Objective. To compare wound infection, revision rates and hospital stay after major lower limb amputation between patients receiving 24 hours versus 5 days of prophylactic antibiotics.

Methods. The outcomes of a consecutive series of 40 major lower limb amputations in patients receiving a short 24-hour course of combined prophylactic antibiotics (flucloxacillin/vancomycin + gentamicin/ciproxin + metronidazole) were retrospectively analysed. Following this a further consecutive group of 40 major lower limb amputations were studied prospectively following the institution of a 5-day combined regime using the same antibiotics.

Results. The 2 groups of patients were similar in terms of demographics, vascular risk factors and level of amputation. The 5-day antibiotic regime led to a significant reduction in wound infection rates (5% vs. 22.5%, P = 0.023) and a reduced length of hospital stay (22 vs. 34 days, P = 0.001). Revision rates were lower (2.5% vs. 10%) but did not reach statistical significance (P = 0.36). More patients in the prospective 5-day antibiotic series were operated on by the vascular trainee. (77.5% vs. 55% P = 0.033).

Conclusions. This data supports the use of a prolonged 5-day course of combined antibiotics after major lower limb amputation. This appears to reduce stump infection rates leading to shorter in-hospital stay.

Keywords: Antibiotic prophylaxis; Wound infection; Surgical site infection; Amputation.
postoperative doses 8-hourly. The regime was as follows: flucloxacillin 1 g or vancomycin 1 g for gram-positive cover. Vancomycin was used for penicillin allergic patients and where MRSA was present or suspected clinically. Gentamicin 120 mgs or ciprofloxacin 200 mgs were prescribed for gram-negative cover. Ciprofloxacin was used instead of gentamicin when there were concerns about renal function. Metronidazole 500 mgs was used for anaerobic cover. All were given intravenously.

Following this audit, a change to the antibiotic protocol was introduced with an intentional 5-day course of the same antibiotic regime given at standard intervals. Oral therapy was used as soon as appropriate beyond the first 24 hours. The outcome of a second consecutive series of below and above knee amputations was prospectively evaluated between January 1st 2005 and April 1st 2006. Wounds were inspected daily from day 5 post amputation until discharge. Infection was defined as the presence of a purulent discharge, or cellulitis with positive wound cultures. The data collection was done according to a preset protocol similar to the one used for retrospective cohort.

**Statistical analysis**

Continuous variables were summarised as medians with interquartile ranges and comparisons were made using the Mann-Whitney rank sum test. Associations between categorical variables were tested with the Chi-square test, or Fisher’s exact if the expected frequency of at least 1 cell was found to be less than 5.

**Results**

38 patients underwent 40 major limb amputations in each 15 month audited period (2 bilateral amputees in each series, 39 being vascular amputations and one for chronic pain and atrophic muscles). The patient demographics and major vascular risk factors are shown in Table 1. The age and gender distribution was similar in both groups as was the incidence of diabetes and hypertension. There were significantly more current smokers (79% vs. 39.5%) in the 5-day antibiotic cohort. There was no significant difference in ASA status. Exactly half the amputations in the 3 dose antibiotic group were above the knee (AKA: BKA ratio 20: 20). There was an almost identical ratio of AKA: BKA in the 5-day antibiotic group (19: 21).

Seven patients (17%) in the 3-dose antibiotic group were given antibiotics that differed from the recommended regime. These were all patients operated on as emergencies out of hours who received a cephalosporin for gram positive and negative cover rather than flucloxacillin and gentamicin. In the prospective 5-day antibiotic cohort, all patients were treated within the recommended regime.

**Fig. 1** shows the wound infection rates in the two cohorts. Patients receiving 5 days of antibiotic cover had significantly lower wound infection rates (5% vs. 22.5%, \( P = 0.02 \)). This was associated with a lower rate of stump revision procedures (2.5% vs. 10%) but due to the small numbers this did not reach statistical significance (\( P = 0.36 \)). Three patients had cellulitis and 6 had a wound discharge with positive cultures in the 3 dose antibiotic cohort. In the 5 day antibiotic cohort 2 patients had both cellulitis and a wound discharge with positive wound cultures. Patients undergoing below knee amputations had a higher incidence of infection in the

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**Table 1. Demographics of the two groups of patients**

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>3 dose antibiotics (( n = 38 )) n (%)</th>
<th>5 day antibiotics (( n = 38 )) n (%)</th>
<th>p.value</th>
<th>Mann-Whitney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>74 (63–83)</td>
<td>75 (63–79)</td>
<td>0.655</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (68.4)</td>
<td>28 (73.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12 (31.6)</td>
<td>10 (26.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15 (39.5)</td>
<td>20 (52.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>23 (60.5)</td>
<td>18 (47.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15 (39.5)</td>
<td>30 (79.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>23 (60.5)</td>
<td>8 (21.0)</td>
<td></td>
<td>&lt;0.001</td>
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<td>Hypertension</td>
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<tr>
<td>Yes</td>
<td>22 (57.9)</td>
<td>23 (60.5)</td>
<td></td>
<td>0.815</td>
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<tr>
<td>No</td>
<td>16 (42.1)</td>
<td>15 (39.5)</td>
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<td>ASA grade</td>
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<td>1</td>
<td>2 (5.0)</td>
<td>0 (0.0)</td>
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<td></td>
</tr>
<tr>
<td>2</td>
<td>4 (11.0)</td>
<td>1 (2.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>17 (45.0)</td>
<td>31 (82)</td>
<td>Chi-square for trend</td>
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</tr>
<tr>
<td>4</td>
<td>15 (39.0)</td>
<td>6 (16.0)</td>
<td>0.603</td>
<td></td>
</tr>
</tbody>
</table>

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retrospective cohort (5 BKA vs. 4 AKA) but this did not reach statistical significance. The incidence of MRSA infection was 4 (10%) in the 3 dose antibiotic group and 0 (0%) in the 5-day group.

