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Review

Long-Term Risks of End-Stage Renal Disease and Potential Health Issues in Living Kidney Donors

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ABSTRACT

The significant challenge is the long-term risk of end-stage renal disease (ESRD) and potential health complications in living kidney donors. While most donors live long and healthy lives after surgery, their chance of getting ESRD is slightly higher than the general population. This increased risk is contributed to by age, obesity, diabetes, and hypertension. Potential medical conditions include surgical risks, hypertension, proteinuria, and impaired kidney function. The donor's long-term health depends upon regular checkups, a healthy lifestyle, and compliance with doctors' recommendations. More research in this area will help us better understand risk factors and long-term outcomes. Outcomes can vary significantly among individuals, making it essential to tailor health interventions to meet specific needs. By fostering a collaborative approach between donors and healthcare professionals, we can enhance overall well-being and ensure more successful transplant results. This review focuses on ESRD and potential long-term health complications in living kidney donors.

Keywords: ESRD, health problems, kidney functions, living kidney donor, long-term outcomes.

Living kidney donation is one of the most effective treatment alternatives for people with end-stage renal disease (ESRD). Living kidney donors are a valuable resource for patients requiring a kidney transplant. The donor's health and long-term effects are highly significant. Living kidney donors face a low chance of acquiring ESRD. However, other studies indicate that the risk of ESRD in donors is slightly higher than in the general population. This higher risk is usually associated with pre-existing risk factors or complications after donation.[1,2]

Understanding End-Stage Renal Disease: Causes and Development

End-stage renal disease has been defined by the gradual destruction of the kidney's functioning units, known as nephrons. Such damage causes a reduction in glomerular filtration rate (GFR) and deterioration of kidney function. The main mechanisms responsible for the pathogenesis of ESRD are glomerular, tubular, and vascular damage, as well as interstitial fibrosis. Glomerular damage harms small blood vessels known as glomeruli, which filter particles from the bloodstream. Glomerular damage leads to proteinuria (protein loss in the urine) and results in a reduction in GFR. Tubules are tiny tubes that transport filtered debris and excess fluid into the urine. Tubular damage may cause electrolyte and acid-base imbalances. Interstitial fibrosis is the accumulation of scar tissue in the kidney and which leads to impaired kidney function. Vascular damage occurs when the blood vessels become damaged, limiting renal blood flow and accelerating kidney disease.[3]

End-stage renal disease is the last stage of chronic kidney disease that occurs when 85-90% of kidney function has been destroyed, and the kidneys are damaged to the point that they can no longer supply what the body requires. In this case, the kidneys are unable to filter blood effectively, which leads to the accumulation of toxins, fluids, and waste products in the body. End-stage renal disease is a life-threatening condition that requires treatments such as dialysis or a kidney transplant. It is a major health disease impacting millions of individuals worldwide.

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According to the research, over 786,000 individuals in the United States have ESRD, with approximately 71% undergoing dialysis. The incidence of ESRD rises with age and is most common in people over 65.[4-6]

Diabetes and hypertension are the main causes of ESRD. Living kidney donors are somewhat more likely to acquire ESRD than the overall population. Based on a meta-analysis, the risk of getting ESRD in donors is 0.04% over 15 years.[1]

Understanding The Genetic Predisposition to End-Stage Kidney Failure

As is well known, ESRD may also be affected by genetic factors, even though diabetes and hypertension are the main causes of the disease. There are various genetic mutations that may lead to ESRD located in a variety of genes. The frequency of genetic mutations in a population varies depending on the type of mutation, ethnicity, and geographic location. Autosomal dominant polycystic kidney disease (ADPKD) is the most prevalent genetic kidney disease.[7,8]

Mutations in the PKD1 or PKD2 genes promote the formation of many cysts in the kidneys, gradually impairing their function. It has an autosomal dominant inheritance pattern, which means that only one copy of the defective gene from one parent is required to generate the disease. The ARPKD is a rare condition caused by mutations in the PKHD1. It usually appears earlier in life than ADPKD and causes cysts in the kidneys and liver. It has an autosomal recessive inheritance pattern, which means that two copies of the defective gene (one from each parent) are required to develop the condition. Alport syndrome is caused by mutations in genes (COL4A3, COL4A4, or COL4A5) that code for a type of collagen required for the construction of the glomeruli (the kidney's filtering units). It can also impair hearing and vision. Inheritance might be X-linked, autosomal recessive, or autosomal dominant, depending on the gene affected. Fabry disease is a rare, X-linked lysosomal storage disorder caused by GLA gene mutations. This results in a deficiency of an enzyme that breaks down certain fats, leading to their accumulation in various organs, including the kidneys, which can eventually result in renal failure. Males tend to be more severely affected than females.[9]

