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Methicillin Resistant *Staphylococcus aureus* in Patients Undergoing Major Amputation

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Objectives: *to examine the impact of MRSA infection on patients undergoing major amputation.*
Setting: *District General Hospital.*
Methods: *patients having had major amputation and positive MRSA cultures January 1995–December 1999 were included. Outcome was compared with a randomly chosen group of patients having major amputation but no positive MRSA culture from the same time period.*
Results: *overall 21% of patients undergoing amputation were MRSA positive. Some 28 patients (30 amputations) with MRSA positive cultures were compared with 44 patients (54 amputations) who did not have positive cultures for MRSA. MRSA was isolated from the wound in 17 of 30 amputations. More patients in the control group had a below knee amputation (38 of 54 compared with 12 of 30,* $p<0.02$*). Mortality in MRSA positive patients was higher than controls, (12 of 28, 43%, versus 4 of 44, 9%,* $p<0.01$*). Primary healing was achieved in only 4 of 17 (24%) amputations where MRSA was isolated from the wound. This compared with 31 of 54 (57%) controls* ($p<0.05$*). Delayed healing due to chronic infection was also more likely in MRSA positive patients* ($p<0.01$*).*
Conclusion: *in view of the high morbidity and mortality in patients with MRSA positive isolates specific antibiotic prophylaxis against MRSA should be considered in patients undergoing major amputation.*

Key Words: Methicillin resistant; Staphylococcus aureus*; Major amputation.*

Introduction

The number of patients being diagnosed as having methicillin resistant *Staphylococcus aureus* (MRSA) infection is increasing.[1] The incidence of MRSA in hospital patients had reached 13.5% of *S. aureus* infections by 1995.[2]

In a previous study we found that MRSA-infected general surgical patients were sicker and had sustained a greater surgical insult than non-MRSA-infected patients.[3]

Patients undergoing arterial operations are at considerable risk of acquiring infection. Patients not receiving prophylactic antibiotics have been shown to have a groin wound infection rate of approximately 25%.[4] Infection of synthetic vascular grafts though uncommon has dire consequences, with high rates of limb loss and death.[5] Though prophylactic antibiotics have proved effective in the past the emergence of MRSA is challenging vascular surgeons and microbiologists alike.

In a recent multicentre survey of patients undergoing vascular operations almost half of wound and graft infections diagnosed were due to MRSA.[6] MRSA-infected wounds were significantly more likely to to progress to major amputation or ongoing infection than wounds infected with other organisms.

The aim of this study was to examine the impact of MRSA infection in those patients who had undergone a major amputation.

Methods

Patients having had major amputation and positive MRSA swabs between January 1995 and December 1999 were included. They were identified by cross checking data from the microbiology laboratory computer against theatre ledgers. During this time it was not hospital policy routinely to screen all patients for MRSA. However, once a positive swab from a primary site (e.g. wound, sputum, blood or urine) was obtained, these patients had swabs taken from nose, axilla, perineum and groin.

This population of patients was compared with

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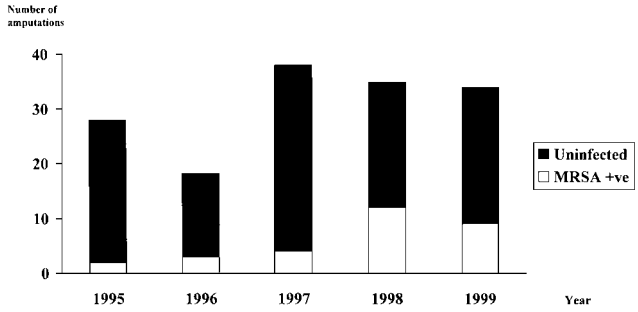

Fig. 1. Total number of major amputations 1995–1999 showing numbers being MRSA positive.

patients who had undergone major amputation without identifiable MRSA infection or colonisation. These "control" patients were identified from the operating ledgers. We randomly chose patients who had operations as close as possible in time to those of the study group. The patients and amputations were not matched in any other way. Not all patients having major amputation during the time of the study were included in this control group.

Stastistical analysis was carried out using Chi-squared test with continuity correction for small numbers.

