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Diabetes Mellitus and Aortic Aneurysm Rupture: A Favorable Association?

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Abstract

Introduction: Recent reports suggest that diabetic patients are relatively unlikely to have abdominal aortic aneurysms (AAAs). This retrospective study assesses the relationship between diabetes mellitus (DM) and aortic aneurysm rupture. **Methods:** Patients with a diagnosis of any aortic aneurysm during a 10-year period were identified from our records. Patients with diagnoses of aortic aneurysm (thoracic, thoracoabdominal, and abdominal, treated and untreated) were included. Patients with nonatheromatous aneurysms (transection, dissection, mycotic, or isolated iliac) were excluded. **Results:** In all, 1830 patients with nonruptured aneurysms and 232 ruptured aneurysms were included giving a total of 2062 patients with aortic aneurysms (abdominal, thoracic, and thoracoabdominal). Of these 1830, 225 (12.3%) patients with nonruptured aneurysm were diabetic; however, only 13 (5.6%) of the 232 patients with ruptured aortic aneurysm were diabetic (odds ratio [OR] = 0.42; confidence interval [CI]: 0.23-0.75, $P = .004$). Considering only those with AAAs, 184 (12.4%) of the 1482 nonruptured AAA were diabetic; however, only 12 (6.4%) of the 188 patients with ruptured AAA were diabetic (OR = 0.48 [CI: 0.26-0.88], $P = .02$). In this study group, the odds of dying due to aneurysm rupture in the diabetic group are significantly lower compared to the nondiabetic groups (OR = 0.31 [CI: 0.13-0.69], $P = .004$), despite the finding that diabetic patients had almost the same life expectancy as nondiabetic patients (DM, 73 years [67-80] vs non-DM, 75 years [68-82] $P = .23$). **Conclusions:** Diabetic patients with aortic aneurysms are significantly less likely to present with rupture or to die from aneurysm rupture when compared to nondiabetic patients with aortic aneurysms. We have identified association only, not causality. However, it is plausible that DM, or the treatment of DM, may have a protective effect on aortic aneurysm rupture.

Keywords

aortic aneurysm, ruptured AAA, diabetes

Introduction

Aneurysmal disease can affect any part of the aorta although abdominal aortic aneurysm (AAA) is more common, particularly among older men, occurring in 7% to 8% in men older than 65 years of age[1,2] but this is often asymptomatic until the catastrophic event of rupture occurs. Ruptured AAA deaths account for 2.1% of all deaths in men aged 65 and older.[3] The size of the aneurysm[4] and rapid expansion[5] are the most commonly used morphological features that predict the risk of rupture. No clinically useful biological factors that could influence risk of aneurysm rupture have been identified so far. Similarly, no therapy has been shown to convincingly slow or halt the rate of small aneurysm growth and prevent or delay the need for surgery, and there is no clear consensus on the factors that influence aneurysm growth. Diabetes mellitus (DM) is an acknowledged risk factor for atherosclerosis.[6] However, recent data from AAA screening suggested that diabetic patients are less likely to develop an AAA,[7-10] and very recent studies have suggested that aneurysms grow slower in diabetic patients.[11-16] This study assesses the risk of aortic aneurysm rupture in diabetic patients.

Methods

We included all patients who were admitted to King's College Hospital with a diagnosis of aortic aneurysm during the period January 2001 to April 2012. Patients were identified from King's College Hospital electronic information records using *International Classification of Diseases, Tenth revision* (*ICD10*). Thoracic aortic aneurysm (TAA; ruptured [TAAr; I171] and nonruptured [TAAnr; I172]), thoraco-AAA (TAAA; ruptured

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Table 1. Demography of the Different Aortic Aneurysm (TAA, TAAA, and AAA) Groups in Diabetic and Nondiabetic Patients.

Description	Demography	DM	Non-DM	*P*
Aortic aneurysm all nonruptured (n = 1830)	Median age (range)	74 (52-89)	75 (43-96)	.32
	≥65 years (%)	23/225 (10.2)	252/1605 (15.7)	.02
	Male:female	185:40	1363:242	.34
Aortic aneurysm who had elective treatment (n = 588)	Median age (range)	75 (63-86)	75 (52-93)	.34
	≥ 65 years (%)	5/76 (6.6)	82/512 (16.0)	.036
	Male:female	69:7	449:63	.57
Ruptured aortic aneurysm (n = 232)	Median age (range)	74 (68-86)	74 (44-96)	.36
	≥ 65 years (%)	0/13 (0)	33/219 (15.0)	N/A
	Male:female	10:3	185:34	.44

Abbreviations: AAA, abdominal aortic aneurysm; DM, diabetes mellitus; TAA, thoracic aortic aneurysm; TAAA, thoracoabdominal aortic aneurysm; N/A, not applicable.

