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Medication in relation to complications after endovascular abdominal aortic aneurysm repair

Medicações referentes às complicações após correção de aneurisma da aorta abdominal endovascular

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Abstract

Objective: **This observational study was undertaken to explore the influence of medication on the occurrence of complications following endovascular repair of abdominal aortic aneurysms.**

Methods: **Clinical data concerning 70 consecutive patients undergoing elective EVAR in two vascular surgical centres over a 3 year period were analysed retrospectively. Complications were graded according to the recommendations of the Ad Hoc Committee on Reporting Standards. A distinction was made between device-related and non-related complications. An adjusted regression analysis was used to assess the association between 12 different medication groups and EVAR outcome.**

Results: **During 70 person years of follow-up 14 mild (20%), 23 moderate (33%) and 7 severe (10%) complications were recorded. Thirty patients (43%) who used coumarin derivates showed significantly less non-device-related complications (OR 0.21; 95%CI 0.05-0.90) compared to non-users. Twenty patients (29%) on anti-emetic drugs during hospital stay showed a fourfold more non-device-related complications (OR 4.37; 95%CI 1.10-17.3) and in-hospital use of analgesics in 25 patients was associated with more device-related complications (OR 3.81; 95%CI 1.32-11.0).**

Conclusion: **Medication seems to be associated with the occurrence of complications following endovascular therapy of abdominal aortic aneurysms. Patients who used coumarin-derivatives experienced fewer non-device-related complications. Patients who used anti-emetic drugs during hospital-stay showed a fourfold number of non-device-related complications. Patients using analgesics during hospital stay were associated with significantly more device-related complications**

Descriptors: **Aortic aneurysm, abdominal, complications. Vascular surgical procedures. Stents, complications.**

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Resumo

Objetivo: **Este estudo observacional foi desenvolvido para pesquisar a influência dos medicamentos na ocorrência de complicações após correção endovascular de aneurismas da aorta abdominal.**

Método: **Foram analisados retrospectivamente os dados clínicos referentes a 70 pacientes consecutivos submetidos à correção endovascular de aneurisma da aorta abdominal em dois centros cirúrgicos vasculares num período de 3 anos. As complicações eram classificadas de acordo com as recomendações do Comitê Designado de Padrões de Tratamento. Foi feita uma distinção entre complicações relacionadas ou não ao stent. Uma análise de regressão foi usada para avaliar a associação entre 12 grupos de medicamentos diferentes e o resultado da correção endovascular.**

Resultados: **Durante um acompanhamento de 70 pacientes-anos, foram relatadas 14 complicações leves (20%), 23 moderadas (33%) e sete graves (10%). Trinta pacientes (43%) que usaram cumarínicos tiveram significantemente menos complicações não relacionadas ao stent (OR. 0,21; 95% CI 0,05-0,90) comparados com os não usuários. Vinte pacientes (29%), tomando medicamentos antieméticos durante internação, mostraram quatro vezes mais complicações relacionadas ao stent (OR. 4,37; 95% CI 1,10-17,3) e o uso de analgésicos no hospital em 25 pacientes foi associado com mais complicações relacionadas ao stent (OR. 3,81; 95% CI 1,32-11,0).**

Conclusão: **Medicações parecem estar associados com a ocorrência de complicações após terapia endovascular de aneurismas da aorta abdominal. Pacientes que usaram cumarínicos tiveram menos complicações não relacionadas ao stent. Pacientes que usaram agentes antieméticos durante internação mostraram um número quatro vezes maior de complicações não relacionadas ao stent. Pacientes usando analgésicos durante a internação eram associados com maiores complicações relacionadas ao stent.**

Descritores: **Aneurisma da aorta abdominal, complicações. Procedimentos cirúrgicos vasculares. Contenedores, complicações.**

INTRODUCTION

Co-morbidity is common in patients with abdominal aortic aneurysms (AAA) [1]. The majority of AAA-patients have manifestations of cardiovascular disease such as myocardial infarction, stroke or hypertension, as well as pulmonary problems [2-4]. These co-morbidities require several medication-controlled treatments at the same time. The importance of medication in the prevention of secondary events is well known [5], but there is a risk of side effects or interaction of drugs in patients undergoing endovascular aneurysm repair (EVAR).

