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Rupture of Abdominal Aortic Aneurysms in Patients Under Screening Age and Elective Repair Threshold

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WHAT THIS PAPER ADDS

All patients treated for ruptured abdominal aortic aneurysm (RAAA) in two hospitals were analyzed to evaluate how many of them were not within the elective repair threshold or screening age. Surprisingly many RAAA patients were under 65, especially among smokers (28%). The mean AAA diameter at the time of rupture was significantly smaller among women: 5.6% of men had a rupture at under 55 mm and 11.5% of women at under 52 mm, which are the operative limits according to the European guidelines. It seems that current practice for AAA screening age and guidelines for size threshold may underestimate the risk of rupture.

Objectives: The objective of this study was to identify the proportion of abdominal aortic aneurysm ruptures that occur before the screening age or threshold diameter for operative repair is reached.
Methods: The study was a retrospective analysis of RAAA patients including all RAAA patients admitted to Helsinki (HUH) and Tampere University Hospitals (TaUH) during 2002—2013. The data for age, gender, and comorbidities were collected from vascular registry and patient records. Computed tomography images taken at the time of admission were used for the measurement of maximum anteroposterior (AP) aneurysm diameter at the time of rupture. Age and diameter data were compared with risk factors.
Results: A total of 585 patients diagnosed with RAAA were admitted to the two hospitals during the 12 year period. The mean age at the time of rupture was 73.6 years (SD 9.5, range 42—96 years). 18.3% of patients were under 65: 21.4% of men and 3.0% of women. Men were on average 8 years younger than women. The odds ratio (OR) for rupture before 65 years of age for smokers was 2.1 compared with non-smokers, and 28.4% of smokers were under 65 at the time of rupture. Of all RAAA patients, 327 had a computed tomography scan confirming rupture. The mean AP diameter of the aneurysm was 75.6 mm (SD 15.8, range 32—155 mm). The mean size was significantly lower in women than in men (70.5 vs. 76.8, $p = .005$).
Conclusions: The data from this study show that a fifth of men would not make it to the screening age of 65 before AAA rupture, the proportion being even larger in active smokers. The data from this study also supports the previous finding that aneurysm size at the time of rupture is significantly smaller in women.

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INTRODUCTION

Ruptured abdominal aortic aneurysm (RAAA) carries a very high mortality that has not been significantly reduced even as treatment methods have evolved.[1—3] Most aneurysms are asymptomatic until rupture. The key in reducing AAA related mortality is to identify patients before rupture. To achieve this, AAA screening programs have been implemented in many countries.[4—6] Most AAA patients do not die of rupture but of other causes, and predicting AAA growth rate and rupture risk is problematic. This makes operative decisions difficult with asymptomatic aneurysms. The decision for operative treatment is mostly based on AAA diameter. According to the practice guidelines of the European Society for Vascular Surgery the AAA diameter beyond which operative treatment should be considered is 55 mm for men and 52 mm for women if the risks for elective repair are not significantly increased.[7] The American practice guidelines published by the Society for Vascular Surgery recommend repair for patients with AAA maximum diameter of 55 mm or larger without significant comorbidities, and suggest that young,

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healthy patients and especially women may benefit from repair even with a maximum diameter between 50 and 54 mm.[8] This lower threshold for women is not based on robust evidence, as aneurysm prevalence among women is markedly lower than among men. A proportion of AAAs rupture before screening age and operative threshold diameter, and currently there is no way of differentiating these patients.

AAA prevalence rises with age. Smoking is a clear risk factor for developing an AAA, another is a positive family history. Smoking is also known to increase the rate of aneurysm growth and the risk of rupture. Women have a higher rupture risk than men, although there is no difference in the rate of aneurysm growth.[9–11] Medical therapy beyond the control of general risk factors of atherosclerotic disease has not been shown to be effective: a recent Cochrane review of pharmacological treatment to reduce the mortality and cardiovascular events in AAA patients found insufficient evidence to draw any conclusions.[12]

The aim of this study was to identify the proportion of RAAAs that occur before screening age or threshold diameter for operative repair is reached and whether there are differences in risk factor profiles between early and late ruptures.

