Risk factors in vascular surgical sepsis

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Summary

The risk factors for sepsis after vascular surgery were studied in 100 consecutive patients with lower limb arterial ischaemia. Patients were randomised either to a short or long course of antibiotic prophylaxis with amoxycillin/clavulanic acid combination (Augmentin®).

Pathogenic organisms were isolated from the skin preoperatively in 39 (36%) cases, significantly more frequently in patients with ischaemic rest pain and skin necrosis (66%) than rest pain alone (21%) (P=0.0004) or claudication/aneurysm (11%) (P=0.0001). All but three organisms isolated (5%) were sensitive to amoxycillin/clavulanic acid.

A wound infection occurred after 21 (19%) reconstructions, significantly more frequently both in patients suffering rest pain with skin necrosis (P=0.001) and rest pain without skin necrosis (P=0.04) compared with claudication/aneurysm. Sixteen of the 21 patients with a wound infection had at least one organism isolated from their skin preoperatively (P=0.0001). Twelve patients (57%) had a similar organism isolated from the skin preoperatively and from the postoperative wound infection. Reducing the course of antibiotic prophylaxis from 5 days to 3 doses did not significantly increase the infection rate. The only other significant risk factor for sepsis was increasing age of the patient.

Although prophylaxis is undisputed in patients having synthetic grafts, antibiotics may not be as important in the prevention of wound sepsis as had been thought. The role of antiseptic agents requires further evaluation.

Introduction

Vascular surgery has been classified as clean surgery but many patients with peripheral arterial ischaemia have distal skin necrosis which may be a source of endogenous infection. Vascular graft infection is rare, occurring after 1–6% of reconstructions but has a high associated morbidity and mortality (1–6). In some patients a wound infection, particularly in the groin, has preceded a graft infection and a causal relationship has been inferred

(1,2,5,6). Therefore prevention of wound infection might decrease the incidence of graft infection. The reported incidence of wound sepsis after vascular surgery varies widely from 0.4% to 22% (7–14). However, many studies of sepsis after vascular surgery specifically exclude patients with distal skin necrosis (9,10,12,14). In Nottingham, patients with distal skin necrosis account for over 40% of all those receiving surgical reconstructions and any policy for reducing sepsis rates must include these patients.

In a prospective study in this unit in 1984, a wound infection rate of 35% was documented in patients having vascular surgery. The prophylactic antibiotic used was ampicillin/flucloxacillin combination (Magnapen®) started at anaesthetic induction and continued for 5 days postoperatively. In the prospective study and in a retrospective review of vascular wound infections in Nottingham it was noted that Gram-negative organisms and anaerobes were surprisingly common. It was considered that a prophylactic antibiotic with a broader spectrum might be more effective, and therefore in the present study a new antibiotic combination, amoxycillin with clavulanic acid (Augmentin®, Beecham Pharmaceuticals), has been investigated in vascular surgical patients. Clavulanic acid alone has only weak antibacterial properties but it is a potent inhibitor of many bacterial beta-lactamases. In combination with amoxycillin the range of sensitive micro-organisms is considerably extended to include penicillin-resistant *Staphylococcus aureus*, many resistant coliforms and some anaerobes (15–17). We have previously shown that amoxycillin/clavulanic acid has serum and tissue penetration suitable for use in vascular surgery (18).

The aims of this study were to investigate the risk factors for postoperative sepsis in 100 consecutive patients having vascular surgical reconstructions and to assess the relevance of preoperative skin bacteriology in relation to the severity of arterial ischaemia and the rate of postoperative wound infection. Antibiotic prophylaxis in general surgery is not usually extended beyond three perioperative doses (19) and we have investigated whether there was any advantage in extending the duration of antibiotic prophylaxis in vascular surgery.

Patients and methods

One hundred patients received 108 lower limb vascular reconstructions. There were 69 men and 31 women with a median age of 70.5 years (43–89 years). There were 16 patients (16%) with diabetes mellitus and 63% were current cigarette smokers. Thirty-five operations (32%) were for claudication or aneurysm, 29 (27%) for ischaemic rest pain with intact skin and 44 (41%) for rest pain with distal skin necrosis.

