

Epidemiology and Management of Surgical Upper Limb Infections in Patients with End-stage Renal Failure

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Abstract

Introduction: Hand infections in patients with end-stage renal failure (ESRF) are more difficult to treat and have had the worse outcomes. This paper examines the epidemiology, bacteriology and outcomes of surgically managed upper limb infections in these vulnerable patients. **Materials and Methods:** All patients from a single centre with surgically-managed upper limb infections between 2001 and 2007 were reviewed. We collected epidemiological data on demographics, type and site of infection, bacteriology, surgical treatment, complications and mortality. **Results:** Forty-seven out of 803 (6%) patients with surgically managed upper limb infections in the study period had ESRF. The average age was 59 years. ESRF was secondary to diabetes in 88% of cases. Patients presented on average 7 days after onset of symptoms. Abscesses (34%), wet gangrene (26%) and osteomyelitis (11%) were the commonest infections. *Methicillin-resistant Staphylococcus aureus* (MRSA) was the commonest pathogen (29%), occurring either in isolation or with other organisms. Eighteen percent of single organisms cultured were gram-negative. Multiple organisms occurred in 29%. A median of 2 operations were required. Thirty-six percent of all cases required amputation. Twenty-five percent of patients had a life-threatening event (myocardial infarction or septic shock) during treatment. **Conclusions:** ESRF patients present late with severe upper limb infections. Nosocomial infections are common. Initial empirical antibiotic treatment should cover MRSA and gram-negative bacteria. Immediate referral to a hand surgery unit is recommended. Multi-disciplinary management of the patient with input from physicians and anaesthetists or intensivists in the perioperative period is necessary to optimise the patient for surgery and to manage active medical comorbidities and complications after surgery.

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Introduction

Hand infections are common in the general population, and their management is usually uncomplicated. Several papers have noted that patients with diabetes mellitus have more severe infections, a different spectrum of bacteriology and a worse outcome.¹⁻⁶ In our experience, of all patients with upper limb infections, those with end-stage renal failure (ESRF) have been the most difficult to treat and have had the worst outcome. In addition to their immunocompromised status, many of these patients have multiple concomitant medical problems including diabetes mellitus, ischaemic heart disease and vasculopathy that complicate their management. They tend to present late and with more severe infections. Healing tends to be slower in

these patients. To the best of our knowledge, there is almost no information in the current literature on the epidemiology and management of hand and upper limb infections in this group of patients.

This retrospective epidemiological study analyses the bacteriology, patterns and sites of infection, complications and outcome of surgically-managed hand infections in individuals with ESRF managed in a large tertiary referral centre for both renal disorders and hand surgery in Singapore.

Materials and Methods

Medical records of all patients with surgically-managed upper limb infections between 2001 and 2007 and who

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also had ESRF, were reviewed, retrospectively. ESRF was defined as a chronic glomerular filtration rate (GFR) of less than 15 ml/min per 1.73m² or creatinine clearance <15 ml/min.⁷ Patients with renal failure of less than 3 months' duration, creatinine clearance $\geq$ 15 ml/min, or acute or chronic renal impairment were excluded. We collected epidemiological data on patient demographics, type and site of infection, bacteriology, surgical treatment, complications, mortality and outcome. All data collected were charted in the patients' medical records. All conditions documented under the patients' "Past Medical History" were considered comorbidities for the purpose of this study, and no further attempt was made to define or assess the severity of these conditions.

Results

Demographics

Of 803 patients with surgically managed hand or upper limb infections during the study period, 47 (6%) had end-stage renal failure. Twenty-seven (57%) patients were on haemodialysis, 12 (26%) were on continuous peritoneal dialysis and 8 (17%) were awaiting renal replacement therapy. Table 1 summarises their demographics. Diabetes mellitus was the commonest comorbidity, occurring in 42 patients (89%), and was the cause of renal failure in 41 patients (88%).

