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Optimising Abdominal Aortic Aneurysm Screening of 65 Year Old Men by Exploring Risk Factor Based Targeted Screening Strategies in the Light of Declining Prevalence of the Disease

Patrik Söderberg [a,b,c,*], **Anders Wanhainen** [a,d], **Sverker Svensjö** [a,b,c]

[a] Department of Surgical Sciences, Vascular Surgery, Uppsala University, Uppsala, Sweden
[b] Department of Surgery, Falun County Hospital, Falun, Sweden
[c] Centre for Clinical Research (CKF), Dalarna, Sweden
[d] Department of Surgical and Peri-operative Sciences, Surgery, Umeå University, Umeå, Sweden

WHAT THIS PAPER ADDS

The ongoing decline in abdominal aortic aneurysm (AAA) prevalence calls into question the justification and effectiveness of programmes with general screening of all 65 year old men. Analysis of comprehensive risk factor data from the Swedish national general AAA screening programme indicates that selectively targeting cohorts based on hypertension and cardiac disease alone would be futile. This study demonstrated that targeted screening based on smoking history is the only plausible selective strategy, and could hypothetically detect most AAAs in the population while screening significantly fewer individuals.

Objective: A decline in abdominal aortic aneurysm (AAA) prevalence calls into question the credibility of general population screening of 65 year old men. Selectively targeting high risk individuals among this group could be more effective in preventing death from AAA rupture. This cross sectional study analysed risk factor data in a cohort of 65 year old men screened in the Swedish general population based AAA screening programme, with the aim of exploring the effectiveness of hypothetical targeted screening strategies.

Methods: All men attending AAA screening in four neighbouring counties in Sweden between 2006 and 2010 completed a health questionnaire on smoking habits and medical history. Abdominal aortic aneurysm was defined as measuring $\geq$ 30 mm. The sensitivity and specificity of different targeted screening strategies, with targeted subpopulations defined by duration of smoking with and without additional risk factors, were explored using receiver operating characteristic (ROC) curves.

Results: A total of 16 232 men were screened, with 236 (1.5%) screen detected AAAs. A strategy combining smoking, presence of coronary artery disease (CAD), or both was associated with the mathematically optimal balance between sensitivity and specificity (optimal threshold) in the ROC analysis. The optimal threshold corresponded to targeting men having smoked for thirty years or more, a history of CAD, or both, where 74.0% of all AAAs could be detected by screening 33.0% of the population, compared with general screening. Targeting men that have smoked for ten years or more indicated that 84.0% of all AAAs could be detected by screening 55.0% of the population. A simplified strategy of targeting ever smokers resulted in detecting 85.0% of all AAAs by screening 61.0% of the population.

Conclusion: Targeted screening of men at high risk of AAA, focusing on smoking history for inclusion, may be a safe and effective alternative to general population screening.

Keywords: Abdominal aortic aneurysm, Duration of smoking, High risk group, Men, Risk factors, Targeted screening
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INTRODUCTION

General population based screening programmes for the early detection of abdominal aortic aneurysm (AAA) by ultrasound in elderly men have been implemented in several countries. Screening programmes with national coverage were justified and designed, based on the results from four large randomised controlled screening trials[1–4] conducted in the 1990s and early 2000s. These studies together

* Corresponding author. Department of Surgery, Falun County Hospital, Lasarettvagen 10, 791 82, Falun, Sweden.
E-mail address: patrik.soderberg@regiondalarna.se (Patrik Söderberg).

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demonstrated that AAA mortality was effectively halved by the early detection of AAAs, with subsequent elective surgery preventing rupture. The prevalence of AAA among elderly men has declined by > 50%[5] in the past two decades.[6] Contemporary population AAA screening studies demonstrate AAA prevalence rates among elderly men of approximately 0.9 — 1.8%[5–8] compared with > 4% in the Multicentre Aneurysm Screening Study.[1] The dramatic reduction in prevalence is mainly attributed to the decrease in smoking prevalence in Western countries over time, as well as improved control of risk factors such as use of statins.[9] Smoking is the strongest known risk factor for developing AAA, believed to account for 75 — 90% of all AAAs.[10,11] Although cost effectiveness of AAA screening can be demonstrated down to prevalence rates of 0.5%,[12] a clearly decreasing prevalence justifies a critical appraisal of the overall clinical plausibility of general population based AAA screening. As a result, various strategies are being investigated to improve the uptake and AAA detection rate. The safety and benefit of alternative screening strategies has not been properly evaluated.