All patients had skin swabs taken preoperatively from the nose, and the groin and toes of the ischaemic foot. A mid-stream urine sample (MSU) was also obtained for culture. Preoperative antiseptics were not used. The patients were shaved for operation on the day before surgery. Patients were randomised either to a short or long perioperative course of antibiotic prophylaxis. A short course was given in 56 operations and consisted of amoxycillin 1 g with clavulanic acid 200 mg (Augmentin 1.2 g) given intravenously (i.v.) at anaesthetic induction and two subsequent doses given at 8-hourly intervals. A long course was given in 52 operations and consisted of amoxycillin/clavulanic acid given as above at anaesthetic induction and continued 8 hourly for 5 days. Oral amoxycillin/clavulanic acid was substituted for i.v. when intestinal function recovered postoperatively. All patients had vascular reconstructions performed under general anaesthesia. Before surgery the skin was prepared with aqueous chlorhexidine. A femoropopliteal graft was inserted on 64 (59%) occasions (51 saphenous vein and 13 polytetrafluoroethylene—PTFE); 26 (24%) were aortoiliac reconstructions; there were 13 (12%) extra-anatomic grafts and 5 miscellaneous operations.

Postoperatively the wounds were reviewed blind by RCBS twice weekly until the patient left hospital. A wound infection was defined as 'the discharge of pus' *(20)*. A cotton-tipped swab was taken from all wound discharges for culture. Serous discharge, particularly from a groin wound where lymphatic damage had occurred, without any bacterial culture was not regarded as a wound infection. The patients were followed in the out-patient clinic and it was noted whether there was any wound discharge during the convalescent period. Follow-up ranged from 6 to 20 months.

Pre- and postoperative swabs were placed in Stuart's transport medium before culture in the laboratory by standard methods. Potential pathogens were identified and their sensitivities performed by agar incorporation methods using 2 and 4 µg/l clavulanate with amoxycillin. Commensal skin organisms were not included unless grown in pure culture.

Patients were included for analysis if they survived to have their wounds reviewed twice, once between the 3rd and 6th postoperative days and once between the 7th and 10th postoperative days. During the study period three patients were excluded who suffered acute myocardial infarctions and died less than 1 week after surgery. The only other exclusions from the study were five patients sensitive to penicillin.

Results

PREOPERATIVE BACTERIOLOGY

Pathogenic organisms were isolated from the skin preoperatively in 39 patients (36%). A total of 67 organisms was isolated. *S. aureus* was the organism most often isolated (60%) and the site most frequently affected was the toe of the ischaemic foot (60%) (Table I). All the organisms isolated preoperatively except *Pseudomonas aeruginosa* and *Candida albicans* (5%) were sensitive to amoxycillin/clavulanic acid. Organisms were isolated in 29 patients (66%) with rest pain and skin necrosis, significantly more frequently than in patients with rest pain alone (21%) ($P=0.0004$) and claudication or aneurysm (11%) ($P=0.0001$) (Table II).

WOUND INFECTION

Twenty-one patients (19%) developed a wound infection. A single infection occurred in an abdominal wound, eight in groin wounds, seven in popliteal wounds and five in both groin and popliteal wounds. Eighteen infections developed during the hospital admission. At the first follow-up clinic visit two patients reported a purulent wound discharge which had been treated by their GPs and a third was readmitted for drainage of a popliteal wound abscess. The mean age of patients with wound infections (70 years) was significantly greater than in those without infections (66 years) ($t=1.92$, $P<0.05$). This could not be entirely accounted for by differences in the severity of the ischaemia, as the mean ages of patients with claudication/aneurysm (65 years), rest pain alone (70 years) and rest pain with skin necrosis (70 years) were broadly similar. The two groups who had different antibiotic schedules were well matched, in particular, distal skin necrosis was present in 20 patients who received the short course and 24 patients who received the long course of perioperative antibiotics. Nine patients who received the short course and twelve patients who received the long course of amoxycillin/clavulanic acid had wound infections ($\chi^2=0.89$, $P=$n.s.). Seven infections occurred in the twenty operations on diabetic patients (35%) compared with 14 infections in 88 operations on non-diabetics (16%), a difference which just