[TAAAr; I175] and nonruptured [TAAAnr; I176]), and AAA (ruptured [AAAr; I173] and nonruptured [AAAnr; I174] were all collected at any level of diagnosis. The *ICD10* codes I718 (nonspecified aortic aneurysm-ruptured) and I179 (nonspecified aortic aneurysm-nonruptured) were also identified from the database, and these 2 codes were then individually classified into one of the previous diagnosis codes of I171 to I176. The search was performed with a filter for DM (including E100-E149 codes) to ascertain DM status (type 1, type 2, diet controlled, or nondiabetic) and also to obtain mortality outcomes.

Data on aneurysm size were obtained from preoperative radiological reports (computed tomography) for patients with elective repair. For patients with a ruptured aneurysm, this information was not available as preoperative scanning was inconsistent (many patients went directly to theatre where aneurysm sizing is notoriously unreliable) and where performed, size calculations can be inaccurate. Information on other medical risk factors was sought from the patients' clinical records on history of hypertension, hyperlipidemia, and smoking history.

Patients who had surgical or endovascular procedures during the study period were identified using procedure codes from the Operation and Procedure Codes-Version 4.4 (OPCS 4.4) database. The procedure codes of L181 to L199 (emergency aortic repair for aneurysm), L201 to L219 (bypass for aortic aneurysm), L254 (operation on aortic aneurysm not included elsewhere), and L271 to L289 (endovascular aneurysm repairs) were included to identify both elective and emergency aortic aneurysm procedures.

Of the identified 2294 patients, patients with nonatheromatous aneurysm pathology (dissection [179 patients], mycotic [4 patients], transection [3 patients]) and pure iliac aneurysmal disease (46 patients) were excluded. This was achieved by identifying anyone with coexisting *ICD10* diagnosis code of I170 (aortic dissection). The *ICD10* series begins with either A or B for infectious disease or S for traumatic cases. All the cases that have *ICD10* diagnosis codes A, B, or S series diagnosis were then individually checked to establish whether these patients should be excluded.

The proportion of patients who had a ruptured aortic aneurysm at ≤65 years ("young ruptures") was compared with the proportion of young patients with the diagnosis of all aortic aneurysms without rupture and those who had elective repair for above threshold size aortic aneurysm. A similar comparison was made for AAA.

Statistical Method

The prevalence of aortic aneurysm rupture, rate of repair, and mortality were compared between the populations with and without DM (considering type 1, type 2, and diet-controlled DM as one group). Group comparisons were made using nonparametric statistical testing. Odds ratios (ORs) were calculated, and chi-square test or Fisher exact test was used to assess the statistical significance of the OR. The 95% confidence intervals (CIs) are given in brackets with the OR. The age was given as years (median with interquartile range [IQR]), and the age difference between the groups was tested using the Mann-Whitney *U* test.

Results

In all, 1830 patients with nonruptured aneurysms and 232 patients with ruptured aneurysms were identified using the search criteria giving a total of 2062 patients (median age 75 [IQR: 66-79], 464 females, and 1598 males). There were 238 diabetic patients and 1824 nondiabetic patients. The distribution of aneurysm type was TAA (32 ruptured and 214 nonruptured), TAAA (12 ruptured an 134 nonruptured), and AAA (188 ruptured and 1482 nonruptured). Overall, there was no significant difference between the patients in the diabetic and nondiabetic groups in terms of hypertension, hyperlipidemia, or current smoking history for ruptured aortic aneurysms (P =.69, P =.64, and P = .77 respectively) or within the nonruptured category, or those having elective AAA repair (see Table 1).

