Multi-Centre Study on Cardiovascular Risk Management on Patients Undergoing AAA Surveillance

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Abstract

Background

The risk of cardiovascular events and death in patients with abdominal aortic aneurysms (AAA) is high. Screening has been introduced to reduce AAA related mortality; however, after AAA diagnosis, cardiovascular modification may be as important to patient outcomes as surveillance. The aim of this study was to assess cardiovascular risk reduction in patients with small AAA.

Methods

Institutional approval was granted for The Vascular and Endovascular Research Network (VERN) to retrospectively collect data pertaining to cardiovascular risk reduction from four tertiary vascular units in England. Patients with small AAA (January 2013–December 2015) were included. Demographic details, postcode, current medications, and smoking status were recorded using a bespoke electronic database and analysed. In a secondary analysis VERN contacted all AAA screening units in England and Wales to assess their current protocols relating to CV protection.

Results

In total, 1053 patients were included (mean age 74 ± 9 years, all men). Of these, 745 patients (70.8%) had been prescribed an antiplatelet agent and 787 (74.7%) a statin. Overall, only 666 patients (63.2%) were prescribed both a statin and antiplatelet. Two hundred and sixty eight patients (32.1%) were current smokers and the proportion of patients who continued to smoke decreased with age. Overall, only 401 patients (48.1%) were prescribed a statin, antiplatelet, and had stopped smoking. In the secondary analysis 38 AAA screening units (84% national coverage) replied. Thirty-one units (82%) suggest changes to the patient's prescription; however, none monitor compliance with these recommendations or assess whether the general practitioner has been made aware of the AAA diagnosis or prescription advice.

Conclusion

Many patients with small AAA are not prescribed an antiplatelet/statin, and still smoke cigarettes, and therefore remain at high risk of cardiovascular morbidity and mortality. National guidance to ensure this high risk group of patients is adequately protected from poor cardiovascular outcomes is lacking.

Keywords

AAA; Screening; Cardiovascular; Protection

What this paper adds

This study suggests that many patients with small abdominal aortic aneurysms are not prescribed an antiplatelet or statin and continue to smoke cigarettes and therefore remain at high risk of cardiovascular morbidity and mortality.

Introduction

Abdominal aortic aneurysm (AAA) is a common cardiovascular (CV) cause of death.1 The current prevalence of AAA in the western world is estimated to be 1.2–3%, based on data from mature screening programmes, and cross sectional studies,2; 3; 4; 5; 6; 7 ; 8 and screening has been shown to be beneficial regarding aneurysm related mortality.4 ; 7 Subsequently, screening is now offered routinely in several countries, including the UK, where males are offered ultrasound screening at the age of 65 through the NHS AAA Screening Programme (NAAASP).9 This has resulted in approximately 6000 people having been diagnosed with a small AAA (3.0–5.5 cm) between 2013 and 2015.3

Small AAAs do not require immediate surgical treatment to prevent rupture, as rupture is unlikely to occur at this size, based on well designed randomised trials.10 However, apart from rupture, patients with a small AAA are at significantly higher risk of major CV events compared with the general population.11 ; 12 Cardiovascular disease and AAA share common predisposing risk factors, including smoking, male sex, hypertension, and hypercholesterolaemia,1; 13 ; 14 and a meta-analysis of large observational cohorts of patients with small AAAs recently demonstrated that the risk of CV death for an individual with a small AAA is 3% per year, significantly exceeding the standard CV risk of a male individual at the age of 65.12

The National Institute for Health and Care Excellence (NICE) and the American Heart Association (AHA) have both produced clear guidance, based on high quality randomised evidence, that supports the use of antiplatelets, statin therapy, blood pressure control, lifestyle modification, and implementation of smoking cessation in any individual deemed to be at high CV risk, using standard CV risk scores.15; 16 ; 17 Furthermore, based on the NAAASP Standard Operating Procedures