This study used collected extensive screening and risk factor data while implementing general population based AAA screening in Sweden.[10] It aimed to explore risk factor based targeted screening strategies to optimise AAA detection, at the same time striving to minimise use of healthcare resources.

MATERIALS AND METHODS

In Sweden, the introduction of population based screening for infrarenal aortic aneurysm with a one time ultrasound in 65 year old men identified in the National Population Registry was initiated in 2006 in the healthcare region of Uppsala. The neighbouring healthcare regions of Dalarna, Gävleborg, and Sörmland successively launched similar programmes and, in 2009, all four independent healthcare regions had up and running programmes. Ultrasound examinations were carried out at the local hospital by an ultrasound technician or a registered nurse with specific competence in aortic ultrasound. The maximum infrarenal anteroposterior leading edge to leading edge diameter[13] was measured, and an infrarenal aortic aneurysm (AAA) was defined as ≥ 30 mm. All men invited to screening between 2006 and 2010 in Uppsala and between 2006 and 2009 in the remaining three counties were asked to complete a health questionnaire. The questionnaire collected information of smoking habits and medical history. Smoking habits were divided into the following: never, former, or current smoker. Current or former smokers reported years of active smoking and were stratified based on duration of smoking (≥ 1, ≥ 10, ≥ 20, ≥ 30, ≥ 40, and ≥ 50 years, respectively). Ever smoker displayed a duration of smoking of one year or more. Coronary artery disease was defined as a history of angina pectoris or myocardial infarction. Hypertension was interpreted as medically treated high blood pressure. Cerebrovascular disease was a history of stroke or transient ischaemic attack, and diabetes mellitus was treated with either diet or drugs.

Using the mapped associations between AAA prevalence and the relevant risk factors in the entire population subjected to general screening, the sensitivity and specificity for a number of different screening strategies, in which individuals were selected and invited based on having certain defined risk factors, were plotted in a receiver operating characteristic (ROC) curve. The mathematically calculated optimal balance (cut off) between sensitivity and specificity in the ROC is the point in the ROC curve with minimum distance to the uppermost left corner, designated as optimal threshold.

The strategies that were explored were as follows: (1) smoking duration stratified by years, including ever smokers and current smokers; (2) smoking duration stratified by years, coronary artery disease, or both; (3) smoking duration stratified by years and coronary artery disease; (4) smoking duration stratified by years, hypertension, or both; (5) smoking duration stratified by years and hypertension.

The mean AAA diameter of the different subgroups of smoking duration was compared by one way analysis of variance. A p value of < .050 was considered statistically significant.

The study DNR 2007/052 was approved by the ethical committee of the Uppsala-Orebro region.

RESULTS

Within the general screening programme, a total of 20 141 65 year old men were invited, of whom 16 232 (81.0%) accepted and had an ultrasound examination of the abdominal aorta and a valid health questionnaire. Of these, 2 129 (13.0%) were current smokers and 8 719 (54.0%) former smokers. In total, 236 AAAs were found, resulting in an overall AAA prevalence of 1.5%.

The distribution of smoking duration and risk factors in the population with the corresponding prevalence of AAA, sensitivity, and 100 specificity for the various selective targeting screening strategies are presented in Table 1. The ROC curves of different selective screening strategies are presented in Figure 1. The combination of a smoking duration of thirty years or more, presence of coronary artery disease, or both constituted the most effective threshold (i.e., the optimal targeting strategy). With this targeting strategy, 74.0% (sensitivity) of all aneurysms in the total population would be detected by screening 33.0% (100 specificity) of the 65 year old men in the population.

A strategy based only on duration of smoking, disregarding presence of other risk factors, was most effective with a threshold of smoking duration of thirty years or more, and resulted in a sensitivity of 64.0% and specificity of 74.0%. The remaining strategies, comprising various combinations of smoking duration, coronary artery disease, and hypertension all had less favourable performance. Exploring the ROC curve on smoking duration only, irrespective of other risk factors, it was apparent that a gain in sensitivity could be attained at a small cost of decreased specificity up to the point representing ten years of smoking duration or more, with 84.0% of the AAAs detected by screening 55.0% of the population. A shorter duration of smoking progressively resulted in little gain in sensitivity, at a high cost of lost specificity. The strategy of ten years of smoking, having coronary artery

Table 1. Outcomes of general screening and selective screening strategies compared with general screening.

