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Review Article

# Novel strategies for the management of renal replacement – A review

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## ABSTRACT

End-stage renal disease (ESRD) is the last stage of kidney disease, and it is life threatening and often causes fatal complications such as cardiovascular disease. ESRD is a growing public health issue with prominent increase and prevalence in developed and developing countries with high rates of morbidity and mortality. It worsens the quality of life. The life expectancy of these patients is up to 4-5 years. Interleukin-6 is a major factor responsible for the mortality in ESRD patients. Treatment cost for renal replacement therapy in ESRD patients is too high annually. Strategies are developed to overcome to minimize the medical expenditure. Novel innovative strategies were developed for ESRD include wearable kidney, nanotechnology, and regenerative medicine. This article focuses on the different advanced strategies such as transplantation of bioengineered kidney, kidney regeneration and cell replacement, wearable kidney – dialysis machine, continuous dialysis therapy at home, and micro-Chinese osmotherapy.

**Keywords:** End-stage renal disease, hemodialysis, renal replacement therapy, transplantation

## Introduction

Chronic kidney disease (CKD) is a common condition most commonly occurs in the elderly population which results in end-stage renal failure.[1,2] CKD in younger patients is associated with loss of kidney function, but of patients over 65 years of age with CKD, 30% do not have a progressive disease with loss of kidney function over time. CKD is associated with an increased risk of cardiovascular disease and chronic renal failure.[3-5] Kidney disease is the 9th leading cause of death in the United States. Patients with CKD Stages 1-3 (glomerular filtration rate [GFR] >30 mL/min/1.73 $m^2$) are generally asymptomatic. Mostly in Stages 3 and 4, endocrine/metabolic derangements or disturbances in water or electrolyte balance become clinically manifest. Imaging studies such as renal ultrasonography, retrograde pyelography, computed tomography, magnetic resonance imaging, and radionucleotide scanning will diagnose CKD (Figure 1).

Pathologic manifestations include anemia, hypophosphatemia, hypocalcemia, hyperparathyroidism, and metabolic acidosis.[6,7]

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Different stages of CKD are as follows:

- Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 $m^2$)
- Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 $m^2$)
- Stage 3: Moderate reduction in GFR (30-59 mL/min/1.73 $m^2$)
- Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 $m^2$)
- Stage 5: Kidney failure (GFR <15 mL/min/1.73 $m^2$ or dialysis)

Stage 5 is termed as end-stage renal disease (ESRD), in which the kidneys stop working totally. There will be a permanent kidney failure which is a fixed one in nature.

ESRD is a growing public health issue with prominent increase and prevalence in developed and developing countries. It worsens the quality of life.[8,9] Treatment cost for renal replacement therapy (RRT) in ESRD patients is too high annually. Strategies are developed to overcome to minimize the medical expenditure.

## ESRD and high potassium level

Majority of the ESRD patients are living with high potassium level which results in irregular heartbeat and weakness, hence reducing the potassium level shall keep away these risks. Potassium level in blood vessels most commonly increases when the kidneys stop excreting extra potassium level effectively.[10] Damaged residual nephrons are another cause for electrolyte disorder.

## Diabetes and ESRD

Low socioeconomic status is associated with an increased risk of ESRD due to diabetes.

## Mortality and morbidity of ESRD patients

Sudden death in ESRD patients is due to hyperkalemia followed by missed dialysis. The another cause is cardiovascular disease and cardiovascular mortality,[11] which is more higher in dialysis patients. ESRD patients at every age have increased the mortality comparatively with nondialysis patients.

# Materials and Methods

Literature review was done extensively using various sources like PUBMED, SCOPUS, MEDLINE, EMBASE.

Novel innovative strategies for ESRD.

## Transplantation of bioengineered kidney

The study published by Song *et al.,* 2013, states a novel strategy about the success of Transplantation of the bioengineered kidney by creating a transplantable graft to permanently replace kidney function. These innovative findings shall address the donor organ shortage and the morbidity associated with immunosuppression (Figure 2).[12]

Such a bioengineered graft possesses the kidney's architecture and function and permits perfusion, filtration, secretion, absorption, and drainage of urine. These transplantable grafts produced rudimentary urine *in vitro* when perfused through their intrinsic vascular bed. When transplanted in an orthotopic position in rat, the grafts were reported to perfused by the recipient's circulation and produced urine through the ureteral conduit *in vivo*. In light of the above study, it is suggested that transplantable bioengineered graft is an alternative remedy for RRT.