Comparison of Ruptured Cases: Diabetic Versus Nondiabetic

Only 1 (3.1%) of the 32 patients with ruptured TAAs was diabetic whereas 26 (12.1%) of the 214 patients with nonruptured TAAs were diabetic. None (0.0%) of the 12 patients with ruptured TAAAs was diabetic, whereas 15 (11.2%) of 134 patients with nonruptured TAAA were diabetic. These numbers are too small to calculate any meaningful CI or OR. However, when comparing AAAs, 12 (6.4%) of 188 patients with ruptured

Table 2. Odds of Diabetes Mellitus in Different Aneurysm Groups.*

		Total (n)	DM (%)	Non-DM (%)	OR (CI)	P
TAA	Ruptured	32	*1 (3)	31 (97)	*	*
	Nonruptured	214	26 (12)	188 (88)		
TAAA	Ruptured	12	*0 (0)	12 (100)	*	*
	Nonruptured	134	15 (11)	119 (89)		
AAA	Ruptured	188	12 (6.4)	176 (93.6)	0.48 (0.26-0.88)	.02
	Nonruptured	1482	184 (12.4)	1298 (87.6)		
All aortic aneurysm	Ruptured	232	13 (5.6)	219 (94.4)	0.42 (0.23-0.75)	.004
	Nonruptured	1830	225 (12.3)	1605 (87.7)		

Abbreviations: AAA, abdominal aortic aneurysm; CI, confidence interval; DM, diabetes mellitus; OR, odds ratio; TAA, thoracic aorticaneurysm; TAAA, thoracoabdominal aortic aneurysm.
* Numbers are too small to calculate a meaningful CI for OR.

Table 3. Odds of Diabetes in Patients With Ruptured AAA Compared to that of Elective Repair.*

	Total (n)	DM (%)	Non-DM (%)	Odds Ratio (CI)	P
TAA (ruptured)	44	*1	31	*	*
Elective repair for TAA	72	8	53		
TAAA (ruptured)	12	* 0	12	*	*
Elective TAAA repair	11	* 0	11		
AAA (ruptured)	188	12 (6.4)	176 (93.6)	0.45 (0.23-0.85)	.02
Elective AAA repair for >5.5 cm (AAA)	516	68 (13.0)	448 (86.8)		
Total aortic aneurysm (ruptured)	232	13	219	0.39 (0.22-0.73)	.004
Total elective aortic aneurysm repair	588	76	512		

Abbreviations: AAA, abdominal aortic aneurysm; CI, confidence interval; DM, diabetes mellitus; TAA, thoracic aorticaneurysm; TAAA, thoracoabdominal aortic aneurysm.
*Numbers are too small to calculate a meaningful CI for OR.

aneurysms were diabetic whereas 184 (12.4%) of the 1482 patients with nonruptured AAAs were diabetic (OR = 0.48 [CI: 0.26-0.88], $P = .02$). Considering all aortic aneurysms together (TAA + TAAA + AAA), 13 (5.6%) of 232 patients with ruptured aortic aneurysms were diabetic, whereas 225 (12.3%) of the 1830 patients with nonruptured aortic aneurysm were diabetic (OR = 0.42 [CI: 0.23-0.75], $P = .004$). These figures are summarized in Table 2.

Comparison of Elective Versus Ruptured AAA Repairs: Diabetic Versus Nondiabetic

Elective repair of above-threshold (5.5 cm) AAAs was performed in 516 patients, of which 68 (13.0%) were diabetic. When this was compared with the 12 diabetic patients in the ruptured group of 188 (6%; including operated and not operated), the odds of DM is significantly lower in the ruptured group (OR = 0.45 [0.23-0.85)], $P = .02$). There was no significant difference between the maximal aortic diameter size in the diabetic group, 5.7 cm, and in the nondiabetic group, 5.8 cm ($P = .21$). There is also no significant difference in the sizes in patients with TAA and TAAA. These figures are given in Table 3.

Aortic Aneurysm Rupture in Young Patients

The proportion of young patients (age $\leq$ 65 years) with ruptured aortic aneurysms was compared with that of all aortic aneurysms and those who had elective repair for above threshold aortic aneurysm. The details of the young patients in each category are given in Table 1. A similar comparison with details relating to AAA is given in Table 4. Male–female ratio was similar in both diabetic and nondiabetic groups. The median age at which aortic aneurysms ruptured in both diabetic patients and nondiabetic patients was 74 years. However, in nondiabetic groups 33 (15%) of the 219 ruptures were in young patients aged $\leq$65 years (young rupture),; however, not even asingle patient with diabetes below the age of 65 had a ruptured aortic aneurysm.

Majority Rupture Age

The age above which 95% of the ruptures occurred (majority rupture age) in diabetic patients and nondiabetic patients was also compared. As far as all aortic aneurysm ruptures are considered, in majority rupture age for nondiabetic patients was 59 years compared to 68 years for diabetic patients. Similarly for patients with AAA, this was 58 and 68 years for nondiabetic and diabetic patients, respectively.