Table 1. Demographics

Total number of patients	47
Males	23
Females	22
Average age	59 years (range, 36 to 85)
Cause of ESRF	
Diabetes mellitus	41 (88%)
Hypertension	2 (4%)
Glomerulonephritis	1 (2%)
Unknown	3 (6%)
Significant Comorbidities	
Diabetes mellitus	42 (89%)
Hypertension	33 (70%)
Peripheral vascular disease	26 (55%)
Ischaemic heart disease	23 (49%)
Previous lower limb amputation	16 (34%)
Previous surgically treated soft tissue infections	12 (25%)
Cerebrovascular accidents	10 (21%)
Gout	4 (9%)

Serum sodium level was 134 mmol/L (range, 125 to 143), potassium was 4.33 mmol/L (range, 3 to 6.1), average creatinine level was 592 μ mol/L (range, 339 to 1370) and urea was 19.1 mmol/L (range, 7.1 to 42.4). Patients with concomitant diabetes always had greatly elevated blood glucose levels on admission, with an average of 15.4 mmol/L and ranging from 12.8 to >29 mmol/L (unrecordable). The average haemoglobin level was 98.94 g/L on presentation (range, 31.0 to 135.0). White blood cell count (WBC) was $12.70 \times 10^3/\mu$ l (range, 4.18 to $28.23 \times 10^3/\mu$ l), C-reactive protein was 135.51 mg/L (range, 3.2 to 408) and erythrocyte sedimentation rate (ESR) was 86.75 mm/hr (range, 1 to 140). HbA1c and albumin levels were only occasionally obtained, and these are not reported here.

Characteristics of Hand and Upper Limb Infections

Table 2 lists the types and etiology of infections encountered. In those patients with an arteriovenous fistula in the upper limb, the infection usually occurred in the opposite limb except when it was a complication of limb

Table 2. Characteristics of Hand and Upper Limb Infections

Location of Infection	
Localised to digits	23 (49%)
Involving the hand	17 (36%)
Proximal to hand (wrist/forearm)	7 (17%)
Etiology	
Unknown	19 (40%)
Nosocomial (intravenous site infections and extravasation)	12 (26%)
Ischaemic gangrene from steal syndrome (distal to arteriovenous fistula)	7 (15%)
Ischaemic gangrene in limb without fistula	3 (6%)
Minor trauma	6 (13%)
Infection	
Subcutaneous abscess	16 (34%)
Wet gangrene	12 (25%)
Osteomyelitis	5 (11%)
Necrotizing fasciitis or myositis	4 (9%)
Suppurative tenosynovitis	4 (9%)
Septic arthritis	2 (4%)
Cellulitis	2 (4%)
Infected open wound	1 (2%)

ischaemia from a steal syndrome. Most infections had no definite cause, but many were nosocomial. There was an average delay of 6.6 days (range, 1 to 60) from the onset of symptoms to the time patients sought treatment or were referred for their infection. Twenty-five patients (53%) were afebrile (body temperature $<37.5^{\circ}\text{C}$) on presentation.

Bacteriology

Blood cultures were not routinely obtained, but aerobic and anaerobic tissue cultures were obtained from all patients during drainage and debridement of the infection. The first dose of intravenous antibiotics had usually been given by this time. The bacteriology is shown in Table 3. The single most common organism was *Methicillin-resistant Staphylococcus aureus* (MRSA). This was present in 28% of tissue cultures. It occurred in isolation in 18% of tissue cultures, and together with gram-negative organisms in 11%. Gram-negative organisms were present in 47% of tissue cultures, including almost a third of single organism cultures and all mixed cultures. Multi-sensitive *Staphylococcus aureus* and *Streptococci* were present in only 18% of cultures. Anaerobic bacteria (*Bacteroides fragilis*) were present in only one tissue culture.

Table 3. Bacteriology

Blood Cultures (n = 30)	
No growth	21 (70%)
<i>Methicillin-resistant Staphylococcus aureus</i> (MRSA)	3 (10%)
<i>Staphylococcus aureus</i>	3 (10%)
<i>Coagulase-negative Staphylococcus</i>	1 (3%)
<i>Klebsiella pneumoniae</i>	1 (3%)
Mixed growth	1 (3%)
Tissue cultures (n = 45)	
Single pathogen	26 (58%)
MRSA	8
Gram-negative bacteria (<i>Pseudomonas aeruginosa</i> 2, others 1 each)	8
Gram-positive bacteria (<i>S. aureus</i> 5, <i>Streptococci</i> 2, <i>Enterococcus</i> 1)	8
<i>Candida</i>	1
<i>Clostridium perfringens</i>	1
Multiple pathogens	13 (29%)
Gram-negative bacteria (<i>P. aeruginosa</i> 3, <i>Aeromonas</i> 1, <i>Acinetobacter</i> 1, others 10)	13
MRSA	5
Gram-positive bacteria (<i>Enterococcus</i> 2, <i>S. Aureus</i> 1, <i>Bacillus</i> 1)	4
<i>Candida</i>	2
No growth	6 (13%)

