Renal function in a narrow-age cohort of adults at 79 and 87 years

SIR—Renal function declines with age [1, 2], but data are limited in those aged over 80. The Italian Longitudinal Study on Ageing included nearly 3,000 participants at baseline and followed up just under 2,000 4 years later [2], but only a small proportion were aged over 80, whereas another Italian longitudinal study based in Chianti comprised 1,055 participants, 246 of whom were 80 years or older [3]. Many people aged over 80 have estimated glomerular filtration rates (eGFRs) less than 60 ml/min/1.73 m² and thus fulfill the criteria for chronic kidney disease (CKD) stage 3, but in just over one-third this does not progress, which has important implications for demand on specialist renal services [4]. Non-progression was associated with lower blood pressure, absence of proteinuria and lower cardiovascular disease burden [4]. The Cardiovascular Health Study followed up 4,380 participants of mean age 72 over 7 years and found that 16% suffered a rapid decline in renal function [5]. Decline in renal function is modifiable in older adults [6]; however, cardiovascular disease is highly prevalent in longitudinal ageing studies of renal function, even in those under 80 years [7], so more careful characterisation may be required to identify specific risk factors. Other risk factors for loss of renal function in older adults include advanced glycation endproducts [3], diabetes [2], lower haemoglobin [7], smoking [2] and elevated fibrinogen levels [2]. We followed up a narrow-age cohort of adults with well-characterised risk factors over 8 years through their ninth decade to evaluate eGFR decline and to identify key determinants.

Methods

Sample
The baseline sample and its renal function have been described previously [8]. Participants were all born in 1921 and on recruitment in response to letters generated from the Community Health Index, were all relatively healthy, community-resident and aged around 79. The study was conducted with permission from the local research ethics committee. All participants gave written informed consent and were living independently in the community; none was on renal replacement therapy. Surviving participants were invited for an almost identical follow-up assessment approximately 8 years later at the same clinical research facility where blood was again taken for creatinine measurement. Blood was taken at a time convenient to the participant without any prior dietary restrictions.

Measures
Baseline assessments are described in detail elsewhere [9, 10], but included childhood IQ, sociodemographic, health and physical examination variables together with a range of blood tests that included haemoglobin, glycated haemoglobin, fibrinogen and creatinine. eGFR was calculated from creatinine values using the modification of diet in renal disease formula as at baseline. Electrocardiograms were scored and principal components extracted relating to ischaemic changes and left ventricular hypertrophy [11].

Statistical analysis
Distributions of eGFR at 79 and 87 years approximated to normal and parametric statistics were therefore used throughout. One value at age 87 fell beyond three standard deviations of the mean, but excluding this had a minimal effect on beta coefficients in the linear regression model. All analyses were performed with the SPSS 16.0 statistical package.

Results
Five hundred and twenty-nine participants had baseline creatinine measured at mean 79.1 (range 77.7–80.6) years, and of these, 185 attended for assessment 8 years later and had creatinine measured at mean 86.6 (range 85.7–87.4) years. Creatinine measures were used to calculate eGFR (Table 1). The 185 participants assessed at age 87 had a mean 11.3 (range 8–20) years of full-time education with mean 168 (sd 25) mmHg sitting and 164 (sd 26) mmHg standing systolic blood pressure with mean 83 (sd 13) mmHg sitting and 83 (sd 13) mmHg standing diastolic blood pressure. Only seven (3.8%) were current smokers. Participants who died in the intervening period had significantly lower baseline mean eGFR than those who survived (dead, n = 199, 67 ml/min, alive n = 329, eGFR 71 ml/min, P = 0.031, one participant’s outcome uncertain). For those participants assessed at both 79 and 87 years, mean eGFR fell significantly more (F = 6.14, P = 0.014) from 72 (sd 14) to 60 (sd 17) ml/min in men than in women where it fell from 69 (sd 13) to 63 (sd 18) ml/min. Moreover, at age 79 years, 19.8% had eGFR<60 ml/min rising to 49.7% by age 87 years; nevertheless, 24.3% had an eGFR higher at 87 years than at 79 years (Figure 1).

