# Renal transplantation in a patient with cystic fibrosis: a changing disease landscape

Daniel H Tewkesbury[1]

Raman Dhanda[2]

Evelyn Looi[1]

Rowland J Bright-Thomas[1,3]

Author details can be found at the end of this article

Correspondence to:
Daniel H Tewkesbury;
daniel.tewkesbury@mft.nhs.uk

## Introduction

Cystic fibrosis is a multisystem disease. Treatment advances have resulted in improved life expectancy for patients with cystic fibrosis, who are now at increased risk of long-term complications secondary to either cystic fibrosis or age-related comorbidities. This article presents a 45-year-old man with cystic fibrosis who received a renal transplant following multiple admissions with infective pulmonary exacerbations and acute kidney injury. The prevalence of chronic kidney disease is increasing in patients with cystic fibrosis; risk factors include cystic fibrosis-related diabetes, use of aminoglycosides and nephrotoxic immunosuppressant medication post-transplantation. This is the first reported case of renal transplantation in a patient with cystic fibrosis who was not on immunosuppressant therapy from previous transplantation. With improved survival and increasing prevalence of chronic kidney disease in adults with cystic fibrosis, renal transplantation may play an important role in improving patients' clinical status and quality of life.

## Discussion

Cystic fibrosis is the most common lethal inherited condition affecting people in the western world. It affects over 10 000 patients in the UK and 35 000 patients in Europe (Elborn,

### Case report

The patient was a 45-year-old man with cystic fibrosis (genotype *ΔF508/711 + 3A>G)* complicated by multilobar bronchiectasis with chronic *Pseudomonas aeruginosa* infection, pancreatic insufficiency, cystic fibrosis-related diabetes and nasal polyps.

He had undergone a right nephrectomy aged 22 years for an incidental ectopic kidney. He was diagnosed with hypertension at 32 years of age which was refractory to multiple agents and by age 40 years had developed stage 3 chronic kidney disease presumed secondary to a combination of diabetic and hypertensive nephrosclerosis. At this time, forced expiratory volume in 1 second ($FEV_1$) was 41% predicted and he required, on average, one course of intravenous antibiotics per year to treat infective pulmonary exacerbations.

At the age of 42 years, he developed nephrotic-range proteinuria and a subsequent persistent transudative pleural effusion. He required nine emergency hospital admissions over the next 2 years secondary to infective pulmonary exacerbations, progressing to acute-on-chronic kidney injury, pulmonary oedema and type 2 respiratory failure. On four occasions he required acute haemofiltration for renal failure with either significant fluid overload or hyperkalaemia and metabolic acidosis. At this stage, he was started on outpatient haemodialysis with dramatic improvement in symptoms and admission frequency, but at the cost of dialysis three times a week in addition to the high burden of his maintenance cystic fibrosis therapies.

After careful consideration of risk, and close liaison between the renal transplant and cystic fibrosis teams, he was listed for renal transplantation which he received 10 months later. His creatinine level improved from 577 mmol/litre to 75 mmol/litre and $FEV_1$ improved from 36% to 44% predicted. He no longer required antihypertensive medication and has not required any renal or respiratory admissions for over 4 years.

In view of his excellent response to renal transplant, and his wishes to improve glycaemic control and diarrhoea secondary to pancreatic insufficiency, he was listed for and received a pancreatic transplant aged 48 years. This has further improved his quality of life by removing his need for both exogenous insulin and pancreatic enzyme replacement therapy.

**How to cite this article:**
Tewkesbury DH, Dhanda R, Looi E, Bright-Thomas RJ. Renal transplantation in a patient with cystic fibrosis: a changing disease landscape. Br J Hosp Med. 2021. https://doi.org/10.12968/hmed.2020.0744

2016; UK Cystic Fibrosis Registry, 2020), and following treatment advances has a median predicted life expectancy in the UK of 49 years (UK Cystic Fibrosis Registry, 2020). The advent of modulator therapies that regulate the faulty cystic fibrosis transmembrane conductance regulator protein looks set to further improve survival (Bell et al, 2020). Most patients are now adults and present increasingly with cystic fibrosis or treatment-related long-term complications and unrelated chronic conditions. As longevity improves, patients with cystic fibrosis are increasingly developing chronic conditions such as chronic kidney disease and their improved overall health status will make them suitable candidates for transplantation. This is the first reported case of a patient with cystic fibrosis receiving a primary renal transplant for chronic kidney disease.

The prevalence of chronic kidney disease is rising in people with cystic fibrosis for multiple reasons. Cystic fibrosis-related diabetes affects 34% of adults with cystic fibrosis (UK Cystic Fibrosis Registry, 2020) and these patients have an increased prevalence of chronic kidney disease, even after adjusting for other factors (Quon et al, 2011). Aminoglycosides and other nephrotoxic medications are frequently used to treat pulmonary exacerbations and patients with cystic fibrosis are also at risk of nephrolithiasis and IgA nephropathy (Nazareth and Walshaw, 2013). Previous reports of renal transplantation in cystic fibrosis have occurred after lung or liver transplantation, in patients receiving nephrotoxic immunosuppressive medications (Berg et al, 2018).

Patients with cystic fibrosis are at increased risk of postoperative respiratory complications and the risks and benefits of major surgery in cystic fibrosis have to be carefully considered (Della Rocca, 2002). However, with close collaboration between cystic fibrosis and renal teams and careful anaesthetic management, these risks can be minimised.

