRFs 78.2%, ≥3 CRFs 90.3%; comparing all groups: *p*<0.0001; comparing no CRFs with any CRF: *p*<0.0001).

Statin therapy

Statin data were available for 628 patients. Almost two-thirds (61.5%) were on a statin. However, the type and dosage of statin prescription varied significantly, with 41.2% being on

Table 1 Proportion of study cohort included from each institution

Trust/local health board	Proportion
Heart of England NHS Foundation Trust	26.9%
Norfolk and Norwich University Hospitals NHS Foundation Trust	26.0%
Aneurin Bevan University Health Board	21.6%
University Hospitals of Leicester NHS Trust	7.4%
Imperial College Healthcare NHS Trust	6.9%
South Tees Hospitals NHS Foundation Trust	5.2%
Betsi Cadwaladr University Health Board	3.4%
Derby Teaching Hospitals NHS Foundation Trust	2.7%

atorvastatin. Among the patients for whom information on atorvastatin dosage was available (*n*=97), 24.7% were on the recommended dosage of 80mg.⁵ There was no difference in statin prescription between the PAD and AD groups (PAD 62.7%, AD 58.0%, *p*=0.56).

Patients with no additional CRFs were less likely to be on a statin than those with an additional risk factor (no CRFs 41.0%, 1 CRF 69.8%, 2 CRFs 73.0%, ≥3 CRFs 88.3%; comparing all groups: *p*<0.0001; comparing no CRFs with any CRF: *p*<0.0001).

Best medical therapy

Almost half (47.3%) of the patients were on both antiplatelet and statin therapy, and 28.9% were on antiplatelet and statin therapy and not smoking. There was no significant difference in antiplatelet and statin therapy between PAD and AD patients (PAD 49.4%, AD 40.8%, *p*=0.06).

Patients with no additional CRFs were less likely to be on both aspirin and statin than those with an additional risk factor (no CRFs 30.9%, 1 CRF 47.2%, 2 CRFs 63.4%, ≥3 CRFs 77.8%; comparing all groups: *p*<0.0001; comparing no CRFs with any CRF: *p*<0.0001).

Smoking

Smoking data were available for 480 patients. Over a third (37.5%) were current smokers, with more PAD patients currently smoking than patients with AD or carotid atherosclerosis (PAD 41.4%, AD 27.5%, carotid 21.0%, *p*=0.003).

Patients with no additional CRFs were more likely to be current smokers than those with an additional risk factor (no CRFs 50.1%, 1 CRF, 30.9%, 2 CRFs 33.3%, ≥3 CRFs 27.1%; comparing all groups: *p*=0.002; comparing no CRFs with any CRF: *p*=0.0002).

Co-morbidities

Data regarding co-morbidities were available for 638 patients, with a standard range of co-morbidities for a cohort of patients with vascular disease (Table 2). Patients with AD were more likely to have a history of ischaemic heart disease (PAD 25.2%, AD 36.5%, *p*=0.012) and a history of stroke/TIA (PAD 7.6%, AD 13.8%, *p*=0.035) whereas PAD patients were more likely to have diabetes (PAD 29.1%, AD 15.8%,

p=0.002). Patients with carotid atherosclerosis had similar co-morbidities to those with PAD. Table 3 shows the frequency of the number of CRFs per patient. No significant difference was found between the PAD and AD cohorts.

Comparison of patients with a history of ischaemic heart disease or a cerebrovascular event and those with primary AD or PAD

Among this cohort of patients, 219 had a prior history (PH) of either an ischaemic cardiac event or stroke/TIA. There was a significant difference in antiplatelet prescribing for these patients when compared with those presenting with no prior cardiovascular risk factors (PH 82.2%, no PH 49.3%, *p*<0.0001) as well as for statin prescribing (PH 75.0%, no PH 41.0%, *p*<0.0001). This was also the case with the number of current smokers (PH 22.8%, no PH 48.8%, *p*<0.0001).

Stratification by age

There was no difference in the proportion of patients on combined antiplatelet and statin therapy between age groups (age <60 years 46.8%, 60–64 years 46.2%, 65–69 years 50.0%, 70–74 years 50.0%, 75–79 years 49.0%, ≥80 years 43.5%, *p*=0.90).