The reported incidence of complications after EVAR varies from 20% to 75% [6]. This morbidity is considerable and requires further investigation [6]. While in the earlier series complications could be attributed to suboptimal device construction, present stent-graft and delivery systems have improved and are fairly standardised [7]. With the use of improved equipment, the patient and doctor related risk factors for failure or complications are becoming more important determinants [6,8,9]. These factors have not been very well defined at the present time [6]. Various conditions may be expected to influence the occurrence of complications such as the learning curve, and anatomic characteristics of the aneurysm [10,11]. Also patient factors such as age, ASA-class and medication may influence the occurrence of complications and prolong hospital stay [2,6].

Until now, no research has been carried out on the influence of medication side effects or interactions on the occurrence of complications in AAA-patients with endovascular aneurysm repair.

METHOD

Subjects

Patients with endovascular abdominal aneurysm repair (EVAR) or attempted EVAR between April 1999 and November 2003 in two vascular surgical centres were included in the study. Experienced surgeons and interventional radiologists jointly performed implantation of stent-grafts. When necessary, adjuvant procedures such as the placement of extension devices of iliac limbs, coil embolisation of side branches, endarterectomy or patch-plasty of the common femoral artery were performed to obtain a satisfactory result. All patients were placed in the intensive care unit for monitoring during the first 4-20 hours after EVAR. On the first post-operative day, patients started with acetylsalicyl-acid (ASA) at a dosage of 80-100 mg per day as a standard medication. The follow-up protocol included contrast-enhanced CT-scanning on the first postoperative day and at 6, 12, 18, 24 months and annually thereafter.

Data assessment

Treatment results were assessed by clinical examination

and by imaging studies of the vascular morphology and endograft during follow-up.In case of death, details of this event were recorded as they occurred.

Medication was assessed from medical records. To obtain the influence of medication on the occurrence of complications, we studied groups of drug as they were used by our patients, such as coumarin derivatives, β-blockers, calcium-antagonists, thiazide-diuretics and lipid lowering medication. Complications were also assessed from medical files and verified thereafter. They were classified into device related (such as rupture or endoleak type I or III) or non-device- related (such as endoleak type II or myocardial infarction) complications according to the SVS-ISCVS-score. Explicit probability of causes of complications was determined. All radiological investigations where therefore reviewed by a vascular surgeon and a radiologist and were judged whether technical satisfaction was obtained. The combination of duplex ultrasound-scan (DUS) and computed tomographic-angiography (CTA) allowed accurate identification of any endoleak source (type I-IV).

Covariates

The study variables included patient characteristics such as smoking, obesity, ASA-class, hypertension and co-morbidity according to the SVS-ISCVS risk score, as well as stentgraft type.

Data analysis

Chi-square analysis was used to compare the baseline characteristics of the subjects. Rates and relative risks were calculated by means of the number of complications in each patient-category. To quantify the correlation between clinical variables, medication, complications and mortality a logistic regression and Cox proportional hazards model was constructed. α of 0.05 was used to define statistical significance. All analyses were performed with The SAS system (version 8.00, SAS Institute, Cary, NC, USA).

RESULTS

The population consisted of 70 patients of which 66 were male. The mean age was 71.8 years (SD: 8.1, Range: 41-86) and the average aneurysm diameter was 62.5mm (SD: 10.3, Range: 50-110). The mean hospital stay was 4.1 days (SD: 4.9 Range: 0-31) and mean follow up 9.9 months (SD: 11.9, Range: 0-37). Eight patients (11%) were classified as ASA class I, 20 patients ASA class II (29%), 34 ASA class III (49%) and 8 ASA class IV (11%). Smoking was encountered in 28 patients (26%), hypertension in 36 (51%) and 11 patients were obese (16%). All operative procedures were planned for non-ruptured asymptomatic aneurysms. The mean duration of operation was 163 minutes (SD: 52.7 Range: 90-320) (Table 1).

Table 1. Patient demographics.