Risk factor or combination of factors used to define the cohort targeted by screening	Prevalence of AAA in screened population* − %	Sensitivity† − %	100 specificity‡ − %
General screening of all 65 year old men	1.5	100	100
Selective screening strategies			
Smoking history, stratified by duration of smoking − y			
≥1 (ever smoker)	2.0	84.8	60.9
≥10	2.2	83.9	54.9
≥20	2.7	75.4	40.2
≥30	3.4	63.6	26.5
≥40	4.3	47.9	15.9
≥50	3.7	11.4	4.4
Current smoker	3.7	31.8	12.8
Smoking history, stratified by duration of smoking, coronary artery disease, or both − y			
≥1 and/or CAD	2.0	87.3	64.1
≥10 and/or CAD	2.1	86.4	58.6
≥20 and/or CAD	2.6	80.5	45.3
≥30 and/or CAD	3.2	73.7	33.3
≥40 and/or CAD	3.7	63.1	24.4
≥50 and/or CAD	3.6	36.9	14.6
Smoking history, stratified by duration of smoking, and coronary artery disease − y			
≥1 and CAD	4.7	25.4	7.6
≥10 and CAD	5.1	25.4	7.0
≥20 and CAD	5.5	22.9	5.7
≥30 and CAD	6.1	17.8	4.1
≥40 and CAD	7.3	12.7	2.3
≥50 and CAD	5.6	2.5	0.6
Smoking history, stratified by duration of smoking, hypertension, or both − y			
≥1 and or hypertension	1.7	89.8	74.5
≥10 and or hypertension	1.8	89.8	70.7
≥20 and or hypertension	2.0	85.6	61.9
≥30 and or hypertension	2.2	80.5	53.8
≥40 and or hypertension	2.7	76.3	47.6
≥50 and or hypertension	2.2	*60.6*	40.4
Smoking history, stratified by duration of smoking and hypertension − y			
≥1 and hypertension	2.9	48.3	23.9
≥10 and hypertension	3.1	47.5	21.6
≥20 and hypertension	3.9	43.2	15.8
≥30 and hypertension	5.0	36.4	10.3
≥40 and hypertension	6.0	25.0	5.8
≥50 and hypertension	4.0	4.2	1.5
Hypertension	2.0	59.2	37.5
Coronary artery disease	3.5	22.0	8.9

AAA = abdominal aortic aneurysm.

* The number of detected AAAs per 100 screened 65 year olds, expressed as %.

† Sensitivity % (for the selective screening strategies this reflects the proportion of AAAs in the population that would be detected in comparison to general screening).

‡ For the selective screening strategies, this reflects the proportion of the screening population that would have to be examined compared with general screening, to reach the corresponding sensitivity.

disease, or both was superior to the smoking only strategy by a few percentiles in sensitivity, but at the cost of loss in specificity, corresponding to 86.0% of the AAAs detected by screening 59.0% of the population.

A selective strategy based on smokers with a history of smoking ten years or more resulted in a AAA prevalence of 2.2 % by screening 55% of the available population compared to a 1.5 % AAA prevalence in a general screening strategy screening 81% of the available population (Figure 2). Selectively targeting ever smokers, duration of smoking more than one year detected 85% of all AAAs by screening 61.0% of the population. Current smokers constitute 15.0% of the entire cohort, and targeting current smokers results in detecting 32.0% of the AAAs by screening 13.0% of the population. Among never smokers (37.0% of the population), the prevalence of AAA was 0.5%, and targeting this group results in detecting 13.0% of the eligible AAAs by screening 37.0% of the population.