(SOPs), individuals with a small AAA should be offered antiplatelet/statin therapy, and lifestyle interventions should be considered, including referral to a smoking cessation service if necessary.9

By systematically addressing the CV risk factors of patients with a small AAA, thousands of which are now discovered nationally through screening, the burden of CV events and CV death could be significantly reduced in this high risk group; however, compliance with the above guidance is unknown. The aim of this study was to assess whether patients with a small AAA are currently offered adequate secondary prevention in terms of antiplatelet and statin therapy as well as lifestyle and smoking cessation interventions. Data from various regions in England were used, all of which have mature screening programmes, and a nationwide online survey of NAAASP screening units was conducted to assess their current CV risk reduction protocols.

Methods

The Vascular and Endovascular Research Network

The Vascular and Endovascular Research Network (VERN) is a collaborative for those involved or interested in the care of individuals with vascular conditions in the UK. The network includes vascular surgical trainees, vascular scientists, vascular nurses, students, and cardiovascular researchers. It aims to help facilitate multi-centre cross-specialty research and audit and was used to record contemporary data relating to the treatment of patients with a small AAA from a series of tertiary vascular centres in England.

Primary study: cardiovascular risk reduction at a vascular unit level

Recruitment and data capture

Members of VERN recorded data using an electronic purpose built database from four tertiary vascular units in areas (England) with mature AAA screening programmes: University Hospital of Coventry and Warwickshire NHS Trust, Coventry; Norfolk and Norwich University Hospital NHS Trust, Norwich; Queens Medical Centre NHS Trust, Nottingham; and Birmingham Heart of England NHS Foundation Trust, Birmingham. Consecutive patients identified to have a small AAA through the respective vascular centre (between January 2013 and December 2015) who were then referred to a vascular outpatient clinic were recorded. This included patients identified both through NAAASP screening and incidentally detected aneurysms.

Clinic letters, electronic patient records, and physical notes were assessed to ensure data completion. Data were captured after the patient had been diagnosed with an AAA and had seen a vascular specialist. Demographic details, medical and surgical history, postcode, current medications, and smoking status were recorded. The most recent cholesterol level was also

recorded. Patients with thoracic, mycotic, or inflammatory aneurysms were excluded. Institutional approval under “audit and service evaluation” was granted by each participating Trust. Data were collected and processed adhering to the Declaration of Helsinki.

Index of Multiple Deprivation score

The Index of Multiple Deprivation (IMD) is the official measure of relative deprivation for various geographical areas across England.18 It is the most widely used of the Indices of Deprivation, published regularly (available online) by the Department for Communities and Local Government. The IMD ranks every small area in England from 1 (most deprived area) to 32,844 (least deprived area) by combining seven domains to produce an overall relative measure of deprivation. The domains that are combined include (weight %): Income Deprivation (22.5%), Employment Deprivation (22.5%), Education, Skills and Training Deprivation (13.5%), Health Deprivation and Disability (13.5%), Crime (9.3%), Barriers to Housing and Services (9.3%), and Living Environment Deprivation (9.3%). The weights were derived from consideration of the academic literature on poverty and deprivation, as well as the levels of robustness of the indicators.18 Based on each individual's latest postcode, IMD scores were calculated.

Secondary study: cardiovascular risk reduction at an AAA screening level

Following approval by the NAAASP research committee, all screening units in England and Wales were contacted (electronically) to assess their current protocols relating to cardiovascular protection. An online survey consisting of 10 questions was sent to each unit, between December 2015 and January 2016. The questions interrogated each unit's prescribing protocol relating to antiplatelets and statins, cardiovascular follow-up, lifestyle modification advice, and measures relating to smoking cessation.

Definitions and outcomes

The primary outcome was the proportion of patients with a small AAA who has been prescribed antiplatelet and statin therapy, as per current national guidance relating to CV secondary prevention. Secondary outcomes included cholesterol levels upon recruitment, smoking habit, differences in pharmacotherapy between different age and IMD score groups. An analysis of full compliance was performed with full compliance defined as prescription of a statin, prescription of an antiplatelet, and the patient being a non-smoker at the time of data collection.