Results

During the five years of the study 153 major amputations were carried out. A total of 28 patients (30 amputations) were found to have MRSA positive swabs. There was a steady increase in the number of patients having amputations who tested positive for MRSA during the first four years of the study, with a slight decrease in 1999 (Fig 1). Overall 20% of amputations were complicated by the patient having MRSA isolated.

Table 1 illustrates the demographic and amputation details of patients with MRSA-positive swabs and controls. In patients with MRSA the indication for amputation was gangrene in 12, ulceration in nine and rest pain in the remainder. For the control patients the indication was gangrene in nine, ulceration in 15, the remainder having rest pain. Of patients who were MRSA positive three had previous contralateral amputations, which had not been complicated by MRSA. Control patients were more likely to have undergone a below knee amputation than patients with positive MRSA cultures. (Chi-squared 6.2, df 1, $p<0.02$).

In 17 cases MRSA was isolated from the amputation wound. Other sites of infection or contamination were skin (13), blood (2), graft (2), urine (2) and an infected feeding line (1). Multiple sites of infection were identified in 8 cases. MRSA was first identified before amputation in 16 and following amputation in 14.

All patients had prophylactic antibiotics to cover the time of the amputation (either metronidazole or penicillin). In addition vancomycin was given in one case and teicoplanin in three. Postoperatively teicoplanin or vancomycin was given to all patients with MRSA isolated from wound, blood or graft site or if they were systemically unwell with sepsis.

Co-existing infections were present in 8 patients, the most common being a coliform urinary tract infection (5). Others included pseudomonas chest infection (2) and clostridium difficile diarrhoea (1).

Outcome is shown in Table 2. Mortality in patients who were MRSA positive was 12 of 28 (43%), compared with four of 44 (9%) in the control patients (Chi-squared 9.42, df 1, $p<0.01$). Patients with MRSA in their wounds fared particularly badly. Nine of seventeen (53%) patients with MRSA in their wound died compared with four of 44 (9%) controls, (Chi-squared 11.6, df 1, $p<0.001$).

There was no difference in mortality in patients having MRSA in their wounds compared with those in whom MRSA was found elsewhere. Primary healing

Table 1. Demographic and amputation details.

	MRSA isolated		Controls	
	n	(%)	*n*	(%)
Patients	28		44	
Men	20	(71)	34	(77)
Age, median (range)	71 (49–90)		73 (41–85)	
Diabetes mellitus	18	(64)	21	(47)
Hypertension	10	(36)	18	(41)
Ischaemic heart disease	10	(36)	16	(36)
Hypercholesterolaemia	3	(11)	2	(5)
Continued to smoke	10	(36)	13	(30)
Amputations	30		54	
Below knee	12	(40)	38	(70)
Above knee	14	(47)	15	(28)
Through knee	4	(13)	1	(2)

Table 2. Outcome: MRSA patients versus controls. Figures in brackets represent percentages.

	MRSA			Controls
	In wound	Not in wound	Total	
n patients	17	11	28	44
n amputations	17	13	30	54
Primary healing	4 (24)	7 (54)	11 (37)	31 (57)
Secondary healing	13 (76)	6 (46)	19 (63)	23 (43)
Delayed healing	4 (24)	2 (15)	6 (20)	0 (0)
Refashioning	5 (29)	0 (0)	5 (17)	10 (19)
Death	9 (53)	3 (27)	12 (43)	4 (9)

occurred in four of 17 (24%) amputations from which MRSA was grown in the wound, compared with 31 of 54 (57%) controls (Chi-squared 4.6, df 1, $p<0.05$). There was no significant difference in the rate of refashioning in the two groups. Healing was delayed for more than six months, due to chronic infection, in six amputations (21%). This only occurred in the presence of MRSA (Chi-squared 8.8, df 1, $p<0.01$). Healing did occur in these patients, but the median time to healing was 12 months (range 6–24 months).

Discussion

Over the period 1984–1991 the proportion of *S. aureus* resistant to methicillin isolated in American hospitals rose from 5%to 29%.[7] This trend is mirrored worldwide. MRSA infection in patients undergoing arterial perations is similarly increasing. Nasim et al showed a five-fold increase between 1993–1998.[8] Our results, with regard to MRSA being diagnosed in patients undergoing major amputation show a similar pattern.