TABLE I *Organisms isolated from the skin preoperatively*

	Toe n=40 (60%)	Nose n=12 (18%)	Groin n=9 (13%)	MSU n=6 (9%)	Total n=67 (%)
Staphylococcus aureus	20	11	7	2	40 (60%)
Esherichia coli	9	1	1	4	15 (22%)
Haemolytic streptococci	5				5 (7%)
Proteus spp.	3		1		4 (6%)
Pseudomonas aeruginosa	2				2 (3%)
Candida albicans	1				1 (2%)

TABLE II *Skin colonisation related to the severity of ischaemia*

	n	Patients with skin isolates (%)		
Claudication/ aneurysm	35	4 (11%)	$\chi^2=1.1$ $P=$n.s.	$\chi^2=23.8$ $P=0.0001$
Ischaemic rest pain	29	6 (21%)		
Rest pain with skin necrosis	44	29 (66%)	$\chi^2=14.4$ $P=0.0004$	

TABLE III *Wound infection related to the severity of ischaemia*

	n	Infections (%)		
Claudication/ aneurysm	35	1 (3%)	$\chi^2=3.9$ $P=0.04$	
Ischaemic rest pain	29	5 (17%)	$\chi^2=2.6$ $P=$n.s.	$\chi^2=11.9$ $P=0.001$
Rest pain with skin necrosis	44	15 (34%)		

TABLE IV *The relationship of preoperative skin colonisation to wound infection*

	n	Infections (%)		
No preoperative isolates	69	5 (7%)	$\chi^2=5.7$ $P=0.02$	
Single preoperative isolate	22	6 (27%)	$\chi^2=4.0$ $P=0.04$	$\chi^2=23.9$ $P=0.0001$
Multiple preoperative isolates	17	10 (59%)		

TABLE V *Comparison of organisms isolated pre- and postoperatively*

Preoperative organisms (%)		Postoperative organisms (%)
40 (60%)	Staphylococcus aureus	14 (31%)
15 (22%)	Esherichia coli	12 (27%)
5 (7%)	Haemolytic streptococci	3 (7%)
4 (6%)	Proteus spp.	4 (9%)
2 (3%)	Pseudomonas aeruginosa	5 (11%)
1 (2%)	Candida albicans	0
0	Bacteroides spp	5 (11%)
0	Anaerobic streptococci	1 (2%)
0	Methicillin resistant S. aureus	1 (2%)

failed to reach statistical significance ($\chi^2=3.4$, $P=0.06$). Infection occurred more frequently after femoropopliteal surgery (35%) than after aortoiliac surgery (11%), though again this did not attain significance ($\chi^2=2.2$, $P=0.12$). Fourteen of 51 femoropopliteal vein grafts and two of 13 PTFE grafts became infected ($\chi^2=1.1$, $P=0.3$).

Eight patients had a re-operation on the day of the original reconstruction, four for bleeding and four for graft thrombosis. Two (25%) of these patients subsequently developed a wound infection. Nine patients had a femoropopliteal graft thrombosis within 1 week of surgery with subsequent amputation. Four (44%) of these patients developed a wound infection and in all cases the site was the popliteal incision.

The risk of wound infection was significantly increased in patients with rest pain ($P=0.04$) or rest pain with skin necrosis ($P=0.001$) compared with operations for claudication or aneurysm (Table III). Though the infection rate in patients with rest pain and skin necrosis (34%) was double that in patients with rest pain alone (17%), the difference was not statistically significant. This corresponded with the observation that wound infection was more frequent in patients with either a single ($P=0.02$), or multiple ($P=0.0001$) preoperative skin isolates compared with none (Table IV). Sixteen patients (76%) with wound infections had at least one preoperative pathogen isolated.

POSTOPERATIVE BACTERIOLOGY

A single organism was isolated from the wound infection in seven cases and multiple organisms in 13 cases. One occurred after hospital discharge and the organism was unknown. *S. aureus* was the most common cause of wound infection. Infection with a single organism was less frequent after a short course of antibiotic prophylaxis. *Bacteroides* spp and *Proteus* spp were isolated more frequently after the short course and *P. aeruginosa* more frequently after the long course of amoxycillin/clavulanic acid. Gram-negative organisms and anaerobes were isolated more frequently from wound infections than from

the skin preoperatively (Table V). Twelve patients (57%) had a similar organism isolated from the skin preoperatively and the wound infection postoperatively.

