

Artificial and biological membranes in acute kidney injury: a biomedical engineering framework on renal replacement therapy in critical care

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ABSTRACT

Background: Acute kidney injury (AKI) is a common complication in critically ill patients and frequently requires renal replacement therapy (RRT). While comparisons between continuous renal replacement therapy (CRRT) and peritoneal dialysis (PD) have traditionally focused on clinical efficacy, less attention has been given to the membrane technologies underlying these modalities. This narrative review compares synthetic membranes used in extracorporeal therapies with the biological peritoneal membrane from a biomedical engineering perspective.

A narrative review of the literature was conducted, integrating evidence from nephrology, critical care medicine, biomaterials science, and biomedical engineering. The review examines membrane transport mechanisms (diffusion, convection, ultrafiltration, and adsorption), membrane biocompatibility, transport behavior during critical illness, and emerging bioartificial renal technologies.

Although synthetic and biological membranes rely on the same fundamental transport principles, they differ markedly in structure and function. Synthetic membranes provide predictable and controllable transport but are affected by blood-material interactions and membrane fouling. In contrast, the peritoneum is a living, adaptive membrane whose transport properties are influenced by vascular physiology, systemic inflammation, and endothelial integrity. These differences reflect distinct engineering approaches underlying CRRT and PD.

A membrane engineering perspective provides a unified framework for comparing RRT modalities beyond conventional clinical outcomes. Artificial membranes emphasize precision and reproducibility, whereas biological membranes offer physiological integration and adaptability. Future renal support systems are expected to combine these complementary properties through hybrid technologies that more closely replicate native kidney function.

Keywords: Acute Kidney Injury, CRRT, PD, Biomedical Engineering, Critical Care, Membrane Transport

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INTRODUCTION

Acute kidney injury (AKI) is one of the most prevalent organ dysfunctions experienced by critically ill patients. Despite advances in intensive care medicine, AKI is an important cause of high morbidity and mortality rates [1,2]. More than 50% of the critically ill patients experi-

ence AKI during their ICU admission, with a significant proportion of those patients ultimately requiring renal replacement therapy (RRT). The development of AKI is independently associated with prolonged hospital length of stay, increased healthcare costs, progression to chronic kidney disease, and increased short- and long-term mortality [3,4]. Therefore, the optimization

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of renal support strategies remains a major focus of research in critical care.

Most discussions of RRT focus on clinical outcomes such as mortality, renal function recovery, dialysis dose, timing of therapy initiation, and modality type [5,6]. While each of these clinical endpoints is important, they do not fully capture the fundamental differences among available renal support technologies. From a biomedical engineering perspective, both extracorporeal therapies and peritoneal dialysis are considered membrane-based transport systems that replicate the filtration and homeostatic functions of the native kidney. This perspective provides an opportunity to move beyond specific renal replacement therapies and to consider the physical and biological properties of the membranes that facilitate transport, thereby offering a novel approach to current treatment methods [7,8].

The native kidney can regulate its transport activity through dynamic biological structures that adapt to meet changing physiologic requirements. In contrast, extracorporeal therapies use non-biological membranes (synthetic polymers) that allow for the predictable regulation and control of transport activity. Peritoneal dialysis represents an intermediate category between biologic and synthetic membranes, as the patient's own peritoneal membrane serves as a biological interface for solute and fluid transport. The peritoneum is a living tissue whose permeability and transport characteristics are influenced by age, degree of inflammation at the time of treatment, vascularization, and systemic disease. The distinction between biological and synthetic membranes is particularly important in critically ill patients, who often experience sepsis, endothelial dysfunction, capillary leak, and systemic inflammatory responses that can significantly affect membrane function [9].

A comparison of the two membrane types (CRRT-programmed artificial membrane and PD-dynamic biological membrane) extends well beyond the question of how efficiently they clear toxins or how they compare in terms of clinical outcome. Rather, it highlights the fundamental differences between two distinct forms of membrane technology: a programmable artificial membrane with consistent transport characteristics and a membrane that is dynamically physiologically integrated and adaptable. For a better understanding of the advantages and disadvantages of each system, basic transport mechanisms such as diffusion, convection, ultrafiltration, absorption, permeability, and biocom-

patibility need to be considered [7].