There was a small but steady increase 1995–1997 with a four-fold increase in the subsequent twelve months. This was not associated with any change in antibiotic prophylactic policy nor in increasing efforts to diagnose MRSA on cultures.

It is difficult to be certain which of the patients in this study had MRSA infection or simple colonisation. However, once MRSA had been isolated the likelihood of death following major amputation is significantly increased. The aggressive nature of MRSA in patients undergoing arterial reconstruction has been established previously. MRSA-infected wounds following reconstruction being significantly more likely to progress to amputation compared with non-MRSA infected wounds.[6] Our data suggest that even after amputation the presence of MRSA continues to exert a negative influence on survival.

Mortality following major amputation depends upon the level of amputation. Patients having above knee amputation have a mortality of 15–20% compared with approximately 10% for below knee amputations.[9] It is possible that part of the high mortality we have shown in MRSA positive patients may be due to the high proportion of above knee amputations in this group. However a mortality in patients undergoing major amputation with clinical evidence of MRSA infection has been described by others.[10] Of 14 patients described by Murphy *et al*. five died (36%). Over half of those amputations were below knee. Primary healing is more likely in patients undergoing above compared with below knee amputations. Despite the case-mix in this study which has resulted in a greater proportion of below knee amputations in the control group, healing in these patients was significantly better than those patients who had MRSA isolated from their amputation wounds. Furthermore, delayed healing was more likely in those patients in the MRSA group.

The choice of above knee amputation for this group of patients probably represents their general frailty. We have previously shown that this group of patients are particularly likely to sustain MRSA infection.[4]

Antibiotic prophylaxis for patients undergoing major amputation has been mainly directed towards preventing gas gangrene using metronidazole or penicillin.[11] This policy should clearly be reassessed. Use of an antibiotic such as vancomycin or teicoplanin can probably be justified in view of the data provided in this study.

References

1 Reacher M, Shah A *et al.* Bacteraemia and antibiotic resistance of its pathogens reported in England and Wales between 1990 and 1998: trend analysis. *BMJ* 2000; **320**: 213–216.
2 Cookson BD. Is it time to stop searching for MRSA? Screening is still important. *BMJ* 1997; **314**: 664–666.
3 Menon KV, Whiteley MS, Burden P, Galland RB. *Surgical patients with methicillin resistant Staphyloccocus aureus*: an analysis of outcome using P-POSSUM. *J Coll Surg Edin* 1999; **44**: 161–163.
4 Pitt HA, Postier RG, MacGowan WAL *et al.* Prophylactic antibiotics in vascular surgery. Topical, systemic or both? *Ann Surg* 1980; **192**: 356–364.
5 Chamberlain J. Sepsis. *Clinical problems in vascular surgery.*

Chapter 9, pp. 71–78. Ed. Galland RB, Clyne CAC; Edward Arnold 1994.
6 Naylor AR, Hayes PD, Darke S. A prospective audit of complex wound and graft infections in Great Britain and Ireland: the emergence of MRSA. *Eur J Vasc Endovasc Surg* 2001; **21**: 289–294.
7 Panlilo AL, Culver DH, Gaynes RP *et al*. Methicillin-resistant *Staphylococcus aureus* in U.S. hospitals 1975–1991. *Infect Control Hosp Epidemiol* 1992; **13**: 582–586.
8 Nasim A, Thompson MM, Naylor AR, Bell PRF, London NJM. Methicillin-resistant *Staphylococcus aureus* infection in vascular patients. *BR J Surg* 2000; **87**: 505–506.
9 Callum KG. Amputations. *Clinical problems in vascular surgery*. Chapter 10, pp. 79–88. Ed. Galland RB, Clyne CAC; Edward Arnold 1994.
10 Murphy GJ, Pararajasingam R, Nasim A, Dennis MH, Sayers RD. Methicillin-resistant *Staphylococcus aureus* infection in vascular patients. *Ann R Coll Surg Engl* 2001; **83**: 158–163.
11 Galland RB. Prevention of infection: Systemic antibiotics. *Infection and the surgical patient*. Chapter 56, pp. 72–90. Ed. Polk HC; Churchill Livingstone 1982.

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