Discussion

In our cohort, patients with a previous ischaemic cardiac or cerebrovascular event were significantly more likely to be taking antiplatelet agents, on statin therapy and to have stopped smoking than those with PAD or AD only. Patients referred to vascular clinics have inadequate cardiovascular protection, putting them at an unnecessarily high risk of stroke, myocardial infarction and death. Less than two-thirds of our patients were on antiplatelet therapy and less than two-thirds were on statin therapy. Of those patients receiving some cardiovascular risk reduction, very few were on high dose (80mg) atorvastatin and among PAD patients receiving cardiovascular risk reduction, the majority were not on clopidogrel as recommended by NICE.⁵ This highlights that physicians may not view PAD or AD as ‘cardiovascular disease’ and guidance must therefore be more clear.

Table 2 Range of co-morbidities for all patients referred to vascular clinics with arterial disease					
Co-morbidities	PAD (<i>n</i> =480)	AD (<i>n</i> =152)	Carotid atherosclerosis (<i>n</i> =24)	Overall (<i>n</i> =656)	<i>p</i> -value (PAD vs AD)
Chronic obstructive pulmonary disease	56/463 (12.1%)	25/139 (18.0%)	2/22 (9.1%)	83/624 (13.3%)	0.10
Ischaemic heart disease (myocardial infarction, angina or coronary artery bypass graft)	117/464 (25.2%)	50/137 (36.5%)	4/22 (18.2%)	171/623 (27.4%)	0.012
Stroke / transient ischaemic attack	35/463 (7.6%)	19/138 (13.8%)	24/24 (100%)	78/625 (12.5%)	0.035
Hypertension	210/466 (45.1%)	72/137 (52.2%)	11/22 (50.0%)	293/625 (46.9%)	0.15
Diabetes	137/471 (29.1%)	22/139 (15.8%)	8/23 (34.8%)	167/633 (26.4%)	0.002
PAD = peripheral arterial disease; AD = aneurysmal disease					

Table 3 Frequency of number of CRFs (history of ischaemic heart disease, hypertension, stroke/transient ischaemic attack or diabetes) per patient

Number of CRFs	PAD	AD	Overall
0	37.3%	31.3%	34.5%
1	32.3%	33.3%	33.2%
2	21.0%	25.0%	22.5%
3 or 4	9.3%	10.4%	10.0%

CRFs = cardiovascular risk factors; PAD = peripheral arterial disease; AD = aneurysmal disease

Data on cardiovascular risk reduction for individuals with arterial disease is well documented. Two-thirds of patients with a non-fatal stroke subsequently die from cardiovascular disease, a proportion almost four times greater than the background population.¹⁹ The presence of PAD increases the cardiovascular risk ratio to at least 1.9 (considerably higher in other studies)^{20,21} and when complicated by diabetes, this increases the standardised cardiac mortality ratio to 2.59.²² The presence of a small abdominal aortic aneurysm confers a risk of cardiovascular death of 3% per year, significantly greater than that of a male individual at the age of 65 years without AD.²³

Despite this evidence, we show suboptimal intervention to minimise this cardiovascular risk. Analysis of the UK Aneurysm Growth Study published in 2017 highlighted similar results, with patients in aneurysm surveillance no more likely to receive cardiovascular medications after entering surveillance.²⁴ Patients with a history of a cardiac or cerebrovascular event are being significantly better managed than those with PAD or AD only; an underlying reason for this may be a lack of clear guidance for these individuals. The patients with AD in our study were less likely to smoke than those in the PAD group. However, given that smoking increases aneurysm rupture rates, more needs to be done to reduce this risk. In addition, although the AD cohort had on average more co-morbidities than the PAD cohort, they were less likely to be on antiplatelet therapy.

Evidence regarding the use of cholesterol lowering therapy in patients with established cardiovascular disease is well described, with reduction in low density lipoprotein-C by 1mmol/l decreasing overall mortality, coronary mortality and any vascular event by 15%, 24% and 22% respectively.²⁵ Moreover, high dose statin therapy can further reduce cardiovascular risk by 15%.²⁶ The use of statin therapy following aneurysm repair has also been shown to improve survival with a hazard ratio (HR) of 0.75 (95% confidence interval [CI]: 0.70–0.80).²⁷ Nevertheless, statin prescription rates in our cohort remained at only 61.5% (with the vast majority of these patients not on a high dose statin) and only 41.0% of patients with no other cardiovascular risk factors were taking a statin, even though they had been referred for an arterial disorder.