Management and Outcome

In all cases, broad spectrum empirical intravenous antibiotic therapy was initiated upon diagnosing the infection, as there was usually an unpredictable delay in getting the patient into the operating room for debridement. Antibiotics were later changed as necessary, based on the tissue cultures. Intravenous antibiotics were used until there were clear signs of the infection reversing, then converted to oral antibiotics for a further 2 weeks for soft tissue infection, and 6 weeks for bone or joint infection.

All patients in this series required urgent surgery and had a median of 2 procedures (range, 1 to 4) before the infection settled. The initial procedure was drainage and excisional debridement for 30 patients (64%), amputation for 14 (30%), arthrotomy for 2, and revision of an infected humeral amputation stump in one patient. A total of 17 patients (36%), all of whom had concomitant diabetes mellitus, required an amputation. This was done either as the initial procedure or subsequent to debridement. Of these, 10 were ray amputations, 3 were through the interphalangeal joints, 2 were below the elbow, and 1 through the elbow. These last 3 were for ascending necrotizing fasciitis, not responding to antibiotics and fasciectomy.

Wounds were sutured immediately in 7 patients (6 following amputation, and one following complete excision of a small subcutaneous abscess). Thirty-two patients had delayed closure by suture (27 patients) or skin graft (5 patients) an average of 14 days after the initial surgery. Eight patients were unfit for further surgery, and left to heal by secondary intention.

Twelve patients (25%) experienced life-threatening events while being treated for their upper limb infection. Seven suffered from myocardial infarction and 5 had septic shock, of whom 3 had disseminated intra-vascular coagulopathy and 2 required inotropic support in the intensive care unit. All patients survived and were discharged home or back to the care of the referring physician. Sixteen patients (34%) subsequently died within 5 years of the episode of hand infection, 11 (23%) of them within a year. These deaths were all unrelated to the hand infection, but due to some other complication of their medical comorbidities.

Discussion

There were 3401 patients on dialysis in Singapore by December 2004.⁸ The incidence and prevalence of ESRF in Singapore has been rising over the last 2 decades and is expected to continue rising.^{8,9} We have seen the vast majority of hand infections in Singapore and our institution is the largest tertiary referral centre for both renal disorders and hand surgery in Singapore. Between 2001 and 2007, 47 patients (roughly 7 patients per year) with ESRF were admitted and underwent surgery for various hand and upper

limb infections. This represents 6% of all hand infection cases admitted under our unit in this same period. This study provides some valuable insights into the nature and outcome of surgical hand infections in this increasing population of immunocompromised and debilitated patients. A major weakness of this study is that it is retrospective. There is also a lack of data on some parameters that could potentially contribute to the severity of infections and the outcome of management. These include the nutritional status, socioeconomic status, smoking, duration of dialysis in those patients that were undergoing dialysis, serum albumin levels and HbA1c. Despite these omissions, we believe the data will help guide future management of these patients, as virtually no other data on hand infections in ESRF patients is currently published.

Well over one-third of our cases were nosocomial, being referrals for intravenous site infections or complications of limb ischaemia from arterial steal syndrome due to an arteriovenous fistula. Interestingly, patients on haemodialysis without limb ischaemia tend to have infections in the limb without the fistula, a phenomenon we dub the “contralateral limb syndrome”. This may be because they are constantly aware of the limb with the fistula and are trained to take care of it. The other limb is therefore more exposed to trauma in daily activities, and any intravenous access or venepuncture by default goes into that limb.