The seniority of the operating surgeon did not appear to influence the stump infection or revision rates. Patients in the 5-day antibiotic group were in fact more likely to be operated on by the Surgical Trainee (year 5/6 surgical residents) than in the 3-dose group (77.5% vs. 55%). The total in-hospital length of stay is shown in Fig. 2. There was a significant reduction in length of stay in the 5-day antibiotic group (22 vs. 34 days, \( P = 0.001 \)). There were 5 in-hospital deaths (12.5%) for the 3-dose antibiotic group and 1 (2.5%) for the 5-day antibiotic group. All deaths were due to myocardial infarction. Mortality was linked to ASA status, 3 of 5 deaths in the 3 dose antibiotic cohort were ASA 4, the single mortality in the 5 day antibiotic cohort was ASA 4. This difference did not reach statistical significance (\( P = 0.2 \), Fisher’s exact test).

Although there were 7 patients in the retrospective 3-dose group who received cephalosporins outside of the recommended regime, only 1 of these patients (14%) developed a wound infection. There was concern about the risk of acquiring *clostridium difficile* infection with the 5-day course of antibiotics. Three patients (7.5%) developed diarrhoea positive for *C. difficile* toxin in this group. The incidence of C.Difficile infection in the retrospective 3-dose group was not recorded.

**Discussion**

The first cohort of 40 amputees in this study had a “standard” antibiotic prophylactic regime with a dose given at the time of surgery and 2 postoperative doses eight hours apart. This protocol however was associated with a high stump infection rate of 22.5%. Anecdotal reports of longer courses of antibiotics reducing infection rates led us to consider introducing a 5 day prophylactic regime.\(^{10}\) Hall and colleagues prospectively randomised 302 patients undergoing vascular reconstructive procedures to a single dose antibiotic regime or a multi-dose regime. The latter was maintained until all lines were removed, a mean of 3 days with a maximum set at 5 days. The multidose group had a lower wound infection rate of 10% vs. 18% \( P = 0.04 \). Earnshaw et al. in a previous, though smaller, study had failed to find any benefit of a longer 5-day course of antibiotics.\(^{5}\) Neither of these studies included amputees. Very few studies have looked specifically at the role of antibiotics in major lower limb amputation. Huizinga and colleagues reported a large reduction in stump infection rates from 77% to 13% with the use of broad spectrum agents rather than penicillin alone.\(^{1}\) The wide range of organisms cultured pre and post amputation in the study of amputees by Berridge et al.\(^{4}\) confirm the need for a broad spectrum of cover by antibiotics. No strong data exists however on the optimum duration of antibiotic administration for amputees.

Despite the fact that longer courses of prophylactic antibiotics are usually not recommended, there is evidence that they are often used especially in cardiovascular surgery.\(^{11}\) We therefore adopted a longer course of prophylaxis and audited the effect on stump infection rates prospectively in a similar group of amputees. No other aspect of routine management was altered. The result was a significant reduction in stump infection rates associated with a reduced overall hospital stay. The impact on hospital stay was a surprising finding since stump healing alone often does not keep patients in hospital. Home adjustments and rehabilitation issues often have a more direct bearing on discharge planning. These may have been delayed in patients with infected stumps leading to slower discharge.

There were amputees in the first cohort who received antibiotics outside of the recommended regime. This highlights the uncontrolled nature of such a retrospective study. However, this subgroup of patients did not result in a large number of infections and therefore did not influence significantly the high overall infection rate. The prospective cohort of patients proved to be well matched in terms of age, gender and major vascular co-morbidities other than higher incident of smoking in this group, which may be an incidental finding. These other factors cannot therefore explain the major reduction in wound infection rate found in this study.

Advocating a 5-day regime of antibiotics for lower limb amputations is controversial. The findings of this

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**Fig. 2.** Scatter plot showing the spread of the hospital stay between the two patient groups.

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study clearly require confirmation in further studies. Ideally a randomised trial would provide more definitive data. Organisation of a multi centred trial was considered after the first audit of stump infection rates. The logistics of this proved to be a major hurdle and a re-audit using a 5 day antibiotic regime within the same single centre was therefore undertaken. The delay between the two audits was largely due to the time spent working on a possible multi centred trial. Other aspects of amputation stump sepsis that require further study, are the rates of pre-existing stump colonisation with bacteria, an extension of the previous work by Berridge and colleagues. Can other techniques such as stump lavage, help in contaminated stumps? Could longer courses of antibiotics be targeted only at amputees with positive intra-operative stump cultures?

Concerns about the development of antimicrobial resistance and Clostridium difficile infections favour shorter regimes of prophylaxis. Clearly there is an important balance to strike with major lower limb amputations between the need to minimise stump infection rates, which are often high, and the detrimental effects of excessive antibiotic usage. However, the significant reduction in wound infection rates in this study cannot be ignored. There may well be a place for targeted more intense antibiotic regimes in major limb amputation, guided by wound culture. Further research into the effect of such an approach is required.

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Conflict of interest

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References


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