Nephronophthisis (NPHP) is a set of autosomal recessive conditions that include cysts at the renal cortex-medulla junction, which lead to progressive kidney fibrosis and failure. A number of genes for NPHP have been identified. Cystinosis is an autosomal recessive condition in which cystine accumulates in multiple organs, including the kidneys, resulting in kidney failure. Primary hyperoxaluria is a set of rare hereditary conditions that result in excessive oxalate production, which can produce kidney stones and ultimately damage the kidneys. Gitelman syndrome and Bartter syndrome are tubulopathies, which are types of genetic conditions that alter the function of kidney tubules to reabsorb salts and electrolytes, potentially leading to kidney problems over time. Thin basement membrane disease (benign familial haematuria) is frequently caused by mutations in COL4A3 or COL4A4. It normally causes chronic blood in the urine but does not lead to renal failure; however, it can in some individuals or families. The PKD, collagen type IV, and NPHP are significant genes and mutations associated with ESRD. The uromodulin (UMOD), renin (REN), and HNF1B are the other genes that can also cause ESRD; however, these mutations are less prevalent. Mutations in the PKD1 and PKD2 genes cause ADPKD, and these are the most prevalent genetic causes of ESRD. The ADPKD affects around one in 400-1000 individuals. The PKD1 mutations are more prevalent than PKD2 mutations and result in more severe disease. Mutations in the collagen type IV genes, including COL4A3, COL4A4, and COL4A5, cause Alport syndrome, and it is a genetic condition that may lead to kidney failure, hearing loss, and loss of vision. It impacts one in 8000-25000 individuals. Mutations in the NPHP1-NPHP11 genes cause NPHP. Nephronophthisis is characterized by abnormal development of the kidney tubules and can lead to ESRD. The incidence is around one in 100,000 individuals. Mutations in rare genes like the UMOD gene may result in medullary cystic kidney disease. The REN gene may result in renal tubular dysgenesis, which is a rare kidney disease. HNF1B gene mutations have also been associated with kidney cysts and diabetes.[9-11]

Diagnosis And Treatment of ESRD

Genetic studies play a crucial role in identifying the hereditary origin of ESRD, as well as the disease's prognosis and therapy alternatives. Genetic screenings may be useful to figure out whether family members are at risk. Early diagnosis and therapy may minimize or prevent the progression of ESRD. Several methods are frequently used in genetic testing. Sanger sequencing is a common choice for deciphering the DNA sequence of a single gene or a specific gene region, proving particularly useful when examining mutations within a known gene. Next-generation sequencing (NGS) offers a way to analyze numerous

genes at the same time. When multiple genetic factors are suspected, NGS approaches like gene panel testing or whole exome sequencing might be preferred. Furthermore, deletion/duplication analysis plays a role in identifying substantial deletions or duplications that can arise in genes. Polymerase chain reaction is a widely used method for this, typically involving the amplification and analysis of a targeted DNA region. A diagnosis of ESRD involves a comprehensive evaluation of clinical conditions, laboratory findings, and radiological assessments. Lab tests consist of blood analysis; evaluation of factors like blood urea nitrogen, creatinine, GFR, electrolytes, hemoglobin, hematocrit, and urinalysis; and checking for proteinuria, haematuria, and bacterial growth. Imaging techniques, such as ultrasound for kidney size, shape, and structure; computed tomography scans for more detailed kidney visuals; and magnetic resonance imaging for in-depth tissue analysis, are also employed.[12,13]

A kidney biopsy may be performed to pinpoint the underlying cause of kidney damage and its severity. Treatment for ESRD focuses on replacing lost kidney function and preventing associated complications. The two primary approaches are dialysis and a kidney transplant. Dialysis utilizes a machine to remove waste and excess fluid from the bloodstream and includes two forms: hemodialysis, typically administered several times weekly at a clinic, and peritoneal dialysis, which can be performed at home via a catheter inserted into the abdomen.[14-17]