MATERIALS AND METHODS

RAAA and patient age

Helsinki and Uusimaa district in southern Finland has a population of 1.6 million. All elective and emergency AAAs are treated in the vascular surgical unit of Helsinki University Hospital (HUH). Similarly, RAAA patients in the Pirkanmaa district (population 520,000) are treated in Tampere University Hospital (TaUH). Hospital records were searched for all RAAA patients who were admitted to HUH and TaUH during 2002—2013. Data for risk factors were collected from the vascular registry and patient records. Data for patient age and gender, smoking status, history of coronary artery disease, hypertension, dyslipidemia, diabetes, pulmonary disease and stroke/transient ischemic attack (TIA) were collected.

In the first analysis, how well the currently used screening protocols would have found the patients who sustained RAAA was evaluated in the first analysis. Patient age at the time of rupture was compared with risk factors.

RAAA and aneurysm size

In the second analysis, to ensure reliable and reproducible measurement of AAA diameter, only patients who underwent computed tomography (CT) imaging confirming a ruptured AAA were selected. CT images demonstrating rupture were reviewed and the maximum AP diameter (outer to outer) was measured. The diameter data were compared with the information of patient risk factors collected from the local vascular registries and patient records.

Statistical methods

Statistical analysis was done using SPSS Statistics (IBM, Armonk, NY, USA). Univariate analysis between age and risk factor data and AP diameter and risk factor data was performed with independent samples *t* test. Multivariate analysis was performed using a logistic regression model with aneurysm size under 55 mm and age under 65 years as dependent factors. The risk factors associated with patient age that had $p < .2$ in univariate analysis were selected for the multivariate model to identify risk factors independently predicting a rupture before the age of 65 years, which is commonly used in screening programs. The maximal AP diameter in relation to the risk factor data was included in a univariate analysis. All risk factors with $p < .2$ were included in the multivariate model to see which risk factors were associated with rupture before reaching 55 mm diameter. How well the threshold for elective aneurysm repair covered RAAA patients was also calculated.

In the cases where the registry data were incomplete, the missing data were acquired from patient records. After completing the data from the case records, the smoking data were available in 71% of the cases. If patients had smoked actively during the past 5 years they were considered to be smokers. If they had never smoked or had quit smoking over 5 years before, they were considered to be non-smokers. Thus many patients labeled as non-smokers actually had a very long history of smoking.

RESULTS

RAAA and patient age

Altogether, 587 RAAA patients, 16.9% of whom were women, were admitted to HUH and TaUH between 2002—

Table 1. Patient demographics in relation to gender. * indicates $p < .05$.

	Men	Women	Total	Missing	*p*
N	486 (83.1%)	99 (16.9%)	585		
Mean age (SD)	72.2 (9.3)	80.7 (7.6)	73.6 (9.5)		<.01*
Smoking	183	25	208	169	.1
	37.7%	25.3%	35.6%	28.9%	
Coronary disease	211	52	263	19	.06
	43.4%	52.5%	45.0%	3.2%	
Diabetes	55	12	67	4	.81
	11.3%	12.1%	11.5%	0.7%	
Hypertension	261	59	320	29	.21
	53.7%	59.6%	54.7%	5.0%	
Pulmonary disease	108	23	131	27	.57
	22.2%	23.2%	22.4%	4.6%	
Previous stroke/TIA	83	12	95	20	.27
	17.1%	12.1%	16.2%	3.4%	
Dyslipidemia	147	30	177	76	.77
	30.2%	30.3%	30.3%	13.0%	
CT scan	267	61	328		.22
	54.9%	61.6%	56.1%		

2013 (Table 1). Three hundred and twenty-eight patients (56.1%) underwent CT examination where rupture was confirmed. The rest of the patients had rupture confirmed with a bedside ultrasound scan in the emergency room, or the diagnosis of RAAA was made based on patient history and clinical symptoms.