Patients with end-stage renal failure tend to be older than those with hand infections in the general population. They also have multiple medical comorbidities, most commonly diabetes mellitus, peripheral vascular disease and ischaemic heart disease, which increase their risk of infection, complicate surgical management and impede recovery. Eighty-eight percent of patients with ESRF had concomitant diabetes mellitus, almost twice the prevalence of diabetes mellitus in ESRF patients in general. Diabetes mellitus is a well-documented risk factor for severe hand infections with poor outcome in the general population.¹⁻⁶ In this series, all patients who had amputations also had diabetes mellitus. Our impression is that the combination of ESRF and diabetes mellitus probably is a worse prognostic indicator than either condition alone, although we were unable to test this statistically in this study.

Patients with ESRF tend to present late, on average almost a week after the onset of their symptoms, and with advanced infections. This finding is similar to that of Gill et al⁶ in patients with tropical diabetic hand syndrome. The reasons for this may include a cultural preference for traditional remedies, and peripheral neuropathy rendering the hand relatively painless until the infection is far progressed. Half of these patients had no fever on presentation, and the white blood count was normal or only mildly elevated in most cases. However, C-reactive protein and erythrocyte

sedimentation rate were frequently elevated.

Although subcutaneous abscesses were the commonest form of infection (34% of cases) in our series, this was in a lower proportion compared to published figures for a diabetic population (42%)¹ and a mixed population (45%).⁸ Wet gangrene was the second most common presentation, followed by osteomyelitis, then by equal numbers of necrotizing fasciitis or myositis and suppurative tenosynovitis. Two cases of “cellulitis” operated on were in fact suspected early necrotizing fasciitis, and progression may have been aborted by the surgical decompression and debridement. Digit and limb threatening infections are therefore more common than in the general population. Early referral to a specialist hand surgery unit is recommended for all hand infections arising in this population.

The single most common organism was MRSA, which grew in almost a third of cases. Gram-negative organisms were present in almost half the cases, mainly as part of a mixed growth. This differs greatly from the general population, where isolated growths of *Staphylococcus aureus* or *Streptococci* are the most common,¹⁰ and is similar to the diabetic population, where a mixed growth with gram-negative organisms predominates.^{1,2} The high incidence of MRSA in our series parallels the high incidence of nosocomial infection. Based on these findings, we would recommend Vancomycin in combination with ciprofloxacin to cover both MRSA and gram-negative organisms including pseudomonas for all inpatient referrals. Amoxicillin/clavulanate is an appropriate choice for community-acquired infection, and covers the same spectrum as multiple antibiotic therapy using penicillin, cloxacillin and gentamicin. The latter may increase the risk of intravenous site infection from more frequent handling in a patient already susceptible to this complication.

Our protocol for treating suppurative infections of the hand and upper limb involves aggressive and complete surgical debridement of all tissues of questionable viability; using antibiotics, rest and elevation as an adjunct. Most patients required 2 or more debridements, and about a third required amputation. In most cases, the wound was only ready for closure on average 14 days after the initial operation, while in 8 cases, closure or reconstruction was not possible due to poor patient or wound conditions. Our amputation rate (36%) is much lower than in published series for diabetic hand infections, where the rate ranges from 78% to 100%.^{5,10} For cultural reasons, there is a very high resistance to upper limb amputation in our population, despite the risks of multiple procedures and a poorly healing wound. We have therefore been radical in debridement, but conservative in amputation.

There was a high incidence of life-threatening events in our series. One in 4 patients in this cohort endured such an

event, but survived. This compares to Gonzalez et al¹ who had 2 mortalities from sepsis in their subgroup of 8 patients with diabetes and end-stage renal failure. In contrast, no life-threatening complications developed in the other 37 diabetic patients in their study, and none were seen in a separate survey of a general population.⁸ A multi-disciplinary team comprising the surgeon, renal and other physicians and an anaesthetist/intensivist should be involved immediately to optimise patient care in the perioperative period.

Finally, despite adequate treatment and resolution of their upper limb infections, up to one-third of these patients die of unrelated causes within 5 years, and a quarter within a year. These are conservative figures, as they only reflect deaths recorded in our hospital. More may have died elsewhere. A severe hand infection may therefore be a potential harbinger of mortality in patients with ESRF, much as a neck of femur fracture is in the elderly. This study does not look into this aspect, and further analysis is needed to confirm this hypothesis.

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