

## STABILISATION OF DECLINING GLOMERULAR FILTRATION RATE AFTER ARTERIOVENOUS FISTULA FORMATION – AN *IN SILICO* MODEL

**Introduction:** Recent observational work based on a retrospective cohort has led to the hypothesis that arteriovenous fistula (AVF) formation may stabilise a previously declining glomerular filtration rate (GFR). In one of 2015's most remarkable publications a number of potential physiological mechanisms were suggested to explain this observation. To explore the validity of this observation we performed an *in silico* experiment with a cohort of virtual patients.

**Methods:** A cohort of patients with mean ( $\pm$ sd) GFR of 60 ( $\pm$ 6.8) ml/min were enrolled and followed for 10 years. From the time of enrolment each patient had a mean ( $\pm$ sd) decline in GFR of 3.0 ( $\pm$ 3.5) ml/min/year, which was linear and constant throughout the follow-up period. They were offered GFR measurement four times per year, but randomly failed to attend a mean of 20% of clinics. GFR measurement was inaccurate, with a 5% coefficient of variation. Conveniently these virtual patients were immortal and un-transplantable and never declined fistula formation, which was 100% successful.

Patients were referred for AVF formation the first time GFR fell below 18.5 ml/min, and commenced dialysis the first time GFR fell below a patient-specific threshold determined at enrolment, with mean ( $\pm$ sd) threshold of 10 ( $\pm$ 3) ml/min. Patients with fewer than three GFR measurements post AVF formation were excluded from analysis of GFR decline.

**Results:** Out of 310 patients enrolled, 135 developed a GFR less than 18.5 ml/min, of whom 128 underwent AVF surgery. Mean ( $\pm$ sd) GFR at time of fistula formation was 16.4 ( $\pm$ 1.9) ml/min. The mean (95% CI) decline in GFR during the 2 years prior to AVF formation was 6.4 (5.8–7.1) ml/min/year, whereas during the 2 years after AVF formation it was 1.4 (0.6–2.3) ml/min/year.

**Conclusion:** In keeping with published observations in real patients, AVF formation in this cohort of virtual patients was associated with a marked improvement in mean GFR decline of around 5 ml/min/year. However, GFR decline in every virtual patient was completely linear throughout the follow-up period; mean decline appeared to change predominantly due to survivorship bias, as patients were removed from observation when they started dialysis.

Apparent change in GFR trajectory following AVF formation is a statistical, not a physiological phenomenon.