Statistical analysis

Continuous data are presented as mean value ± standard deviation (SD) if normally distributed and median value ± interquartile range (IQR) if non-normally distributed. Distributions were assessed using skewness and kurtosis as a measure as well as using the Kolmogorov–Smirnov test. Categorical data are presented as counts and percentages (%) per group. Comparisons of continuous variable among different groups were performed using analysis of variance (ANOVA) testing and chi-square test for categorical variables. All statistical analyses were performed using the SPSS software package (SPSS version 22.0, IBM, Armonk, NY, USA). A p value <.05 was considered to be statistically significant.

Results

Vascular unit level

Overall, data were obtained for 1053 patients with a small AAA from the four participating centres (mean age 74 ± 9 years, all men), who had attended a vascular clinic following diagnosis of a small AAA, not requiring immediate surgical treatment. Of the 1053 patients, 745 patients (70.8%) had been prescribed an antiplatelet agent (Table 1) and 787 (74.7%) a statin (Table 2). The age group most likely to be prescribed an antiplatelet agent included those aged 70–74.9 years (82.2%), with those aged 65–69 years (56.4%) being least likely to be prescribed an antiplatelet (OR 1.4, 95% CI 1.29–1.64, p<.001). Statin prescription was also greatest in those aged 70–74.9 years (83.7%), with those aged <65 years least likely to be prescribed a statin (67.6%, OR 1.23, 95% CI 1.04–1.48, p=.007). Overall, only 666 patients (63.2%) were prescribed both a statin and antiplatelet, suggesting that over a third of patients under surveillance for AAA (36.8%) were not on optimal pharmacological therapy (Table 3).

Table 1.

Patients receiving antiplatelet by age group.

	No antiplatelet		Antiplatelet	
n	%	n	%	
<64.9	27	38.0	44	62.0
65–69.9	158	43.6	204	56.4
70–74.9	24	17.8	111	82.2
75–79.9	40	21.2	149	78.8
80–84.9	29	19.3	121	80.7
>85	30	20.5	116	79.5
Subtotal	308	29.2	745	70.8

Table options

Table 2.

Patients receiving statin by age group.

	No statin		Statin	
	n	%	n	%
<65	23	32.4	48	67.6
65–69.9	98	27.1	264	72.9
70–74.9	22	16.3	113	83.7
75–79.9	42	22.2	147	77.8
80–84.9	35	23.3	115	76.7
>85	46	31.5	100	68.5
Subtotal	266	25.3	787	74.7

Table options

Table 3.

Patients receiving antiplatelet and statin therapy by age group.

	Antiplatelet + statin			
	No		Yes	
	n	%	n	%
<65	32	45.1	39	54.9
65–69.9	164	45.3	198	54.7
70–74.9	33	24.4	102	75.6
75–79.9	60	31.7	129	68.3
80–84.9	43	28.7	107	71.3
>85	55	37.7	91	62.3
Subtotal	387	36.8	666	63.2

Table options

Cholesterol levels were available for 574 patients (Table 4), while smoking data were available for 834 patients (79.2% completeness) (Table 5). From this, 566 patients were non-smokers, 491 were ex-smokers, 75 had never smoked, and 268 (32.1%) were current smokers, suggesting that a third of patients continue to smoke. The proportion of patients who continue to smoke decreased with age, being greatest in the <65 year age group (48.3%) and lowest in the >85 age group (15.1%, OR 3.2, 95% CI 2.0–5.1, p<.001). Overall, only 401 patients (48.1%) were fully compliant (Table 6).

Table 4.

Mean cholesterol by age group.

Cholesterol level, mmol/L

Mean SD

<65 4.4 1.0

65–69.9 4.3 1.3

70–74.9 4.2 1.1

75–79.9 4.1 .9

80–84.9 4.2 1.1

>85 4.1 1.0

Subtotal 4.2 1.0

Table options

Table 5.