Comparison of Mortality Figures: Diabetic Versus Nondiabetic

In total, 525 patients (79 diabetic and 446 nondiabetic) died during the study period with a diagnosis of aortic aneurysm. Of the 79 patients who died with a dual diagnosis of aortic aneurysm and DM however only 7 (8.8%) of these deaths were attributable to a ruptured aneurysm. In comparison, of the 446 patients who

Table 4. Demography of the Different AAA Groups in Diabetic and Nondiabetic Patients.

Description	Demography	DM	Non-DM	*P*
All AAA nonruptured (n = 1482)	Median age (range)	74 (53-89)	75 (44-96)	.35
	≥65 years (%)	18/184 (9.7)	207/1298 (15.9)	.038
	Male:female	152:32	1102:196	.48
AAA who had elective treatment (n = 516)	Median age (range)	75 (64-86)	75 (52-93)	.37
	≥65 years (%)	4/68 (5.8)	70/448 (15.6)	.039
	Male:female	62:6	393:55	.53
Ruptured AAA (n = 188)	Median age (range)	74 (68-86)	74 (44-96)	.34
	≥65 years (%)	0/12 (0)	26/176 (14.7)	N/A
	Male:female	10:2	149:27	.90

Abbreviations: AAA, abdominal aortic aneurysm; DM, diabetes mellitus; N/A, not applicable.

Table 5. Ten-Year Mortality Data of Patients With AAA and Total Aortic Aneurysm With Regard to Diabetic Status.

	Total	Died Due to Rupture	Died With Intact Aneurysm	Odds Ratio (CI)	*P*
Patients with diabetes who died with AAA	75	6 (8%)	69 (92%)	0.37 (0.15-0.88)	.03
Nondiabetic patients died with AAA	397	76 (19%)	321 (81%)		
Patients with diabetes who died with aortic aneurysm (TAA + TAAA + AAA)	79	7 (8.9%)	72 (91.1%)	0.31 (0.13-0.69)	.004
Nondiabetic patients died with aortic aneurysm (TAA + TAAA + AAA)	446	107 (24.0%)	339 (76.0%)		

Abbreviations: AAA, abdominal aortic aneurysm; CI, confidence interval; TAA, thoracic aorticaneurysm; TAAA, thoracoabdominal aortic aneurysm.

died with the diagnosis of aortic aneurysm but without a history of DM, 107 (23.9%) patients died due to a ruptured aortic aneurysm. This information with a breakdown of aneurysm type is given in Table 5. In this study group, the odds of dying due to aneurysm rupture in the diabetic group are significantly lower compared to nondiabetic group (OR = 0.31 [0.13-0.69], $P = .004$), despite the finding that diabetic patients had almost the same life expectancy as patients in the nondiabetic group (DM, 73 years [67-80] vs non-DM, 75 years [68-82] $P = .23$).

Discussion

This is the first study to specifically address this issue and suggests that diabetic patients with aortic aneurysms are significantly less likely to present with rupture or to die from aneurysm rupture when compared with nondiabetic patients with aortic aneurysms. Although the median age of aortic aneurysm is similar in both diabetic and nondiabetic patients, about 15% of the ruptures occurred in young patients (≤65 years) in the nondiabetic group and none in the diabetic group. Previous studies of ultrasound screening and of prospective clinical diagnosis of AAA have shown that diabetic patients are less likely to have aortic aneurysmal disease.[7-10] It has also been shown that when AAAs exceed 4.0 cm in diameter compared with 3.0 to 3.9 cm, there is a negative association with DM in the larger AAA group (OR 0.78, [95% CI: 0.65-0.94]) whereas there are significant positive associations with age, smoking, and male gender.[9,10] Recent studies have reported that AAA enlargement progresses more slowly in diabetic patients.[11-16] Diabetes mellitus or its medications or both seem to have a negative effect on AAA growth. It was argued that the hyperglycemia rather than the medications is responsible for slower aneurysm growth rate.[10] The Health in Men study reported a negative association between fasting glucose and aortic diameter in 2859 nondiabetic patients.[17] Stanford investigators reported that hyperglycemia in mice was associated with slower AAA enlargement and that this effect was decreased by insulin therapy.[18] These findings suggest that it is hyperglycemia, rather than its treatment, which retards aneurysm growth.

