High mortality after pelvis and lower limb fractures in ESRD

Sir,
The high mortality rate associated with hip fracture in the general population, as well as in the end-stage renal disease (ESRD) population, is well described. However, the mortality associated with pelvis and lower limb fractures in ESRD patients remains unknown.

We reviewed the medical records of all chronic haemodialysis or peritoneal dialysis patients hospitalized at Maisonneuve-Rosemont Hospital for a fracture from 1 July 1995 to 1 February 2007. Femoral neck, pelvis, femoral condyle, tibial plateau, patella, tibia and malleolus fractures were considered. Femoral neck and pelvis fractures were analysed separately, while the other fractures were analysed together as lower limb fractures. All patients who died during the study period were identified and mortality rates were calculated.

During the 127-month-long study period, 60 dialysis patients were hospitalized for a total of 68 fractures. Seven patients had two fracture episodes, and one patient had three fracture episodes. The three most common fracture sites were hip (40 cases), pelvis (13 cases) and malleolus (8 cases) (Table 1). The 1-year mortality rate after a hip fracture was 42.5% (17 patients), with an in-hospital mortality rate of 20%. Two patients died during their hospitalization for a pelvis or lower limb fracture. One-year mortality rates were 30.8% after a pelvis fracture and 20% after a lower limb fracture. Median survival during the observation period was 427 days after a pelvis fracture and 581 days after a lower limb fracture.

Hip fracture is associated with a 1-year mortality rate of 24% in the general population [1]. In ESRD, the 1-year mortality rate after a hip fracture approximates 50% [2]. Our results are consistent with previously reported mortality rates.

Few studies have described the mortality associated with pelvis or lower limb fractures in the general population. In a British study, the 1-year mortality rates were 8.7% after pelvis fracture and 2.4% after a lower limb fracture [3]. In our ESRD cohort, the 1-year mortality rates for pelvis and lower limb fractures were increased 3.5- and 8.3-fold, respectively. In fact, the impact of pelvis and lower limb fractures on mortality in ESRD patients appears very similar to the impact of hip fracture in the general population. Like hip fractures [4,5], pelvis and lower limb fractures are probably markers of poor nutritional and general health status in this population.

With a 1-year mortality rate similar to that of hip fracture in the general population, our data delineate for the first time the poor outcomes associated with pelvis and lower limb fractures in ESRD patients. The incidence, risk factors, clinical and functional outcomes of such fractures in ESRD patients need to be evaluated in larger, registry-based studies.

Conflict of interest statement. None declared.

Table 1. One-year mortality by fracture type

| Fracture sites | Number of fractures | One-year mortality (%) |
|----------------|---------------------|------------------------|
| Hip            | 40                  | 17 (42.5%)             |
| Pelvis         | 13                  | 4 (30.8%)              |
| Malleolus      | 8                   | 0 (0%)                 |
| Femoral condyle| 2                   | 1 (50.0%)              |
| Tibial plateau | 2                   | 0 (0%)                 |
| Tibia          | 2                   | 2 (100.0%)             |
| Patella        | 1                   | 0 (0%)                 |

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doi: 10.1093/ndtplus/sfn135

Advance Access publication 23 August 2008

Mycophenolate mofetil as a possible therapeutic option for idiopathic membranoproliferative glomerulonephritis

Sir,
A 20-year-old Caucasian woman with no significant past medical history was referred to the nephrology clinic for new-onset edema of the lower extremities and four positive proteinuria on dipstick. Her serum creatinine was 2.7 mg/dl with an estimated glomerular filtration rate (eGFR) of 24 ml/min/1.73 m². The 24-h urine protein was measured at 18.8 g. A thorough biologic and immunologic work-up was negative. The renal biopsy revealed type III membranoproliferative glomerulonephritis (MPGN). The patient was started on high dose intravenous methylprednisolone (500 mg/day for 3 days) followed by oral methylprednisolone (16 mg/day) and mycophenolate mofetil (MMF) (500 mg twice a day). Six weeks later, serum creatinine improved to 1.7 mg/dl and proteinuria decreased to 5.5 g/24 h. The MMF dose was subsequently increased to 500 mg three times a day. At 6 months, her
Table 1. Summary of studies on the role of MMF in the treatment of MPGN