The association between different risk factors and patient age at the time of rupture was analyzed using the data for all 585 RAAA patients admitted to HUH and TaUH between 2002—2013. The mean age at the time of rupture was 73.6 years (SD 9.5, range 42—96 years). Of the 107 patients, 18.3% were under 65 years of age, 21.4% ($n = 104$) of men and 3.0% ($n = 3$) of women. Men were on average 8 years younger than women at the time of rupture. Among all smokers 28.4% ($n = 59$) were under 65 years at the time of rupture whereas 13.0% ($n = 27$) of non-smokers had a rupture before the age of 65 ($p < .001$). Among male smokers the proportion of under 65 year olds was the highest, 31.7% (Fig. 1). Other factors besides smoking that were more common among those under 65 in univariate analysis were male gender, history of hypertension, coronary artery disease, history of stroke/TIA, and pulmonary disease (Table 2). In the logistic regression model, only smoking (OR 2.1, 95% CI 1.2—3.7), male gender (OR 15.4, 95% CI 12.1—115.1), and coronary artery disease (OR 0.4, 95% CI 0.2—0.7) were independent predictors of rupture under the age of 65 (Table 3).

Table 2. Factors associated with patient age. * indicates $p < .05$.

		n	Mean age, years (SD)		*p*
Sex	Male	486	72.2	(9.3)	<.001*
	Female	99	80.7	(7.6)	
Smoking	Yes	208	69.5	(8.8)	<.001*
	No	208	75.0	(8.9)	
Diabetes	Yes	67	74.3	(7.9)	.544
	No	514	73.6	(9.7)	
Dyslipidemia	Yes	177	73.9	(8.7)	.667
	No	332	73.5	(9.7)	
Hypertension	Yes	320	74.5	(8.9)	.010*
	No	236	72.4	(10.1)	
Coronary disease	Yes	263	76.8	(8.0)	<.001*
	No	303	71.0	(9.9)	
Pulmonary disease	Yes	131	75.0	(7.8)	.019*
	No	427	73.0	(9.9)	
Previous stroke/TIA	Yes	95	76.1	(8.7)	.006*
	No	470	73.1	(9.6)	