This review analyzes renal replacement therapies for critically ill patients from a biomedical engineering perspective. The development of a framework that relates membrane structure, transport physics, the physiological state of the critically ill patient, and new developments in renal support technologies is sought. This analysis provides insight into both the current limitations of renal replacement therapy and the potential future development of hybrid systems that combine the precision of engineered artificial systems with the adaptive capabilities of biological tissue.

■ METHODS

Patient selection

This study was conducted as a narrative review and is intended to provide a biomedical engineering perspective regarding renal replacement therapies employed in the Intensive Care Unit (ICU), specifically continuous renal replacement therapy and peritoneal dialysis. The primary goal of this study was not to perform a quantitative synthesis of the evidence as is typically done in systematic reviews. Rather, it was to integrate contemporary knowledge from nephrology, critical care medicine, biomaterials science, membrane engineering, and physiology into a comprehensive conceptual framework. The literature search was conducted between 10th of June and 5th of July 2026, utilizing the PubMed and Google Scholar databases. There was no minimum publication date for inclusion in the search. All publications available through 30 June 2026 were included in the search. The search strategy was developed using the following keywords: acute kidney injury, renal replacement therapy, continuous renal replacement therapy, peritoneal dialysis, dialysis membrane, diffusion, convection, ultrafiltration, adsorption, hemocompatibility, glomerular filtration barrier, peritoneal membrane, bioartificial kidney, critical care. Eligibility for selection was based upon whether each publication addressed one or more aspects relevant to the objectives of this review. Eligible publications included original research articles, systematic reviews, narrative reviews, clinical practice guidelines, engineering studies, experimental investigations, and landmark physiological studies addressing membrane transport, biomaterials, dialysis membrane design, peritoneal membrane physiology, and renal replacement therapy in critically ill patients. Excluded from consideration were publications related

to areas other than renal replacement therapy and articles written in languages other than English. In developing this study, particular attention was paid to identifying similarities and differences between synthetic and biological membranes from a biomedical engineering perspective, rather than comparing clinical outcomes.

The native kidney as a biological transport system

Before assessing contemporary renal replacement therapies, it is necessary to examine the physiological system they are designed to replace. From a biomedical engineering standpoint, the kidneys can be thought of as an adaptable, dynamic membrane-based system of filtration, diffusion, convection, and active transport over many scales of space and time. In contrast to most currently available artificial renal support devices (which are mostly passive mechanisms), the kidney integrates both passive and active processes within living tissue and can respond to changes in physiological needs. The kidney's ability to adaptively adjust to physiological demand is one key factor distinguishing renal function from contemporary renal replacement treatments [10]

Glomerular filtration

The first step in renal function occurs at the level of the glomerulus, which filters plasma water and small molecules from the blood into Bowman's space. The glomerular filtration barrier is formed of three layers of cells: a layer of capillary endothelium that has pores; an intervening matrix known as the glomerular basement membrane; and podocytes' slit diaphragms. These three layers form a semi-permeable membrane that can filter based upon size, charge, and shape [11].

From an engineering standpoint, glomerular filtration results from pressure differentials (Starling's principles) across the filtration barrier. Water will move through the barrier as a result of the net force generated by pressure differences across it. The presence of proteins in the filtrate will be determined by the barrier's porosity and its permeability to protein movement. Despite its extremely high hydraulic conductivity, the glomerular barrier also maintains surprisingly good selective permeability, excluding larger molecules.

The combined effect of a very large effective membrane surface area, a large pressure gradient favoring filtration, and a unique structure that facilitates filtra-

tion all contribute to its ability to produce such high volumes of filtrate, with an adult healthy kidney producing over 180 L/day [12]. Artificially created hemofiltration membranes can mimic some of the filtration characteristics of the glomeruli but cannot match the size and charge selectivity exhibited by the glomeruli. In addition, there is continuous modulation of filtration rate in response to changes in renal blood flow, hormonal influences, and local regulatory responses to changes in intra-glomerular pressures. In contrast, most artificial membranes used for extracorporeal support exhibit relatively fixed transport properties [13].

Tubular processing

Although glomerular filtration is the most obvious component of renal function, it does not account for how the kidney maintains homeostasis. After filtration, the tubules actively modify the components of the ultrafiltrate using specific transport proteins organized in a coordinated manner.

The proximal tubule is responsible for reabsorption of approximately all filtered electrolytes, bicarbonate, glucose, amino acids, and water. The Loop of Henle is responsible for creating the medullary osmotic gradient, which enables urine concentration. Distal segments of the tubule and collecting ducts regulate fine electrolyte balance and acid-base homeostasis through hormonal control [14].