## Kidney regeneration and cell replacement

### *Induced pluripotent stem cells for disease modeling and drug therapy*

The induced pluripotent stem cells used for the reprogramming process of the kidney from mesangial cells. This is a novel strategy in ESRD patients. According to Sharon *et al.,* enormous amount of somatic cells can be efficiently reprogrammed into induced pluripotent cells and simultaneously redifferentiated into other cell types that recapitulate disease phenotypes. In this view ,the induced pluripotent stem cells aids *in vitro* modeling system that could absolutely lead to novel drug development and testing. The induced pluripotent stem cell technology in kidney disease modeling offers an opportunity to develop self-renewing models that will facilitate mechanistic aspect of the disease (Figure 3).[13]

## Wearable kidney – Dialysis machine

Dialysis on daily basis will be uncomfortable and cumbersome issue to implement. Miniaturized ambulatory continuous renal replacement device approved by FDA is available for end-stage renal failure patients

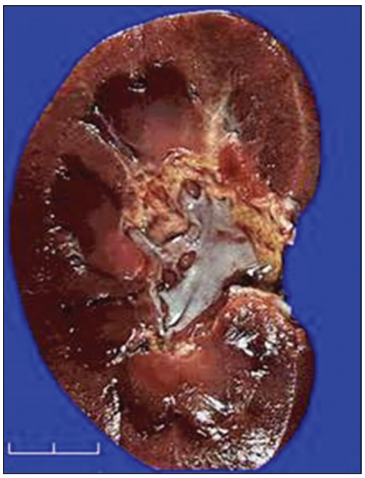

**Figure 1:** End-stage renal disease

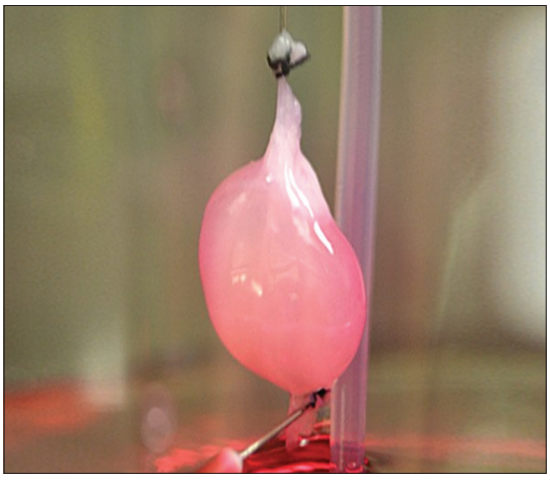

**Figure 2:** Bioengineered graft/rat

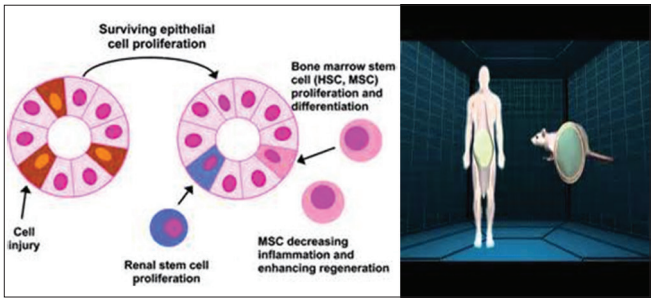


**Figure 3:** Kidney regeneration and cell replacement

that they can wear permanently. This can be worn as a belt operated with batteries of weight <5 lbs. The development of such a strategy will reduce the cost and increase the survival rate by reducing the mortality in ESRD patients.[14]

## Continuous ambulatory peritoneal dialysis (CAPD)

RRT with dialysis and transplantation is the only option of prolonging life for patients with ESRD. Although transplantation is the treatment of choice, the number of donor kidneys is limited and transplants may

fail. Hence, many patients require prolonged or even life-long dialysis. CAPD is an alternative to hospital or home hemodialysis for patients with ESRD (Figure 4).[15,16]

## Traditional Chinese medicine

### *Micro-Chinese medicine osmotherapy*

Micro-Chinese medicine osmotherapy is an advanced natural therapy which is based on Chinese Herbal Medicine. It is an external application and is used for kidney disease. The core technology of micro-Chinese medicine osmotherapy is to make the effective herbs of kidney disease superfinely shattered.[17] Then, with the help of effective penetrant and osmosis devices, the effective medicines are permeated into kidney lesions by external application, thus achieving the goal of treating kidney disease. Clinical practices have been proved that this application method is both effective and convenient. Micro-Chinese medicine osmotherapy can improve kidney functions; thereby, it does help patients to increase the chance to get rid of dialysis (Figure 5).

**Figure 4:** Wearable kidney

**Figure 5:** Continuous dialysis therapy

**Figure 6 :** Micro-Chinese osmotherapy

## Conservative management of ESRD

Conservative (non-dialytic) management of ESRD includes careful attention to fluid balance, treatment of anemia, and correction of acidosis and hyperkalemia. Blood pressure and calcium/phosphorus metabolism must also be managed.[18,19] There is emerging evidence that dietary modifications may be helpful in prolonging life and decreasing symptoms.[20] Providing palliative care is essential for prolonging the quality of life for ESRD patients (Figure 6).[21]

## Conclusion

ESRD is a growing public health issue with prominent increase and prevalence in developed and developing countries. It worsens the quality of life. Treatment cost for RRT in ESRD patients is too high annually. Strategies are developed to overcome to minimize the medical expenditure. These recent advances such as bioengineered graft, wearable kidney, CAPD, and micro-Chinese osmotherapy throw a light on the management of ESRD and minimize the RRT.

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