GRAFT INFECTION

A total of three patients with artificial grafts developed a wound infection, one of whom subsequently developed a graft infection with the same organism. This occurred 3 months after surgery in a PTFE femoropopliteal graft inserted for severe claudication. The graft was removed and the claudication returned. The wound infection resolved in the second patient with local therapy, and the third patient died of bronchopneumonia after 3 weeks with an active wound infection but no signs of graft infection. The other graft infection occurred in a femoropopliteal vein graft after 10 days and caused a secondary haemorrhage. This resulted in an amputation and eventual death from bronchopneumonia. Both patients who had graft infections had a preceding wound infection with a similar organism.

SURGICAL COMPLICATIONS

Other complications included three chest infections two urinary infections, three non-fatal myocardial infarctions and one pulmonary embolism. Three patients included in the trial died, one from a stroke and the other two from bronchopneumonia. A second course of antibiotics was required in 18 patients for chest, urinary and wound infections, and was equally distributed between the two groups having different antibiotic regimens. Antibiotics were only used for wound infection if there was cellulitis or the possibility of infection in a synthetic graft. The mean hospital stay after operation was 32 ± 10.8 days in patients with infections and 13 ± 7.7 days in those without infections ($t=6.99$, $P<0.001$).

Possible side effects from amoxycillin/clavulanic acid included two mild rashes (one which did not recur after rechallenge) and an episode of vomiting on the 5th day of a long course. No serious side effects were noted.

Discussion

The incidence of graft infection (2%) in this study was similar to previous reports and the serious nature of the complication was confirmed (1–6). The incidence of postoperative wound infection (19%) was high but patients

with skin necrosis were not excluded as in some other series and all cases had peripheral arterial ischaemia, whereas some reports include patients having carotid surgery *(8)* and even patients having varicose vein surgery *(10)*. All the infections extended into subcutaneous tissue—Szilagyi grade 2 *(2)*, and were severe enough to prolong hospital stay by an average of 19 days. Three infections which occurred after hospital discharge were also included. Both the patients who suffered a graft infection had a preceding wound infection and it is likely that there is a relationship between the two. Reducing wound infection may be the most important method of limiting graft sepsis.

The most important risk factor identified was the severity of the arterial ischaemia. Patients with rest pain and skin necrosis had a high incidence of skin contamination with pathogenic organisms preoperatively as might have been expected and also the highest wound infection rate. Over one-half of the patients with wound infection had a similar organism isolated from the skin preoperatively, which provides evidence that endogenous infection is the most important cause of sepsis after vascular surgery, though transmission of organisms via the lymphatics could not be ruled out. Increasing age of the patients was also shown to be a risk factor for infection, though this may have been partly accounted for by the lower mean age in patients with claudication or aneurysm. The site of surgery and the presence of diabetes influenced the sepsis rate, though not to a statistically significant extent. Diabetic patients and those having femoropopliteal grafts had a higher incidence of rest pain and skin necrosis which might have been responsible for their increase in infection. Continued limb ischaemia due to early graft thrombosis may have increased the risks of subsequent infection in the popliteal wound.

It is generally agreed that patients having reconstructive surgery using prosthetic graft material require antibiotic prophylaxis *(21,22)*, though only 68% of the members of the Vascular Surgical Society use antibiotics in all vascular cases *(23)*, and there is no consensus on which antibiotic is best. Parenteral antibiotics have been shown to reduce the risk of wound infection *(9–11,14)* but the incidence of graft sepsis is so low that studies designed to demonstrate reduced graft sepsis would have to contain many hundreds of patients. Also graft sepsis may present many months after surgery and studies with short follow-up are inadequate. Topical antibiotics have also been shown to reduce wound infections after vascular surgery *(10)* and the ideal route for prophylaxis is still uncertain. Graft sepsis is often stated to be more frequent and severe in patients with synthetic grafts *(2)* but in this study one of the cases occurred in a vein graft, with a fatal outcome.