Smoking rates by age group.

Non-smoker

Smoker

n % n %

<65 31 51.7 29 48.3

65–69.9 111 55.8 88 44.2

70–74.9 70 58.8 49 41.2

75–79.9 120 71.9 47 28.1

80–84.9 110 76.9 33 23.1

>85 124 84.9 22 15.1

Subtotal 566 67.9 268 32.1

Table options

Table 6.

Full compliance (antiplatelet + statin + not smoking) by age group.

Fully compliant

No

Yes

n	%	n	%		
<65	39	65.0	21	35.0	
65–69.9		127	63.8	72	36.2
70–74.9		63	52.9	56	47.1
75–79.9		79	47.3	88	52.7
80–84.9		55	38.5	88	61.5
>85	70	47.9	76	52.1	
Subtotal		433	51.9	401	48.1

Table options

Prescription of both an antiplatelet and statin was highest in the 75–79.9 year age group (46.6%) and lowest in the 65–69.9 year age group (19.9%). IMD scores were available for 910 patients. Mean IMD rank and decile for the cohort were 16,708±8917 and 5.61±2.70, respectively. Mean IMD decile was not significantly different between patients receiving and not receiving combined antiplatelet and statin therapy (5.55±2.78 vs. 5.72±2.57; p=.339, Table 7).

Table 7.

Deprivation scores by BMT uptake group.

Deprivation indices	Antiplatelet + statin + not smoking (BMT)				
Between groups					
Yes					
No					
Mean	SD			p value	
IMD rank		16,552	9136	16,946	8577	.508
IMD decile		5.55	2.78	5.72	2.57	.339

Table options

AAA screening survey

Overall, 38 screening units (84% national coverage) replied. All units perform an assessment of the patient's CV risk factors once they have been diagnosed with an AAA, regardless of size, but none use a standardised validated CV risk score. Most units (68%) perform these assessments during the first clinic-visit, when the patient is diagnosed (face to face); the remaining units perform this assessment on a second visit. Thirty-one units (82%) suggest prescription of an antiplatelet agent (63% aspirin, 37% clopidogrel), 33 (87%) a statin, and 52% antihypertensive treatment once the diagnosis of AAA has been made; however, no units monitor compliance with these recommendations or assess whether the GP has been made aware of the AAA diagnosis or

prescription advice. If a change to the patient's medication is decided, all units contact the general practitioner (GP) by post; however, only 21% inform the patient directly. Twenty-one units (56%) may refer to a smoking cessation clinic if the patient accepts, and 34 (89%) directly offer lifestyle modification advice, usually written (67% provide a leaflet).

Discussion

This study suggests that the majority of patients (52%) currently under surveillance for a small AAA are not compliant with established secondary prevention guidance on the use of antiplatelets, statins, and smoking cessation to reduce their risk of major cardiovascular events. Importantly, the youngest patients in this study (<70 years old) who have the most to gain from cardiovascular risk factor modification, had the poorest compliance. Despite evidence that patients with a small AAA are at significantly higher risk of major CV events compared with the general population,12 there does not appear to be a uniform national strategy to address the CV risk of these patients. This study also highlights that although many patients have their high cardiovascular risk identified at AAA screening and appropriate pharmacological or lifestyle advice may be given, no mechanism currently exists for either monitoring compliance or ensuring the recommendations are received by the patient's family doctor. This may contribute towards a low compliance with best medical therapy.

Patients with AAA are known to have multiple CV risk factors,19 often including smoking, hypertension, male sex, older age, and hypercholesterolaemia,19 and one meta-analysis suggested that the risk of CV death is 3% per year in an individual with a small AAA,12 equivalent to that of a 70 year old male diabetic smoker with hyperlipidaemia and hypertension. Previous studies have demonstrated the strong relationship between AAA diagnosis and cardiovascular risk, for example Newman and colleagues20 in a longitudinal cohort study demonstrated that rates of cardiovascular mortality (34.3 vs. 13.8 per 1000 person years), and cardiovascular disease (47.3 vs. 31.0 per 1000 person years) were higher in patients with AAA than in those without, while The United Kingdom Small Aneurysm Trial21 showed that for every 8 mm increase in aneurysm diameter the hazard ratio for cardiovascular mortality increased by 1.34.