We have shown that the aneurysmal size was no different between the diabetic and nondiabetic groups, being 5.7 cm and 5.8 cm, respectively, for patients with AAA elective repair, that is, there is no evidence for a difference in patient selection for elective surgery based on aneurysm size simply because someone is diabetic. Despite this, the DM group ruptured less often. Intuitively, it would seem sensible to question whether this is simply, because patients in the DM group died of other causes before they had a chance to rupture. However, this cannot be the case in this study as the life expectancy in the DM group was almost identical to the non-DM group. Furthermore, on the limited additional data we have on medical risk factors (hypertension, hyperlipidemia, and smoking history), there was no significant difference between the diabetic and the nondiabetic groups. Therefore, this study suggests that even if aneurysms grow large enough to warrant elective aneurysm repair, diabetic patients are less likely to present with aneurysm rupture or die from it.

This interesting observation may question the current understanding about atherosclerosis, particularly in diabetic patients. It is possible that atherosclerosis in diabetic patients may be different from that of nondiabetic patients.

This study only showed that patients with DM are less likely to present with rupture, and this protective effect could be either direct or indirect. There could be several possibilities for this protective effect. Diabetes mellitus may change the biology of the aortic wall. A recent study suggested that hyperglycemia associated with diabetes has been shown to stabilize the collagen network by inducing cross-linking of collagen networks in the aortic wall media, and this cross-linking resists proteolysis and inhibits secretion of the matrix metalloproteinases (MMPs) thought to mediate aortic aneurysm formation.[14] Further, DM was also found to suppress plasmin that activates the matrix MMPs.[19] These effects could decrease aortic wall degradation directly and may also explain the thicker abdominal aortic wall observed in DM.[20] A limitation of this study is the lack of availability of information on the severity of hyperglycemia for these diabetic patients. Hemoglobin A_{1c} measurements would have been useful to attempt to correlate the degree of hyperglycemia with rupture risk. However, given the very low number of patients with DM developing a rupture anyway, such analysis may be fruitless.

It is also possible that medications other than those used to control hyperglycemia may have a role for this low-rupture rate in diabetic patients. A better secondary prevention medication instituted in diabetic patients may play a role in protecting diabetic patients from aortic aneurysm rupture. The lower blood pressure (BP) target for diabetic patients may be another possible explanation for this protective effect. However, antihypertensives failed to show any beneficial influence on aneurysm growth or rupture in nonselected patients. In 2006, a Canadian population-based case–control study[21] suggested that angiotensin-converting enzyme (ACE) inhibitors prevent the expansion and rupture of aortic aneurysms. This study also suggested that other antihypertensives such as β-blockers, calcium-channel blockers, α-blockers, angiotensin-receptor blockers, or thiazide diuretics failed to protect from aortic aneurysm rupture. However, another recent study suggested that ACE inhibitors in fact increase the risk of aortic aneurysm growth.[22] It is possible that DM may have been a confounding factor in the Canadian study resulting in a reduced rupture rate in patients taking ACE inhibitors.

Smoking is known to increase the aneurysm growth rate[11] and possibly this would be a confounding factor in this study if most diabetic patients were nonsmokers. Although unlikely, it is possible that diabetic patients were more health conscious, maintained meticulous attention to secondary prevention, and did not smoke; however, we believe this is improbable.

Further studies are required to identify the actual protective factor or multiple factors. If the secondary prevention and a tighter BP control would prove to be the most important, then future studies should focus on maximizing secondary prevention and tighter BP targets in nondiabetic aneurysmal patients. On the other hand, if the biological changes on the aortic wall due to DM are proved to be the reason, then future studies might focus on identifying the exact mechanism with a view to developing targeted pharmacological therapy.

In spite of increasing life expectancy due to improved overall health care, the incidence of aortic aneurysm rupture is declining over recent decades, and Anjum et al report this is mostly due to a decrease in smoking habits in the population and an increase in elective repair.[23] However, it is possible that increasing diabetic incidence could also be partially responsible for these declining aortic aneurysm rupture rates. If diabetic patients are indeed protected from aneurysm rupture it would be tempting to question whether diabetic patients with an aortic aneurysm of 5.5 cm might be managed more conservatively with a higher threshold aneurysm size for elective repair. Urgent studies are required to test these hypotheses.

Conclusion

In conclusion, this study showed that diabetic patients are less likely to present with aortic aneurysm rupture and less likely to die from aneurysm rupture suggesting that DM may have a protective effect against aortic aneurysm rupture. This protection is perhaps due to biological changes in the aortic wall from DM or due to an indirect benefit from secondary prevention or tighter BP control. Future studies should focus on identifying the exact mechanism by which patients with DM are protected against aortic aneurysm rupture.