Age		Mean (SD)
Aneurysm diameter		71.8 years (8.1)
Procedure duration		62.5 mm (10.3)
Hospital stay		163 min (52.7)
Length of follow-up		4.1 days (4.9)
		9.9 months (11.9)
Smoking		n (%)
Hypertension		28 (26)
Obesity		36 (51)
ASA Class		11 (16)
	1	8 (11)
	2	20 (29)
	3	34 (49)
	4	8 (11)

Overall, 41 patients (59%) experienced one or more complications (N=67) of which 24 were device-related and 43 non-device-related complications (Table 2). Most complications were in the early post-operative period. There were 20 endoleaks (29%) of which 8 were type I (11%), 4 endoleaks type II (6%), 4 endoleaks type III (6%), 0 type IV and 4 unspecified endoleaks (6%). No stent-graft infections or AAA-ruptures were encountered. Four patients died postoperatively (6%) of which two due to a malignancy after 2 months, one due to a pulmonary embolus at 3 months and one (1.4%) died within the 30 day period due to respiratory insufficiency. No cause of death was aneurysm-related in this study.

Table 3 shows an overview of the medication and number of complications. All patients (n=70) used thrombocyte aggregation inhibitors (ASA 80-100mg) by protocol. Other frequently used medication were

β-blockers (49%), RAS inhibitors (44%), coumarin-derivatives (43%). The in-hospital medication consisted of analgesics (36%), lipid-lowering drugs (23%), anti-emetics (29%) and calcium-antagonists (23%) respectively.

Patients who used analgesics during hospital stay (36%) showed more device related complications (P= 0.01) compared to patients who did not used this drug during hospital stay. Patients using anti-emetic drugs during hospital-stay (29%) showed more non-device-related complications (P= 0.036) compared to non-users. Patients who used coumarin-derivatives showed less non-device-related complications (P= 0.035) compared to non-users. The grade of severity of complications is presented in Table 4.

Table 2. Overview of complications

Complications*			
Device Related	24 (36%)	Non-Device Related	43 (64%)
Stent Migration	3 (4%)	Stroke	9 (13%)
Stent Occlusion	5 (7%)	Myocardial infarction	7 (10%)
Endoleak type I	8 (12%)	Pulmonary embolus	9 (13%)
Endoleak type II	4 (6%)	Other / Unspecified	18 (27%)
Endoleak type III	4 (6%)		
Endoleaks unspecified	4 (6%)		
Rupture	0		

** N= 67 complications (in 41 patients)*

Table 3. Overview: medication variables and number of complications.

Medication type	Use	Complications			
	n (%)	Device related n (%)	P-value	Non-device related n (%)	P-value
Coumarin derivative	30 (43)	12 (40)	.120	4 (13)	.035
Lipid lowering	23 (33)	5 (22)	.120	4 (17)	.952
?-Blocker	34 (49)	9 (27)	.310	9 (27)	.895
RAS inhibitor	31 (44)	10 (32)	.775	9 (29)	.930
Loop diuretic	12 (17)	3 (25)	.377	3 (25)	.940
Thiazide diuretic	10 (14)	1 (10)	.201	3 (30)	.360
Calcium antagonist	16 (23)	7 (44)	.321	5 (31)	.769
Proton-pump inhibitor	13 (19)	4 (31)	.897	5 (39)	.111
Analgesics in hospital	25 (36)	14 (56)	.010	7 (28)	.813
Anti-emetics in hospital	20 (29)	5 (25)	.052	7 (35)	.036
Opioids in hospital	13 (19)	3 (23)	.274	4 (31)	.774
Other*	27 (39)	11 (41)	N/A	5 (19)	N/A
All patients	70	25 (36)		16 (23)	

** = Immunosuppressive drugs, Anti-histaminic, Laxative, Heart-glycoside, Tranquillizers, Hormones, Anti-gout, Anti-diabetics, Action-potential enlarger, Anti-conceptive, Folic acid and Inhaling drugs*