The overall mean diameter of the AAAs detected was 38.2 mm (95% CI 36.8 − 39.5). No significant difference in mean AAA diameter was seen between subgroups stratified by smoking years (range 37.7 − 39.2 mm, $p = .98$). Of the 23 AAAs with a diameter ≥ 55 mm in the total screened population, 21 were found among men with a duration of smoking of ten years or more. No additional large AAAs were found in men with a history of smoking between one and ten years. Therefore, two (8.7%) of all the large AAAs in

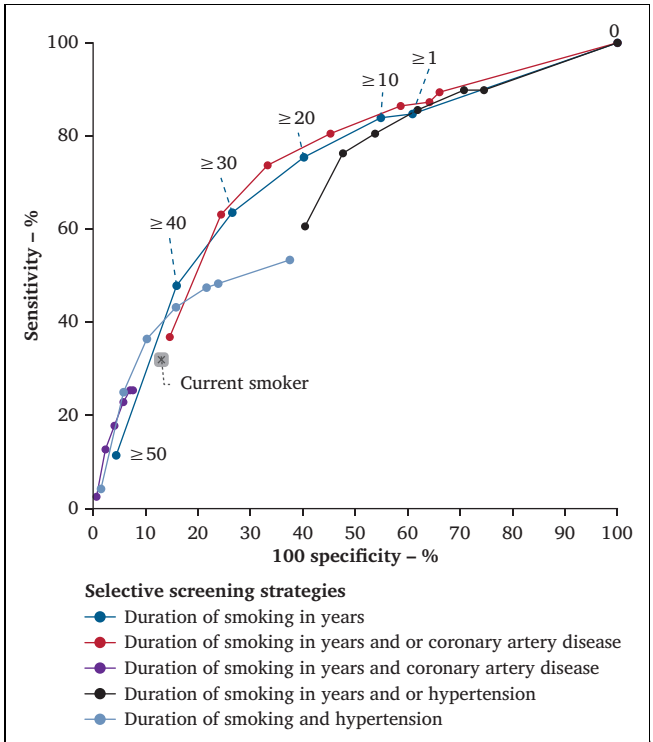

Figure 1. Receiver operating characteristic curve (ROC) showing the performance of different selective screening strategies compared with general screening targeting 65 year old men. All selective screening strategies are presented with the same seven thresholds (≥0, ≥1, ≥10, ≥20, ≥30, ≥40, and ≥50 years) in duration of smoking (points in the graphs) defining the cohort targeted for screening. The blue line represents selective screening based only on duration of smoking and the other coloured graphs represent duration of smoking combined with an additional risk factor to constrain the cohort targeted for screening. The single grey cross represents selectively targeting only current smokers. Sensitivity (%) represents the proportion of all abdominal aortic aneurysms in the population that can be detected and 100 specificity (%) represents the proportion of the total population designated for targeting screening for different screening strategies. The top most right point (100% sensitivity and 100 sensitivity % = 100%), reflects the performance of general screening of all 65 year old men.

the population would be missed by targeted screening based on smoking history.

DISCUSSION

This cross sectional study of 65 year old men demonstrated that targeted screening of 65 year old men for AAA based on smoking history could be effective in maintaining a high AAA detection rate while significantly reducing the proportion of the population to be screened.

On the basis of the changing AAA epidemiology with declining prevalence,[1,10,11] the European Society for Vascular Surgery 2024 guidelines on the management of abdominal aorto-iliac artery aneurysm[14] revised their recommendation on screening, from previsously targeting all 65 year old men to a more non-specific high risk population, depending on local epidemiological conditions. The current AAA prevalence among 65 year old men is just below 1% in Sweden,[6] which is in line with contemporary data from the UK AAA screening programme showing a

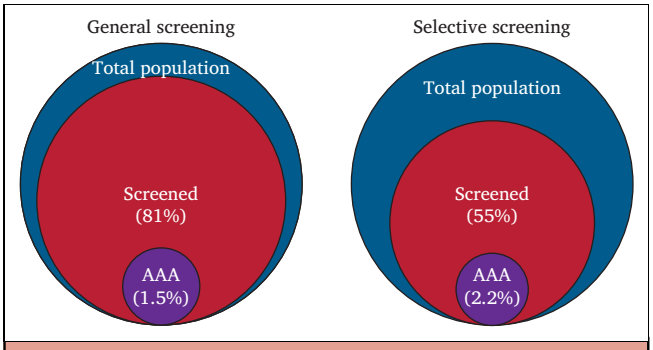

Figure 2. Screening target group and abdominal aortic aneurysms (AAA) in the population for a general screening strategy targeting all 65 year old men compared with a selective screening strategy targeting the part of the population of 65 year old men with a history of ten or more years of smoking. The blue area represents the total population of 65 year old men, the red area the proportion screened (including compliance), and the purple area the number of AAAs detected with the respective strategy. AAA = abdominal aortic aneurysms.

prevalence of 0.9%.[8] This is dramatically lower than in the randomised controlled trials conducted in the 1990s; the question is whether all 65 year old men can be defined as a high risk population, given today's epidemiology.