The ideal prophylactic antibiotic for vascular surgery would have a suitable spectrum, good serum and tissue penetration and cause few side effects. Amoxycillin/clavulanic acid was chosen for this study because of the high infection rate in our retrospective review where ampicillin/flucloxacillin was used. The new combination has an extended spectrum which has recently been stated to be advisable in vascular surgery *(23)*. However, despite the fact that 95% of the organisms cultured from the skin preoperatively were sensitive, and the fact that amoxycillin/clavulanic acid has been shown to have a

suitable spectrum and penetration *(18)*, the wound infection rate of 19% was high and over one-half of the patients had similar organisms isolated from the wound infection and the skin preoperatively. Thus, either the antibiotic regimen was ineffective, or antibiotics are not as important as originally thought. There was no difference in infection rates between the two antibiotic regimens and therefore the latter may be true. When infection results from defective surgical technique such as skin necrosis due to undercutting of skin edges, failure of accurate skin apposition, damage to lymphatics in the groin and haematoma formation, antibiotics cannot be expected to provide complete protection.

There remains considerable disparity in the length of time for which antibiotic prophylaxis is prescribed *(23)* but in this study no increase in infection rate was demonstrated after reducing the course of amoxycillin/clavulanic acid and it is therefore not necessary to give more than three perioperative doses for optimum effect. Indeed the use of more than one dose of antibiotic for prophylaxis has recently been criticised *(24)*.

The evidence from this study that vascular infection may be endogenous means that the preoperative use of antiseptic agents to reduce skin contamination may be beneficial in prevention of wound infection *(13,25)*. The antiseptic agent used to cleanse the skin at surgery may also be important. Randomised trials comparing operative antiseptics have not been performed, though retrospective analysis of one study suggested that iodine based preparations may be superior *(9)*. The role of antiseptics in vascular surgery is worthy of further study.

This report may help explain the low incidence of wound infection detailed in some studies, being dependent on the number of patients in the study with rest pain and skin necrosis. It is important that the severity of limb ischaemia is documented in future reports on sepsis in vascular surgery.

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Notes on books

Rheumatoid Arthritis Surgery of the Complex Hand and Foot edited by F W Hagena. 190 pages, illustrated. Karger, Basle. £80.50.

The Proceedings of the 3rd Congress of the European Rheumatoid Arthritis Surgical Society held in Finland in 1985. Twelve papers on surgery of the hand and eleven papers on surgery of the foot. Many black and white photographs and line diagrams.

A Colour Atlas of Mastectomy with Immediate Reconstruction by David J T Webster. 63 pages, illustrated. Wolfe Medical Publications, London. £17.

Number 38 in the Single Surgical Procedures series describes and illustrates both the Patey and the Halstead mastectomy techniques together with various methods of breast reconstruction. Latissimus dorsi reconstruction, rectus abdominus reconstruction and subpectoral mammary prosthesis insertion are the reconstructions described.

Atlas of Endourology edited by Kurt Amplatz and Paul H Lange. 344 pages, illustrated. Year Book Medical Publishers, Chicago. £91.

Endourology is here defined as being any procedure on the kidney and upper collecting system performed through a percutaneous approach or to retrograde ureteroscopy. Most of the chapters in this atlas relate to percutaneous manipulations of one sort or another and is therefore of interest to both the urologist and the radiologist. Large format, glossy paper, numerous line drawings and radiographs, some colour illustrations, succinct text.

1986 Yearbook of Digestive Diseases edited by N J Greenberger and F G Moody. 479 pages, illustrated. Year Book Medical Publishers, Chicago. £41.

Eighty journals containing more than ten thousand articles have been surveyed to abstract some two hundred and fifty articles for presentation and comment in this volume. Many of the abstracts are of interest to surgeons and the volume should prove a useful update for many readers of this notice.

1986 Yearbook of Urology edited by J Y Gillenwater and S S Howards. 378 pages, illustrated. Year Book Medical Publishers, Chicago. £43.

Another useful volume in the Year Book series which will provide urologists everywhere with an update of the world literature during the year ending January 1986. Over two and a half thousand articles have been reviewed to provide two hundred and fifty digests in this volume which cover both adult and paediatric urology. As usual an editorial comment is appended to each review.

Urologic Complications edited by Fray F Marshall. 451 pages, illustrated. Year Book Medical Publishers, Chicago. £62.

Complications in surgery are best prevented by anticipation. It is hoped that this book will help urologists to anticipate many possible clinical problems both in the adult and in the child. The complications that are covered include both medical and surgical. Each of the 34 chapters concludes with an editorial comment by Dr Marshall giving a personal view.