Table 4. Overview: medication variables and classification of complications

Medication type	Use	Complications					
	n (%)	Mild n (%)	P-value	Moderate n (%)	P-value	Severe n (%)	P-value
Coumarin derivative	30 (43)	7 (23)	0.312	12 (40)	0.135	0 (0)	0.940
Lipid lowering drug	23 (33)	4 (17)	0.836	5 (22)	0.158	1 (4)	0.963
?-Blocker	34 (49)	4 (12)	0.173	9 (27)	0.155	4 (12)	0.961
RAS inhibitor	31 (44)	6 (19)	0.286	11 (36)	0.541	3 (10)	0.871
Loop diuretic	12 (17)	2 (17)	0.602	2 (17)	0.959	2 (17)	0.963
Thiazide diuretic	10 (14)	2 (20)	0.295	0 (0)	0.957	1 (10)	0.978
Calcium antagonist	16 (23)	5 (31)	0.252	7 (44)	0.166	3 (19)	0.758
Proton-pump inhibitor	13 (19)	3 (23)	0.512	4 (31)	0.893	1 (8)	0.904
Analgesics in hospital	25 (36)	8 (32)	0.068	10 (40)	0.274	2 (8)	0.265
Anti-emetics in hospital	20 (29)	4 (20)	0.474	8 (40)	0.213	1 (5)	0.991
Opioids in hospital	13 (19)	4 (31)	0.356	2 (15)	0.232	2 (15)	0.486
Other*	27 (19)	5 (19)	N/A	8 (30)	N/A	4 (15)	N/A
All patients	70	14 (20)		23 (33)		7 (10)	

** = Immunosuppressive drugs, Anti-histaminic, Laxative, Heart-glycoside, Tranquillizers, Hormones, Anti-gout, Anti-diabetics, Action-potential enlarger, Anti-conceptive, Folic acid and Inhaling drugs.*

DISCUSSION

Presently, little is known about the influence of medication on the occurrence of complications after endovascular aneurysm repair (EVAR), whereas recognizing certain patterns in pathology and causes of complications is important [12,13] . As delivery and stent-graft systems have improved and are fairly standardized [6,14,15], risk profiles such as co-morbidity and medication are becoming more important factors for making evidence based decisions concerning elective endovascular therapy in patients with an aneurysm of the abdominal aorta (AAA) [6]. It is also important to detect whether in the post-operative period the risks for developing complications might be diminished. When more patient-related factors will be identified, appropriate alternatives in follow-up or medication may be developed. This study was designed to investigate whether additional medication is associated with any risk of complications in AAA-patients after EVAR.

The EVAR population consists of cardiovascular patients [16-18]. The preventive effect of thrombocyte-aggregation inhibitors in this population is already proven and therefore implemented in the EVAR-protocol [12,19-21]. Many cardiovascular patients are using coumarin-derivatives on a daily basis besides standard acetylsalicylic acid [3,12,19]. In our population the use of both thrombocyte aggregation inhibitors (by protocol) and coumarin-derivatives was quite common (e.g. 43%). This combination provides a protective effect against acute vascular events [5,20]. There are different opinions about the use of coumarin-derivatives next to thrombocyte-aggregation inhibitors after a device implant. Because of the anti-thrombotic effect of coumarin-derivatives [5] it was expected that more endoleaks could occur because of the occurence of a hyperthrombenemic state. This could not be confirmed in the present study. Patients using coumarin-derivatives in this study had less non-device-related complications than patients who did not.The use of analgesics during hospital stay was associated with significantly more device-related complications.

Patients using anti-emetic drugs during hospital-stay had more non-device-related complications. We have no explanation for these outcomes.

The mortality rate of 1.4% in the present study population is comparable to those of the EVAR-1 trial and the DREAM trial [22-24]. In these studies a mortality rate of 2.7% and 3% was recorded for elective EVAR. The initial survival advantage over open aneurysm repair, however, was not sustained after the first postoperative year. The main cause of late postoperative death in both trials was cardiovascular, confirming the impact of comorbidity in EVAR patients.

The EVAR-2 study was conducted in patients unfit for open aneurysm repair. It showed that EVAR is not a safe procedure in such high-risk patients [23]. It also raised concern about the medical treatment of these patients, fuelling the attention for co-morbidity and medication.

In conclusion, medication seems to be associated with the occurrence of complications following endovascular therapy of abdominal aortic aneurysms. Patients on coumarin-derivatives experienced fewer non-device-related complications. Patients who used anti-emetic drugs during hospital-stay showed a fourfold number of non-device-related complications. Patients using analgesics during hospital stay were associated with significantly more device-related complications.

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