Targeted screening strategies in this study based on hypertension or coronary artery disease alone, not including smoking, resulted in detecting one half or less of the AAAs. These data support that basing screening on these risk factors alone is not a plausible alternative. Several studies have highlighted the association between AAA and different common cardiovascular risk factors. However, it is believed that only one previous study has analysed risk stratified targeted population screening for AAA.[15] In a randomised controlled trial, Lindholt *et al.*[15] showed that only screening a high risk population for AAA (cardiovascular disease and chronic obstructive pulmonary disease) identifies 46.0% of all AAAs by screening 27.0% of the population. With this approach, fewer were screened but at a cost of most of all AAAs remaining undetected.

Smoking, and specifically the duration of smoking in years, is an essential and useful risk factor to identify a high risk group that harbours most AAAs in the population. The association between smoking and AAA is well known and was first described by Hammond and Horn in 1958.[16] Smoking is considered to be associated with almost nine out of ten AAAs.[10] In a case control study, the duration of smoking was statistically significantly associated with an increased risk of AAA.[17]

The optimal cut off point in the ROC curve displays the most efficient screening strategy. However, with AAA being a potentially lethal disease and given the safety[21,22] and cost efffectiveness of ultrasound screening,[12] it is reasonable to accept a lower specificity to achieve a higher sensitivity in an AAA screening programme.

The United States Preventive Services Task Force recommendation statement recommends a one time screening for AAA in men aged 65 — 75 years who are ever smokers (defined as having smoked > 100 cigarettes in a lifetime).[17] However, the results from the present study suggest that a more restrictive threshold for smoking to a duration of ten

years or more may improve the specificity, whereas the sensitivity is preserved, making this an alternative with high precision and low use of resources.

Only offering smokers screening will inherently result in a different risk factor profile in men identified with AAA and later operated on. Smokers potentially have a higher surgical peri-operative mortality and morbidity, as well as a higher overall mortality rate compared with non-smokers, somewhat reducing the profit with targeted screening. However, 90% of all AAAs have a history of smoking, and only offering smokers screening will result in a similar population to that identified through a general population based screening programme[7] or incidentally.

The smoking pattern in Sweden, and in many other countries, has dramatically changed in the last thirty to forty years. In Sweden, 6% of all men aged 16 − 84 years report daily smoking as of today; in contrast, almost 30% of all men reported daily smoking in the late 1980s.[18] A continued decline in smoking in society should result in targeted screening based on smoking habits becoming an even more effective strategy, with fewer men at risk of AAA.

The rate of incidental detection of AAA in conjunction with medical imaging for other reasons, and its effect on population screening, is an important issue to consider. In the Swedish screening programme, all 65 year old men identified in the National Population Registry are invited to a one time screening for AAA, even if they are under surveillance or have already been operated on for an AAA. In a previous study, this group found a prevalence of screening detected AAA of 1.7% and an additional prevalence of incidentally detected AAAs (already known) of 0.5% in the eligible population, resulting in a total prevalence of 2.2%. Therefore, 23% of the AAAs in the population were already known.[10] It is likely that this relationship may change over time with the increasing use of imaging. Furthermore, it may be influenced by the target population's risk factor profile, and it may also differ between different healthcare settings. This is a key factor that needs to be factored into the calculation of the benefit of different AAA screening strategies. A suitable target group for AAA screening should, in addition to a sufficiently high prevalence, also have a reasonably low degree of incidental detection, regardless of whether it is general population based or targeted high risk screening.

Although men with a smoking history of less than ten years seem to have a low risk of AAA at the age of 65 years, it does not mean that they are excluded from developing AAA of clinical relevance later in life. The increasing life expectancy in the population justifies that screening for AAA of certain risk groups, even at older ages, should be evaluated in the future.