One prospective cohort study22 including patients with both small and medium AAA who had no known history of cardiovascular disease compared 476 patients with AAA and 339 controls, and found that the AAA group had higher levels of high sensitivity CRP (2.8 mg/L, IQR 1.2–6.0, vs. 1.3 mg/L, IQR 0.5–3.5, p<.001) and heart type fatty acid binding protein (4.6 µg/L, IQR 3.5–6.0, vs. 4.0 µg/L, IQR 3.3–5.1, p=.011), suggesting that the AAA group had an excess risk of cardiovascular disease. The same study 22 showed a higher crude mortality rate in people with AAA (69.1/1000 person years) compared with those without, which persisted after adjustment. This demonstrates that patients with no cardiovascular history who are found to have an aneurysm at screening (a common scenario in AAA screening), may benefit from cardiovascular risk modification.

Acquired CV risk factors, such as hypertension and hypercholesterolaemia, are often modifiable through pharmacological therapy, and patients with established CV disease should receive aggressive pharmacotherapy in that direction; however, a national framework to guide cardiovascular modification in patients with AAA is lacking.13 ; 23 This would be especially helpful in

patients found incidentally to have AAA as this group are not covered by standard NAAASP guidelines. Aside from the inherent cardiovascular risk, one meta-analysis of over 15,000 participants found that smoking was an independent risk factor for both aneurysmal growth ($p<.001$) and rupture (HR 2.02, 95% CI 1.33–3.06; $p=.001$), with aneurysm growth rates twice as fast as non-smokers. Smoking is an integral part of the aetiology and natural progression of AAA and it is recommended that patients are given smoking cessation advice on AAA diagnosis. Despite this, the present study suggests that half of patients under surveillance for AAA in the youngest included age group (<65 years) continue to smoke.

One approach to improving smoking cessation rates would be for clinicians to ask and address the smoking habits of their own patients. Counselling of just 3 min has been estimated to increase the odds of quitting by 1.3 relative to no counselling.23 An understanding of local guidelines and available options is vital, for example behavioural therapies have been shown to approximately double, and together with pharmacotherapy quadruple, the likelihood of successful quitting.24 Bohlin and colleagues25 recently investigated smoking habits after screening for AAA, and in their cohort of 8150 65 year old men, those with AAA reduced their consumption of cigarettes significantly more than men with no AAA and recalled having been informed about the importance of smoking cessation at the time of screening more often than men with no AAA.

Statins play a large role in the primary prevention of cardiovascular events in the general population and patients with a 10% 10 year risk (QRISK 2 score) are currently recommended to receive atorvastatin daily.16 Statin use is associated with a significant reduction in cardiovascular mortality and has demonstrated a reduction in low density lipoprotein (LDL) cholesterol of greater than 40%.14 ; 24 Guidance from the European Society of Vascular Surgery (ESVS)26 suggests that statin therapy should also be continued into the peri-operative period as it significantly reduces the risk of a post-operative myocardial infarction (HR 0.55; 95% CI 0.34–0.88, $p=.01$). 27 Despite the clear association between a diagnosis of AAA and cardiovascular risk,12 antiplatelet therapy is not specifically recommended by NICE for patients with AAA as it is not considered a secondary prevention intervention. Prescription of an antiplatelet has, however, been recommended by the ESVS26 and the results of this study, which demonstrates that up to 30% of patients do not take a regular antiplatelet, are similar to that shown previously by Bahia and colleagues in the UK.28