Postoperatively, immunosuppression and risk of opportunistic infections in transplant recipients need to be balanced against the risks of end stage organ disease. Patients with cystic fibrosis have multilobar bronchiectasis and chronic respiratory infection but are immunocompetent and have not been shown to be at additional risk from immunosuppression. Patients with chronic kidney disease may have an increased incidence of infection as a result of factors such as endothelial dysfunction, coagulopathy and left ventricular dysfunction (Wang et al, 2011). Both the patient presented here and a previous report of renal transplant in a patient with cystic fibrosis following liver transplantation (McKeon et al, 2005) demonstrated improvement in lung function and a reduction in the need for intravenous antibiotics post renal transplant.

Patients with cystic fibrosis remain eligible for cystic fibrosis transmembrane conductance regulator modulators following renal transplant, although manufacturers advise caution in prescribing these to patients with an estimated glomerular filtration rate of less than 30 ml/min. The long-term impact of modulators on renal disease in patients with cystic fibrosis remains to be seen. There are high levels of expression of cystic fibrosis transmembrane conductance regulator in the nephron but this does not appear to have a direct impact on renal function (Nazareth and Walshaw, 2013). Cystic fibrosis transmembrane conductance regulator modulators may decrease the need for nephrotoxic drugs to treat pulmonary exacerbations but are unlikely to directly affect the prevalence of renal disease. However, as patients live longer, the prevalence of renal disease will increase.

Previous reports of renal transplants in patients with cystic fibrosis occurred in the context of other solid organ transplants, where survival is more likely to be determined by the primary transplant organ. A graft half-life of 20 years has been reported for renal transplants (Ponticelli, 2004). Despite treatment advances, cystic fibrosis remains a lethal disease with a median life expectancy in the UK of 49 years (UK Cystic Fibrosis Registry, 2020). As primary renal transplantation becomes more common in patients with cystic fibrosis, pulmonary status remains the most important prognostic factor, but this balance may change in the future if life expectancy continues to improve.

Survival and prevalence of age and treatment-related complications such as chronic kidney disease in adults with cystic fibrosis continue to increase. Renal transplantation in carefully selected patients may help reduce the burden of disease and significantly improve quality of life. Cystic fibrosis lung disease should not be deemed a contraindication to renal transplantation.

## Learning points

- Patients with cystic fibrosis have multiple risk factors for chronic kidney disease, including cystic fibrosis-related diabetes and the use of nebulised and intravenous aminoglycosides to treat pulmonary exacerbations.
- People with cystic fibrosis are living longer, so chronic conditions such as chronic kidney disease are becoming more common in this population.
- This is the first reported case of a patient with cystic fibrosis receiving a primary renal transplant for chronic kidney disease.
- Pulmonary disease in a patient with cystic fibrosis should not be deemed a contraindication for solid organ transplantation. Transplantation may improve patients' pulmonary outcomes and quality of life.
- The long-term effects of cystic fibrosis transmembrane conductance regulator modulator therapies are unknown but may indirectly increase the prevalence of chronic conditions such as chronic kidney disease.

**Author details**

[1]Manchester Adult Cystic Fibrosis Centre, Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, UK

[2]Department of Renal and Pancreas Transplantation, Manchester Royal Infirmary, Manchester University NHS Foundation Trust, Manchester, UK

[3]Division of Infection, Immunity and Respiratory Medicine, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

## References

Bell SC, Mall MA, Gutierrez H et al. The future of cystic fibrosis care: a global perspective. Lancet Respir Med. 2020;8(1):65–124. https://doi.org/10.1016/S2213-2600(19)30337-6

Berg KH, Ryom L, Faurholt-Jepsen D, Pressler T, Katzenstein TL. Prevalence and characteristics of chronic kidney disease among Danish adults with cystic fibrosis. J Cyst Fibros. 2018;17(4):478–483. https://doi.org/10.1016/j.jcf.2017.11.001

Della Rocca G. Anaesthesia in patients with cystic fibrosis. Curr Opin Anaesthesiol. 2002;15(1):95–101. https://doi.org/10.1097/00001503-200202000-00014

Elborn JS. Cystic fibrosis. Lancet. 2016;388(10059):2519–2531. https://doi.org/10.1016/S0140-6736(16)00576-6

McKeon DJ, Haworth C, Bradley JR, Bilton D. Cystic Fibrosis pulmonary disease is not a contra-indication to live-related renal transplantation. Nephrol Dial Transplant. 2005;20(3):664–664. https://doi.org/10.1093/ndt/gfh647

Nazareth D, Walshaw M. A review of renal disease in cystic fibrosis. J Cyst Fibros. 2013;12(4):309–317. https://doi.org/10.1016/j.jcf.2013.03.005

Ponticelli C. Renal transplantation 2004: where do we stand today? Nephrol Dial Transplant. 2004;19(12):2937–2947. https://doi.org/10.1093/ndt/gfh511

Quon BS, Mayer-Hamblett N, Aitken ML, Smyth AR, Goss CH. Risk factors for chronic kidney disease in adults with cystic fibrosis. Am J Respir Crit Care Med. 2011;184(10):1147–1152. https://doi.org/10.1164/rccm.201105-0932OC

UK Cystic Fibrosis Registry. UK cystic fibrosis registry annual data report 2019. 2020. https://www.cysticfibrosis.org.uk/sites/default/files/2020-12/2019%20Registry%20Annual%20Data%20report_Sep%202020.pdf (accessed 31 August 2021)

Wang HE, Gamboa C, Warnock DG, Muntner P. Chronic kidney disease and risk of death from infection. Am J Nephrol. 2011;34(4):330–336. https://doi.org/10.1159/000330673