The outcome of the US screening programme targeting ever smokers, aged 65 − 74 years, within the framework of Medi-Care is discouraging, with a low attendance rate.[19] The reason for this low efficiency is certainly multifactorial, but it is probably crucial that the invitation to screening is easily comprehensible, easy to implement, and does not allow for any doubt about the individual's eligibility for screening. Clinical studies of the acceptance rate of any targeted high risk screening strategy are needed before it can be implemented in clinical practice.

Limitations

General population based screening for AAA is an established and well accepted method for detecting AAA, but real life risk stratified and targeted screening for AAA is currently unproven. The results in this study are based on theoretical strategies, and mathematical associations between risk factors and AAAs and further studies need to evaluate the feasibility of targeting a desired high risk group. All men were invited to screening but not all accepted the invitation. Only data from attendees were, therefore, included. The reasons why some invitees did not attend targeting screening for AAA are unclear and require further investigation.

Conclusion

With declining AAA prevalence, the ongoing population based AAA screening programmes targeting the entire 65 year old male population can rightly be called into question. Nevertheless, AAA is a prevalent and lethal disease. Modifying the screening strategy into targeting male smokers with a smoking duration of ten years or more could potentially ensure that the group with highest risk of AAA is offered continued protection from premature sudden death, while maintaining a high cost efficiency and clinical relevance of the screening programmes.

CONFLICT OF INTEREST

None.

FUNDING

None.

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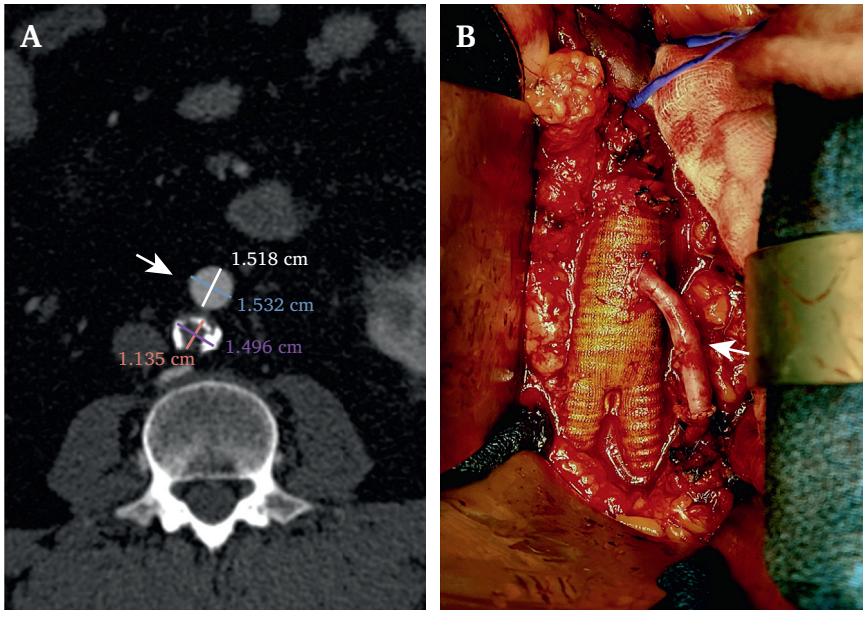
Eur J Vasc Endovasc Surg (2025) 69, 421

COUP D'OEIL

An Inferior Mesenteric Artery Too Good To Go

Marco Campolmi [a,*], **Xavier Berard** [b]
[a] Section of Vascular Surgery, Department of Excellence of Experimental and Clinical Medicine, University of Florence, Florence, Italy
[b] Department of Vascular Surgery, Bordeaux University Hospital, Bordeaux, France



A 66-year-old active smoker, previously treated by left iliac artery stenting, presented with critical lower limb ischaemia. Imaging revealed an occlusion of the infrarenal aorta and a concomitant aneurysm of the inferior mesenteric artery (IMA), the sole blood supplier to the limbs with a diameter greater than the aorta (A, arrow). After infrarenal aortic endarterectomy, an aortobifemoral Dacron bypass was implanted. Due to its poor and non-pulsatile backflow, the IMA aneurysm was replaced by an autologous saphenous vein graft, pre-implanted on the graft (B). The patient was discharged with normal peripheral pulses on single antiplatelet therapy.

* Corresponding author. Section of Vascular Surgery, Department of Excellence of Experimental and Clinical Medicine, University of Florence, Florence, Italy.
E-mail address: marco.campolmi@unifi.it (Marco Campolmi).

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