Antiplatelet therapy reduces the risk of serious vascular events in patients with PAD by 22 events per 1,000 patients

treated for two years,²⁸ with the CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events) trial showing that clopidogrel is likely to be the antiplatelet of choice, particularly in current smokers.^{29,30}

Smoking cessation in patients with coronary heart disease or after myocardial infarction reduces their risk of cardiovascular mortality by 36–61%.^{31,32} Furthermore, smoking is associated with a significant reduction in the ten-year mortality rate in PAD patients from 54% to 18%.³³ Post hoc analysis of the CAPRIE trial suggests that current smokers increase their risk of ischaemic events compared with never smokers (HR: 1.24, 95% CI: 1.08–1.42) and ex-smokers (HR: 1.32, 95% CI: 1.18–1.47).³⁰ In addition, the use of clopidogrel in current smokers significantly reduced their risk of ischaemic events compared with aspirin therapy. Less than two-thirds of patients in our study were taking antiplatelet agents; the majority of these were on aspirin. Although antiplatelet therapy was more widely used in the PAD cohort, the lack of adherence to NICE guidelines¹⁸ regarding use of clopidogrel in these patients is somewhat surprising.

Smoking rates were significantly lower in those with a history of cardiovascular disease, which could be explained by previous exposure to both primary and secondary care physicians, and also by patients having a prior trigger event.^{34,35} In juxtaposition to this, however, is that the majority of patients with multiple diagnoses related to smoking who continue to smoke are the least likely to respond to any further attempt at intervention regarding smoking cessation.³⁵

In this study, patients who had a prior history of either an ischaemic cardiac event or stroke/TIA were significantly more likely to be taking antiplatelet therapy, statin therapy and to have ceased smoking. It is unknown whether this is due to a better understanding of cardiovascular risk management in this cohort of patients by the general practitioner or whether these changes were instigated in secondary care, which would highlight the need for secondary care to encourage uptake of best medical therapy. Indeed, the onus is on the entire multidisciplinary team to improve outcomes. All members should therefore ensure that management plans are optimised, not just the general practitioner.

Although rate of prescriptions for antiplatelet and statin agents are improving for patients with abdominal aortic aneurysm,¹⁶ previous work by VERN has shown that those under aneurysm surveillance also have poor uptake of best medical therapy,³⁶ suggesting that both primary and secondary care must improve further. Future work must evaluate patient compliance in the long term with reducing cardiovascular risk.

This study is limited by the lack of evidence regarding adherence to antiplatelet and statin therapy, and long-term smoking data. In addition, medication doses were not known for a large percentage of patients. The time lag of approximately one year from appointment to data collection ensured that all patients had a true diagnosis of arterial disease as further investigations were reviewed to determine this. However, the extent of disease is unknown, as is aneurysm size and whether these were primary referrals or patients on a surveillance programme.

In addition, data were not collected on referrals for smoking cessation, or advice given to patients regarding antiplatelet and statin therapy or smoking cessation. Previous work by VERN has highlighted that advice given to patients on abdominal aortic aneurysm surveillance programmes is insufficient, with only 66% of patients given full cardiovascular risk reduction advice and only 82% of surveillance units advising changes to the patient's prescription.⁵⁶ Further work is required to determine uptake of this advice and compliance in the longer term.

Conclusions

This study highlights deficiencies in cardiovascular risk minimisation in patients with known arterial disease warranting secondary cardiovascular protection; there is a clear discrepancy compared with those patients with a history of cardiac or cerebrovascular disease. A drive to ensure individuals with PAD and AD receive optimum secondary cardiovascular protection is required. Arterial disease should be integrated into risk scoring algorithms. In the era of computerised medical records, consideration should be given to incorporating alerts within the primary care setting to recommended treatments on entering a diagnosis (such as clopidogrel for patients with PAD).

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