Declaration of Conflicting Interests

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References

1. Lucarotti M, Shaw E, Poskitt K, Heather B. The gloucestershire aneurysm screening programme: the first 2 years' experience. *Eur J Vasc Surg*. 1993;7(4):397-401.
2. Norman PE, Jamrozik K, Lawrence-Brown MM, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. *BMJ*. 2004; 329(7477): 1259-1262.
3. Essential elements in developing an abdominal aortic aneurysm (AAA) screening and surveillance program. Aneurysm screening committee report. Vascular Society of Great Briton and Ireland; May 2010 (Version 2.2).
4. Creager MA, Loscalzo J. Diseases of the aorta. In: Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York, NY: McGraw-Hill Companies Inc; 2008:1563-1567.
5. The UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet*. 1998;352(9141):1649-1655.
6. Law MR, Morris J, Wald NJ. Screening for abdominal aortic aneurysms. *J Med Screen*. 1994;1(2):110-115.

7. Lederle FA, Johnson GR, Wilson SE, et al. Prevalence and associations of abdominal aortic aneurysm detected through screening. Aneurysm detection and management (ADAM) veterans affairs cooperative study group. *Ann Intern Med.* 1997;126(6):441-449.
8. Törnwall ME, Virtamo J, Haukka JK, Albanes D, Huttunen JK. Life-style factors and risk for abdominal aortic aneurysm in a cohort of Finnish male smokers. *Epidemiology*. 2001;12(1): 94-100.
9. Lederle FA. The strange relationship between diabetes and abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2012; 43(3):254-256.
10. Lederle FA, Johnson GR, Wilson SE, et al. The aneurysm detection and management study screening program: validation cohort and final results. *Arch Intern Med*. 2000;160(10):1425-1430.
11. Sweeting MJ, Thompson SG, Brown LC, Powell JT, RESCAN collaborators. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *Br J Surg*. 2012;99(5):655-665.
12. Brady AR, Thompson SG, Fowkes FG, Greenhalgh RM, Powell JT, UK Small Aneurysm Trial Participants. Abdominal aortic aneurysm expansion: risk factors and time intervals for surveillance. *Circulation*. 2004;110(1):16-21.
13. Vega de Céniga M, Gómez R, Estallo L, Rodríguez L, Baquer M, Barba A. Growth rate and associated factors in small abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg*. 2006;31(3): 231-236.
14. Golledge J, Karan M, Moran CS, et al. Reduced expansion rate of abdominal aortic aneurysms in patients with diabetes may be related to aberrant monocyte–matrix interactions. *Eur Heart J*. 2008;29(5):665-672.
15. Ferguson CD, Clancy P, Bourke B, et al. Association of statin prescription with small abdominal aortic aneurysm progression. *Am Heart J*. 2010;159(2):307-313.
16. Thompson A, Cooper JA, Fabricius M, Humphries SE, Ashton HA, Hafez H. An analysis of drug modulation of abdominal aortic aneurysm growth through 25 years of surveillance. *J Vasc Surg*. 2010;52(1):55-61.
17. Le MT, Jamrozik K, Davis TM, Norman PE. Negative association between infrarenal aortic diameter and glycaemia: the health in men study. *Eur J Vasc Endovasc Surg*. 2007;33(5):599-604.
18. Miyama N, Dua MM, Yeung JJ, et al. Hyperglycemia limits experimental aortic aneurysm progression. *J Vasc Surg*. 2010; 52(4):975-983.
19. Dua MM, Miyama N, Azuma J, et al. Hyperglycemia modulates plasminogen activator inhibitor-1 expression and aortic diameter in experimental aortic aneurysm disease. *Surgery*. 2010;148(2): 429-35.
20. Astrand H, Ryde?n-Ahlgren A, Sundkvist G, Sandgren T, Laünne T. Reduced aortic wall stress in diabetes mellitus. *Eur J Vasc Endovasc Surg*. 2007;33(5):592-598.
21. Hackam DG, Thiruchelvam D, Redelmeier DA. Angiotensin-converting enzyme inhibitors and aortic rupture: a population-based case–control study. Lancet. 2006;368(9536):659-665.
22. Sweeting MJ, Thompson SG, Brown LC, Greenhalgh RM, Powell JT. Use of angiotensin converting enzyme inhibitors is associated with increased growth rate of abdominal aortic aneurysms. *J Vasc Surg*. 2010;52(1):1-4.
23. Anjum A, von Allmen R, Greenhalgh R, Powell JT. Explaining the decrease in mortality from abdominal aortic aneurysm rupture. *Br J Surg*. 2012;99(5):637-645.