| Study               | Number of patients | Steroid therapy | Pre-MMF creatinine clearance (ml/min) | Pre-MMF proteinuria (g/24 h) | Post-MMF creatinine clearance (ml/min) | Post-MMF proteinuria (g/24 h) | Comment |
|---------------------|--------------------|-----------------|--------------------------------------|----------------------------|---------------------------------------|----------------------------|---------|
| Jones et al. [1]    | 5                  | +               | 105.3                                | 5.08                       | 1.96                                  |                            | Significant reduction in proteinuria over 18 months (creatinine clearance significantly reduced in the control group while no change in proteinuria) |
| Levin [3]           | 1                  | +               | 56                                   | <0.1                       | 98–106                                | 16                         | Excellent response at 12 months both for creatinine clearance and for proteinuria |
| Segarra et al. [4]  | 15                 | –               | 54.5                                 | 6.05                       | 52.3                                  | 3.1                        | Although mean proteinuria for the ‘whole group’ significantly decreased at 12 months, it had remained unchanged in 53% of the patients |
| Choi et al. [5]     | 1                  | −               | 31e                                  | 3.9f                       | 31e                                   | 4.9f                       | Serum creatinine initially decreased but returned to baseline after reduction in MMF dose |
| Present case        | 1                  | +               | 24                                   | <3                         | 50                                    | 18.8                       | At 24 months, improvement in creatinine clearance and major reduction in proteinuria |

*MMF: mycophenolate mofetil.

MPGN: membranoproliferative glomerulonephritis.

For the studies including more than one patient, this number reflects the ‘mean’ creatinine clearance.

For the studies including more than one patient, this number reflects the ‘mean’ proteinuria.

The study does not mention creatinine clearance. The current creatinine clearance has been calculated according to the MDRD formula based on the information provided in the paper.

This number reflects the random urine protein/urine creatinine ratio.

serum creatinine continued to improve to 1.4 mg/dl with a proteinuria of 2.8 g/24 h. She has continued this regimen associated with an angiotensin converting enzyme inhibitor for the past 24 months with no major complications while her kidney function remains stable with an eGFR of 50 ml/min/1.73 m² and a proteinuria persistently <3 g/24 h.

Idiopathic MPGN (IMPGN) is a rare disorder and accounts for only 6.4 to 7.3% of all primary glomerular diseases [1]. It is generally regarded as a progressive disease. Compared to secondary forms of MPGN, the renal outcome in these patients is usually poor, with a 10-year renal survival of 32–40% and only 5–7.6% of patients achieving at least partial remission [1]. Up to 50 to 60% of untreated patients will progress to end-stage renal disease within 10–15 years; spontaneous improvement occurs in <10% of cases [2].

While steroids have frequently been used for the treatment of IMPGN, it should be noted that studies evaluating the role of steroids have often been conducted in children; there has been no systematic evaluation of steroid therapy for IMPGN in adults. Indeed, retrospective studies have not shown any clear benefit from steroid therapy.

MMF is an antimetabolite agent with potent antiproliferative properties against T cells and B cells, as well as a number of non-lymphoid cell types. It has previously been used in a number of primary glomerular diseases (e.g. lupus nephritis) with promising results in reducing proteinuria. Recently, MMF has been introduced as a potential therapeutic option for MPGN. Some studies reported that proteinuria significantly diminished with therapy while no change was observed in untreated control patients [1]. Other reports have also suggested the benefit of treatment with MMF (Table 1). Our observations, coupled with previous reports, provide evidence that MMF may have a role in the treatment of IMPGN. Further randomized studies with adequate sample size and extended follow-up are clearly needed to confirm these observations and to evaluate the long-term safety of this management strategy.

Conflict of interest statement. The authors have no potential conflicts of interest to declare with respect to this paper. The results presented in this paper have not been published previously in whole or part, except in abstract format.