The Health Implications for Living Kidney Donors

Kidney transplantation involves surgically implanting a healthy kidney, often sourced from a deceased or living related/compatible donor.[18] The chosen treatment plan is adapted to the patient's special conditions and requirements. Untreated ESRD can cause a variety of serious medical conditions, the most prevalent of which is cardiovascular disease; ESRD dramatically raises the risk of heart attack and stroke. This risk can be elevated by lifestyle choices like smoking, genetic predispositions, and mental health concerns such as anxiety or depression.[19,20]

Anemia is another common problem; it develops when the kidneys can't produce enough erythropoietin, a hormone that encourages the formation of red blood cells. Bone disease can also be caused by ESRD; the kidneys' inability to maintain calcium and phosphorus balance has a severe impact on bone health.[21] Neurological problems may also occur; toxin build-up can cause nerve damage, seizures, and even coma. The immune system's weakened condition makes it more vulnerable to infections. Finally, issues, including loss of appetite, nausea, and vomiting, can contribute to malnutrition. These significant effects emphasise the necessity of early ESRD diagnosis and therapy.[22,23]

Research on the long-term health risks of living kidney donors generally shows encouraging outcomes. Most living kidney donors live healthy lives after donating their kidneys. However, some studies have shown that living kidney donors are somewhat more likely to suffer certain long-term health problems. The most serious of these concerns is the possibility of developing ESRD. The chance of acquiring ESRD in living kidney donors is slightly higher than in the general population, but it is still extremely rare. Numerous studies have demonstrated that most living kidney donors do not acquire ESRD over their lifetime.[24,25]

Living kidney donors may also suffer from hypertension. Living kidney donors may experience a slight increase in hypertension. Yet this risk can usually be kept under control. Some living kidney donors may develop protein leakage in their urine (proteinuria). However, this disease rarely affects kidney function. Living kidney donors are extremely unlikely to acquire kidney failure. In some uncommon circumstances, compensatory mechanisms arising from living with a single kidney can produce a slight decrease in kidney function over time.[26-28]

Donors with a family background of kidney failure are also at increased risk of developing it. Additionally, smoking is an important risk factor contributing to kidney damage and ESRD among donors. Being aware of these risk factors and taking precautions to avoid them is crucial for the health of living kidney donors. In addition to the risks mentioned above, living kidney donors may experience some health issues following kidney donation. These issues are usually minor and temporary. The most common types are postoperative complications. Infections, bleeding, and pain are all possible complications of kidney donation operations. However, these effects usually can be cured. Furthermore, kidney donation could cause psychological issues such as anxiety, stress, and depression for some individuals. These issues are frequently handled with psychological support. Living kidney donors can take efforts to preserve their health and reduce the dangers of surgery.[27-31]

Advances in technology, genetics, and personalised medicine are driving significant evolution in the landscape of ESRD management and living kidney donation. Future research and clinical practice will likely focus on several key areas to mitigate long-term risks and maximize outcomes for both patient populations. A multifaceted approach that involves technological innovations, genetic insights, and a patient-centred focus will be essential to achieving these improvements and reducing the ongoing problems associated with renal failure and the altruistic act of kidney donation.[32-35] Further research on this topic will help us better understand risk factors and long-term outcomes and optimize donor care.

In conclusion, the most crucial safeguard is to have regular health check-ups. Donors should visit a doctor on a regular schedule to carefully assess their kidney function and identify any health issues as early as possible. Maintaining a healthy lifestyle is also crucial. Donors should aim to maintain their ideal weight, exercise regularly, eat a nutritious diet that is balanced, avoid smoking, and limit their consumption of alcohol. Furthermore, taking their doctor-prescribed medications on a regular basis is essential for sustaining their health. By following these precautions, living kidney donors can live a long and healthy life. Living kidney donation is a life-saving procedure. However, it is important to remember that donors may experience health problems during and after the surgery. Therefore, the long-term health outcomes of potential donors should be carefully considered. Donor selection, informed consent, long-term follow-up, and psychological support are critical to protecting donor health and addressing ethical issues.

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