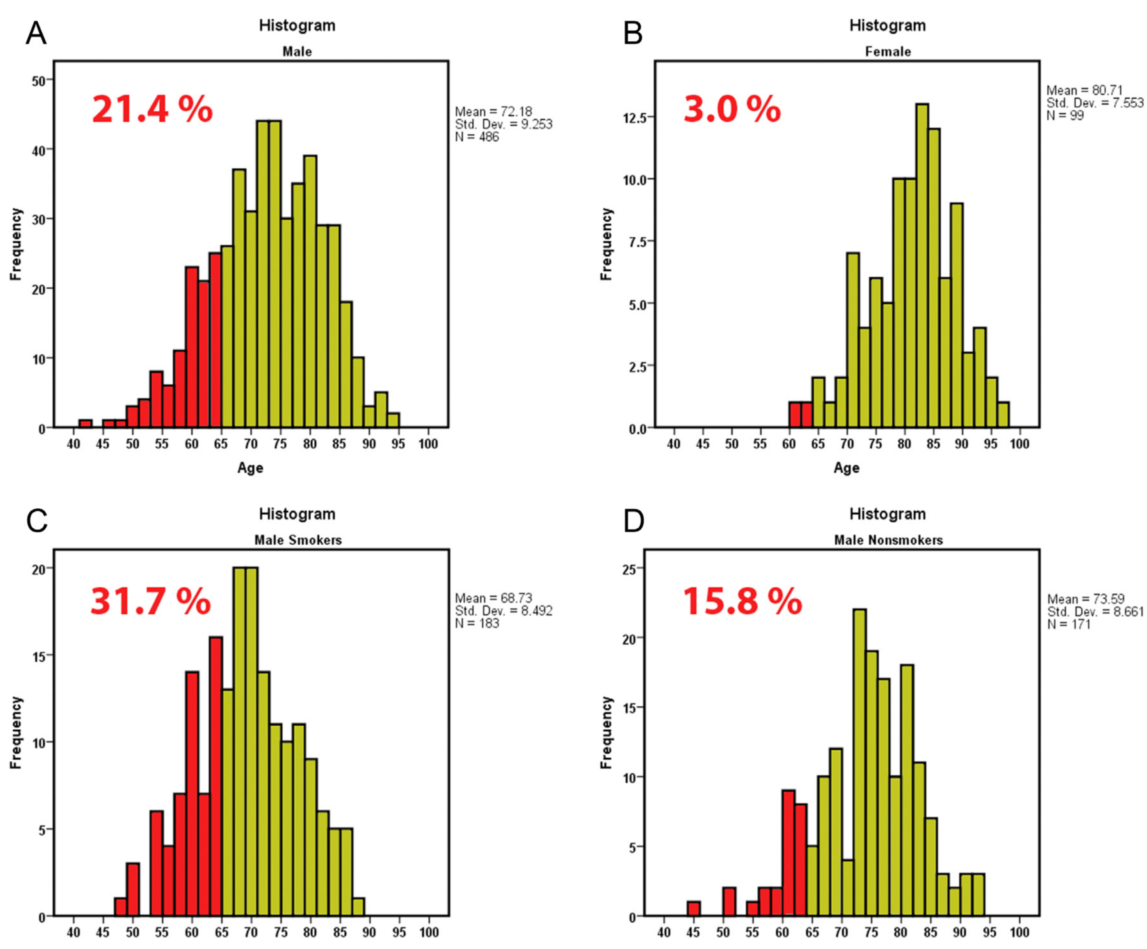

Figure 1. Histogram image showing the number of ruptured abdominal aortic aneurysm patients in relation to patient age. Red columns correspond to patients under 65 years of age with corresponding percentages: (A) men; (B) women; (C) male smokers; (D) male non-smokers.

Table 3. Factors associated with patient age less than 65 years on multivariate analysis. * indicates p<.05.

	OR	95% CI		p
Male sex	15.448	2.073	115.127	0.008*
Smoking	2.113	1.210	3.687	0.008*
Hypertension	0.707	0.409	1.220	0.213
Coronary disease	0.371	0.194	0.709	0.003*
Pulmonary disease	0.704	0.345	1.436	0.704
Previous stroke/TIA	0.553	0.218	1.406	0.553

RAAA and aneurysm size

CT scans for 220 patients from HUH and 108 patients from TaUH were analyzed (Table 4). The CT images for one patient were not available, so measurement data were available for 327 patients in total. The mean AP diameter of the AAA at the time of rupture was 75.6 mm (SD 15.8, range 32—155 mm). The mean size was significantly lower in women than in men (70.5 vs. 76.8, $p = .005$). Smoking status, history of coronary artery disease, diagnosed hypertension, and dyslipidemia did not have a significant effect on the rupture size (Table 5). In the logistic regression analysis (adjusted for coronary disease) female sex had an OR of 3.2 (95% CI 1.4—7.5) for rupture under 55 mm compared with men.

In total 94.4% of men had a rupture at or over 55 mm and 88.5% of women at or over 52 mm, which are the operative limits in the European guidelines. Thus 93.3% of all RAAA patients were over the operative threshold of these guidelines.

DISCUSSION

After analyzing all RAAA patients admitted to HUH and TaUH during a 12 year period, it was found that 18% of the patients had an aneurysm rupture before the age of 65, the age at which aneurysm screening commonly takes place.[4—6] The existing screening programs only invite men to participate. Thus considering only at male patients, 21% of ruptures would have happened even if there was a screening program in Finland, which currently there is not, and every 65 year old male would have attended. There seems to be a significant correlation between the age at the time of rupture and several risk factors, most notably smoking. Since aneurysm growth is faster in smokers, it seems logical that their aneurysms rupture at a younger age.[9] In this study population, 32% of male smokers would have had a rupture before screening.