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High prevalence of *Chlamydia pneumoniae* infection in patients with myeloperoxidase antineutrophil cytoplasmic autoantibody (MPO-ANCA)-associated glomerulonephritis

Sir,

Exposure to *Chlamydia pneumoniae* (*Chlamydia pneu-moniae*, CP) is very common in the general population [1]. CP infection has been proposed as a risk factor of atherosclerosis as a chronic vascular inflammation [2], though current clinical data do not warrant the use of antibiotics for prevention or treatment of cardiovascular diseases [3]. Interestingly, it was recently reported that CP infection might be associated with myeloperoxidase antineutrophil cytoplasmic autoantibody-associated glomerulonephritis (MPO-ANCA-associated GN) [4], which is attributable to systemic vasculitis and subsequently carries an increased risk for end-stage renal disease (ESRD) and death. The pathogenesis of MPO-ANCA-associated GN is still unclear, and the association with CP infection has not been closely investigated in clinical settings yet. In this study, we examined cross sectionally a prevalence of CP infection in patients with MPO-ANCA-associated GN, compared with those with immunoglobulin A nephropathy (IgAN).

Thirty-three case patients with MPO-ANCA-associated GN (mean age 70.2 ± 12.0 years, mean MPO-ANCA 321 ± 240 U/ml) and 40 control patients with IgAN, who were of similar age to the MPO-ANCA-associated GN group (mean age 69.5 ± 4.9 years), were investigated. The levels of anti-CP IgM-, IgA-, IgG-antibodies were measured as markers of active, chronic persistent active and past inactive CP infection, respectively. Multivariable logistic regression models were used to assess the association of CP infection with MPO-ANCA-associated GN, adjusting for age, sex and estimated glomerular filtration rate (eGFR).

As a result, MPO-ANCA-associated GN patients had a higher prevalence of CP infection in each phase than IgAN patients, though the difference was statistically significant only for active CP infection (Table 1). This result was consistent with the previous report [4]. Multivariable analyses suggested that active CP infection was significantly associated with MPO-ANCA-associated GN (OR = 9.79, \( P = 0.001 \)), while insignificant were chronic persistent active infection (OR = 3.10, \( P = 0.11 \)), and past inactive CP infection (OR = 2.93, \( P = 0.11 \)).

In a separate analysis, the difference in renal prognosis (progression to ESRD) between MPO-ANCA-associated GN patients with and without CP infection was also examined, but MPO-ANCA-associated GN patients with CP infection in each infection phase were not statistically different in the renal outcome from those patients without CP infection. This study confirmed the high prevalence of active CP infection in patients with MPO-ANCA-associated GN, and active CP infection could potentially enhance the risk of MPO-ANCA-associated GN. However, the difference in renal prognosis between MPO-ANCA-associated GN patients with and without CP infection was not identified in the present study maybe due to the small sample size. Further analyses are required to examine closely whether CP infection is involved in the pathogenesis of MPO-ANCA-associated GN, and the evidence linking CP infection might lead to the benefit from antibiotic treatment to prevent or cure MPO-ANCA-associated GN by eradicating CP as a causative agent.

Conflict of interest statement. None declared.

Table 1. Prevalence of *Chlamydia pneumoniae*

|                      | MPO-ANCA-associated GN (\( n = 33 \)) | IgA nephropathy (\( n = 40 \)) | \( p \)-value |
|----------------------|--------------------------------------|-------------------------------|---------------|
| Age (years)          | 70.2 ± 12.0                         | 69.5 ± 4.9                    | 0.76          |
| Sex (male, %)        | 66.7                                | 52.5                          | 0.22          |
| eGFR (ml/min)        | 19.4 ± 14.7                         | 46.7 ± 24.0                   | <0.001*       |
| Seropositivity       |                                     |                               |               |
| CP IgM-antibody (%)  | 39.4                                | 7.5                           | 0.003*        |
| CP IgA-antibody (%)  | 72.7                                | 50.0                          | 0.06          |
| CP IgG-antibody (%)  | 66.7                                | 45.0                          | 0.07          |

\( ^* P < 0.05. \)

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doi: 10.1093/ndtplus/sfn102

doi: 10.1093/ndtplus/sfn155