Currently all men are offered a one-off screening ultrasound in the year of their 65th birthday to identify AAA. Men found to have a small AAA (30–54 mm) are offered surveillance based on the size of the aneurysm,29 and, after screening, all men with AAA are seen by a nurse specialist29 who advises regarding blood pressure optimisation, smoking cessation, healthy living and exercise, and any interventions required by the general practitioner. This intervention does not necessarily occur for patients who are incidentally found to have an AAA, although the cardiovascular risk of these patients is likely to be at least equivalent to that of those identified through screening. One issue raised by this study is that there is no follow-up to ensure that a patient's general practitioner receives or acts on advice given. Two recent studies7 ; 30 using data from the Swedish AAA screening programme have demonstrated that a modern screening programme consisting of ultrasound screening with best medical management remains cost effective, and that, assuming a

10% reduction in all cause mortality, the incremental cost of screening would be €175 per person and year.

A meta-analysis of secondary prevention trials,31 totalling 17,000 individuals at high average risk, found that aspirin therapy was associated with a reduction in serious vascular incidents (6.7% vs. 8.2% per year), with reductions in ischaemic strokes and coronary events. Despite antiplatelet and statin therapy being recommended by NAAASP SOPs following diagnosis of a small AAA, practice varies between screening units in England and Wales, as per the results of this survey. None of the units directly monitor prescription of pharmacological risk factor modification and this may be an opportunity missed.

Limitations

This study was retrospective, data on medication drug dose were not available, and information on drug intolerances, which may explain some of those patients not on any antiplatelet and/or statin, were also not available. Data on medical contraindications to the use of aspirin (or any other antiplatelet) and/or a statin were not collected and data on prescription of these medications prior to AAA diagnosis (for existing cardiovascular disease) also were not collected. Statin intolerance is thought to affect approximately 10–15% of patients,32 and although the number of patients intolerant to clopidogrel is approximately 1%,33 the number intolerant or allergic to aspirin is less clear.

Data were collected on current or former smoking retrospectively and did not include data on the recommendation of smoking cessation, psychological or pharmacological therapies to aid smoking cessation. The vascular unit's role is clearly to provide an intervention or recommendation for the patient to stop smoking and it is possible that this approach underestimates the actual input of the unit. By analyzing actual smoking in this group of patients, it has been demonstrated, however, that in the youngest patients with known small AAA, just under half still use cigarettes therefore more could be done. Data were collected using clinic letters, electronic patient records, and physical notes after the patient was assessed by a vascular specialist (nurse or doctor). It is possible that in some cases patients started/stopped smoking or that their prescription was changed but that this was not transcribed and therefore this would be missed. Time between diagnosis and data collection was also not recorded.

Furthermore, although it was possible to collect data on prescription of medications, compliance with taking that medication was not assessed. An assessment of compliance with these medications would probably have demonstrated an even lower number of patients receiving the full complement of cardiovascular protective medications. Furthermore, no further validation of the data collected was attempted after initial data collection at each respective site. This study included not only patients identified at screening but also those patients with small AAA identified incidentally. Patients with AAA found incidentally are more likely to be older, more comorbid, and therefore more likely to be prescribed an antiplatelet and statin for other reasons; however, NAAASP

regulations and/or guidance on the use of best medical therapy do not directly apply to this cohort. Despite this, even in the 80–85 year age group, only 59% were on the full complement of cardiovascular protection. This may be because patients with AAA identified incidentally are not subject to the same pathways as those identified through NAAASP, therefore they do not necessarily receive the same best medical therapy or lifestyle advice. Those younger patients with the most to gain from cardiovascular protection are the group least likely to be on the full complement of an antiplatelet, statin, and a non-smoker. The implications of this are that regardless of how the AAA is identified, there is room for improvement.

Conclusion

Cardiovascular risk factor modification in patients under surveillance for small AAA can be improved. National guidance is sought to ensure that all patients under surveillance for small AAAs are appropriately risk assessed and counselled regarding cardiovascular risk factor reduction including smoking cessation.

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