If a screening age of 60 was used, the percentage of ruptures before this age would drop to 13.7%, and using 55 years, to 5.5% for male smokers. For non-smokers the respective values would be 4.7% and 2.3% and for all men 8.6% and 3.7%. Lowering the screening age for men to 60 and maybe even younger for smokers should be considered. This could, however, mean that a second screen at a later age would be required, especially for those patients with an aortic diameter of 25—30 mm who would not otherwise be followed. This could, however, affect the cost-effectiveness of screening. None of the current screening programs routinely include women as the cost-effectiveness of screening women has not been established.[13] The data here also indicate that screening women at 65 is unlikely to be cost-effective as ruptures are extremely rare in women under 65. This is in line with previous studies showing that AAAs in general are rare in women under 65. In a population wide study in Tromsø, Norway, the AAA prevalence in the female population under 65 was 1.2% compared with 8.8% in men, and only 0.1% of women under 65 had an AAA over 39 mm.[14] In a New Zealand population, the prevalence of AAA was 0.4% in women aged 55—64.9 compared with

Table 4. Demographics of patients with RAAA and available CT scan in relation to gender. * indicates $p < .05$.

	Men	Women	Total	Missing	p
n	267 (81.4%)	61 (18.6%)	328		
Mean age (SD)	72.2 (9.3)	80.2 (7.3)	73.7 (9.5)		<.001 *
Mean AP diameter (SD)	76.8 (15.7)	70.5 (15.5)	75.6 (15.8)		.005 *
Smoking	100	16	116	96	.287
	37.5%	26.2%	35.4%	29.3%	
Coronary disease	131	36	167	7	.170
	49.1%	59.0%	50.9%	2.1%	
Diabetes	35	10	45	1	.508
	13.1%	16.4%	13.7%	0.3%	
Hypertension	141	32	173	18	.955
	52.8%	52.5%	52.7%	5.5%	
Pulmonary disease	71	18	89	12	.527
	26.6%	29.5%	27.1%	3.7%	
Previous stroke/TIA	52	8	60	8	.258
	19.5%	13.1%	18.3%	2.4%	
Dyslipidemia	86	23	109	43	.465
	32.2%	37.7%	33.2%	13.1%	

Table 5. Factors associated with RAAA AP diameter (mm). * indicates $p < .05$.

		n	AP diameter	(SD)	p-value
Sex	Male	266	76.8	(15.7)	
	Female	61	70.5	(15.5)	.005 *
Hospital	Helsinki	219	75.2	(16.5)	
	Tampere	108	76.4	(14.1)	.504
Age	<65	62	75.8	(14.2)	
	≥65	265	75.5	(16.0)	.899
Smoking	Yes	116	74.2	(14.6)	
	No	116	76.6	(17.1)	.250
Diabetes	Yes	45	78.6	(16.3)	
	No	281	75.1	(15.7)	.174
Dyslipidemia	Yes	109	76.6	(16.5)	
	No	176	76.2	(15.1)	.865
Hypertension	Yes	172	76.6	(16.6)	
	No	137	74.3	(14.5)	.206
Coronary disease	Yes	167	74.5	(15.8)	
	No	153	77.1	(15.5)	.137
Pulmonary disease	Yes	89	74.2	(17.2)	
	No	226	76.5	(15.3)	.249
Previous stroke/TIA	Yes	60	75.7	(14.5)	
	No	259	75.7	(16.1)	.987

1.3% in men.[15] In Chichester, UK, 3,052 women and 2,342 men were scanned with ultrasound for AAA. Of the 218 women under 65, none had an AAA compared with 10 of 169 men screened (5.9%).[16] As it seems that aneurysms develop later in women, screening may be cost-effective at a later age or for specific subgroups, and this should be further investigated in future studies and evaluated if screening for AAA is considered.