In a stepwise linear regression where baseline eGFR, sex and period between measurements were forced into the model, significant predictors of eGFR at age 87 were eGFR at age 79 (B = 0.76 ml/min, 95% confidence intervals 0.61, 0.92 ml/min higher for per mol/min at age 79, P < 0.001), sex (B = 5.3 ml/min, 95% confidence intervals 0.61, 9.2 ml/min higher for female at age 79).

Table 1. Mean (standard deviation) of eGFR at ages 79 and 87

<table>
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<tr>
<th></th>
<th>Men Estimated mean (sd)</th>
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<td>GFR at age 79 years (ml/min)</td>
<td>225</td>
<td>72 (16)</td>
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<tr>
<td>GFR at age 87 years (ml/min)</td>
<td>87</td>
<td>61 (17)</td>
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Renal function continues to decline into the ninth decade. This decline is greater in men than in women. It has important clinical implications because at 79 years only around one-fifth of the people have CKD stage 3, whereas by 87 years one-half meet the diagnostic criteria according to eGFR. Nevertheless, this decline is not all pervasive: about one-quarter had better renal function at 87 than at 79. Apart from being male, high systolic blood pressure is a key predictor of greater decline. Clinical trials may be able to clarify whether lowering blood pressure would reduce the number of people entering CKD stage 3 where regular monitoring of renal function is recommended [6]. Since there are useful interventions available to people for CKD even in advanced old age [6, 12] and many older people are prescribed drugs eliminated through the kidney, intermittent monitoring of renal function is worthwhile, even in those with eGFR $>$60 ml/min, particularly for men with elevated blood pressure.

Key points
- At 79 years, only around one-fifth of people have CKD stage 3, but by 87 years one-half meet diagnostic criteria.
- Decline in renal function is significantly greater in men and in people with higher systolic blood pressure.
- Intermittent monitoring of renal function is advisable in people over 80, especially for men and those with elevated blood pressure.
**Research letters**

Conflicts of interest

None declared.

**References**


**N-terminal probrain natriuretic peptide predicts 1-year mortality following acute stroke: possible evidence of occult cardiac dysfunction among patients with acute stroke**

**Background**

SIR—Brain natriuretic peptide (BNP) is a vasoactive peptide hormone synthesised in the cardiac atrium [1] and ventricular myocardium [2]. Increased levels of BNP are associated with various cardiovascular insults [3, 4]. In response to fluid overload, BNP is cleaved from its precursor proBNP resulting in the release of N-terminal (NT)-proBNP. NT-proBNP is an established diagnostic marker of sub-clinical heart failure [5] and predicts cardiovascular events and mortality among asymptomatic patients as well as in patients with coronary artery disease (CAD) [6] independent of conventional cardiovascular risk factors.

In view of the high mortality and morbidity associated with acute stroke, recent studies have focused on non-neurological variables that may affect stroke outcomes [7–9]. Plasma BNP has been shown to predict the risk of stroke and atrial fibrillation (AF) [10]. In the acute phase of stroke, plasma levels of natriuretic peptide have been reported to be elevated [11] and correlate with risks of mortality [12–14]. Conversely, another study has concluded that NT-proBNP concentrations did not confer additional prognostic advantage over conventional cardiovascular risk factors in acute stroke patients [15]. The aim of this study was to investigate the role of NT-proBNP in predicting 1-year mortality of acute stroke in relation to various cardiovascular and biochemical parameters.

**Patients and methods**

We recruited consecutive patients of all ages with an acute ischaemic or haemorrhagic stroke, who were able to provide an informed written consent with mild and moderate level of dependency pre-admission on modified Rankin Scale [16] of <5. All patients were treated with similar protocol and care pathways by the stroke team and underwent chest radiography, electrocardiography (ECG) and computed tomography of brain and were examined for clinical stroke severity using Scandinavian Stroke Scale (SSS) and Oxford Community Stroke Project (OCSP) classification. Echocardiogram was not routinely performed as this was not within the study protocol. Patients were assessed for cardiovascular disease: existing heart failure on standard clinical and radiography features, history of CAD, current AF based on ECG findings and use of antihypertensive drugs. Assessors were blinded for diagnosis of stroke and past medical history. Serum creatinine was measured at the same time as blood samples were taken for NT-proBNP, on the same day as the detailed clinical assessment was performed.