The finding that a history of cardiovascular disease was more common in RAAA patients over 65 years might be due to better management of risk factors in these patients, better control of hypertension, and use of statins. A similar effect was seen in the large meta-analysis by Thompson et al.,[9] where a history of cardiovascular disease was associated with slower aneurysm growth. However, after adjustment for all demographics, medical and drug history, the effect disappeared. The same would probably be true for the patients here. Another possibility is that patients with cardiovascular disease are under tighter surveillance and their aneurysms are more likely to be discovered before rupture and repaired electively.

Diabetes is known to be protective against aneurysm disease.[17] In the analysis here, it did not seem to have a clear effect on rupture size. However, there were no diabetics with rupture at under 55 mm: the number of diabetics was small, but still not less than the prevalence of diabetes in the general population in Finland.

It was found that the maximum AP diameter of the aneurysm was under the operative threshold set in the European guidelines for 5.6% of men and 11.5% of women. If a common operative threshold of 55 mm were used for both sexes, 18.0% of women would have a rupture before that. Furthermore, women were less likely to be treated operatively. This is probably partly explained by the fact that women were on average 8 years older at the time of rupture. This would indicate that even with a lower threshold for women, a smaller percentage of female patients with AAA are caught before rupture. The data here seem to support the higher risk of rupture for women and correspond to earlier findings that women have AAA ruptures at a smaller size.[9]

There are several limitations to this study. Because of the retrospective nature of the study and the quality of registry data there were quite a lot of missing data, which could have had an effect on the final results. For example, approximately half of the patients did not undergo CT imaging. It could be that those patients with larger aneurysms were more unstable and less likely to undergo CT imaging. This would mean that this study would underestimate the average RAAA diameter. However, it seems unlikely that RAAA diameter itself has a direct correlation with a patient's hemodynamic stability in the event of a rupture. It would also have been more informative to quantify smoking status more thoroughly, such as using pack years, but unfortunately this was not possible using the data available. The fact that this was a retrospective study also means that it was not possible to draw direct conclusions about the causality of the tested risk factors and RAAA. For example, the fact that there were more non-smokers among the older RAAA patients might be because in that age group there were fewer smokers in the general population or that they had had more time to stop smoking or that most of the smokers had died of other causes before RAAA. However, the suggestion that AAAs rupture earlier in active smokers seems to fit well with previously available data. Also, designing a prospective study to address this issue would be very difficult. Another clear limitation is that this analysis included only RAAA patients that were admitted to a tertiary vascular center. It is estimated that a third to a half of all RAAA patients die before reaching the hospital. It is likely that the patients that die at home are generally older and have more comorbidities. This probably causes a bias towards younger and healthier patients in these data if compared with all patients sustaining RAAA. Furthermore, lack of a control group of AAA patients without rupture did not permit analysis of the independent risk factors increasing the risk of rupture.

Whether the result would be applicable to other countries beside Finland is another important question. In an analysis of Vascunet data, the average age of rupture seemed to be quite similar in all participating countries, which could indicate that these result are more widely applicable.[18] However, the number of smokers in each country is likely to have a significant effect on rupture age and should be considered when planning screening programs. Obviously, careful cost-effectiveness analysis is required before starting new screening programs or modifying existing ones. Earlier screening would probably mandate a second screening later on, which would be likely to effect the cost-effectiveness.

Even though aneurysm mortality seems to be declining[19–21] and rupture rates of aneurysms above the operative threshold in patients unfit for elective repair seem to be lower than previously expected,[22] RAAA related mortality remains high and the number of ruptures in patients under screening age or operative threshold diameter is not insignificant, as shown in this study. This suggests that critical evaluation of current screening protocols and treatment guidelines is warranted in order to reduce RAAA related mortality.

In conclusion, on the basis of these findings the validity of using 65 as the age of AAA screening is questioned. The data from this study show that over a fifth of men that experienced RAAA would not have made it to the screening age before AAA rupture, the proportion being even larger in active smokers. The data from this study also support the previous findings that aneurysm size at the time of rupture is significantly smaller in women and that female RAAA patients are significantly older than men.

CONFLICT OF INTEREST

None.

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