All these processes utilize energy-dependent transport proteins embedded within cellular membranes. There are many types of transport proteins, including sodium-potassium ATPase, ion exchangers, aquaporins, and cotransporters. These transport proteins regulate the rate at which they transport components based on the body's physiological requirements. Therefore, the kidney acts as a biological processing unit that can change the behavior of its components in real time [15].

This concept has important implications when comparing native renal physiology to renal replacement therapies. Current dialysis modalities can partially replace both filtration and waste removal but cannot reproduce active tubular transport, endocrine signaling, metabolic activity, and adaptive regulation. Therefore, even the most advanced dialysis systems are not complete substitutes for native renal function.

Engineering lessons from native kidney function

The study of the native kidney reveals several engineer-

ing principles. These include: 1. the native kidney has continuous, rather than intermittent, transport; 2. renal transport is an adaptive process; 3. the kidney utilizes multiple simultaneous transport mechanisms; 4. the kidney contains intrinsic biological mechanisms for maintenance and repair.

These principles establish the conceptual framework of this review. Rather than comparing dialysis modalities solely based on clinical outcomes, the biomedical engineering approach presented in this review evaluates the extent to which different membrane systems reproduce the transport characteristics of the native kidney. In this context, both continuous renal replacement therapy and peritoneal dialysis may be viewed as alternative strategies to approximate the function of the highly sophisticated biological transport organ, the kidney.

Fundamental principles of membrane transport

The structures and functions of the native kidney, peritoneal membrane, and extracorporeal dialysis membranes differ greatly; however, they each functionally rely upon the same basic processes. Solutes and fluid move across both biologic and synthetic membranes via 4 primary mechanisms: diffusion, convection, ultrafiltration, and absorption [6]. An understanding of these mechanisms is necessary to assess the performance of renal replacement therapies and the similarities and differences between biologic and synthetic membrane systems.

Diffusion

Diffusion is defined as the movement of molecules from an area of high concentration to an area of low concentration. It is the method by which most small solutes are removed from the body via conventional hemodialysis and accounts for a large proportion of solute transfer during peritoneal dialysis. The theoretical mathematical modeling of diffusion is based on Fick's law [16,17]:

The theoretical basis of diffusion is described by Fick's law:

$$J = -D \frac{dc}{dx}$$

where J represents solute flux (the amount of solute moving), D is the diffusion coefficient, which is characteristic of the membrane (how easily solutes can pass through it), and dC/dx is the concentration gradient across the membrane (the difference in concentration

across the membrane).

Renal replacement therapy uses diffusion as the primary mechanism to remove low-molecular-weight solutes such as urea, creatinine, and potassium. Several parameters affect the efficiency of solute diffusion, including membrane surface area, thickness, molecular size, concentration gradient, and membrane material characteristics.

Most hemodialysis machines employ a countercurrent flow system to maintain a concentration gradient along the length of the membrane. This maximizes the amount of solute removed [16]. Peritoneal dialysis utilizes a concentration gradient generated between blood flowing through the patient's abdominal capillaries and dialysate in contact with those capillaries within the abdominal cavity [17]. Although the underlying transport mechanism is identical, diffusion efficiency differs substantially due to variations in membrane architecture and transport distances.

Convection

Transport by convection occurs when solutes move across membranes via mass flow of the solvent itself. Unlike diffusion, which is driven entirely by solute concentration gradients, the primary factor in convective transport is the movement of the solvent. As the solvent moves through the membrane, it carries all its solutes with it, a phenomenon known as solvent drag. The efficiency of convective transport can be quantitatively expressed as the Sieving Coefficient (the ratio of solute transported with the solvent to the total amount of solute available for transport). For substances with a middle molecular weight, such as inflammatory mediators and uremic toxins, convective transport is significant [7].

Ultrafiltration

Ultrafiltration refers to the flow of water through a semi-permeable membrane driven by a pressure gradient across it. Fluid removal represents one of the most clinically important functions of renal replacement therapy, particularly in critically ill patients with fluid overload.

Most of the fluid removal during extracorporeal therapies results from pressure differences between the blood and dialysate compartments. The higher blood compartment pressures push water through the mem-

branes. Since CRRT systems provide precise control over transmembrane pressure and ultrafiltration rate, they enable controlled fluid loss [18].

Unlike this concept, peritoneal dialysis removes fluid from the body through a completely different mechanism. Instead of using hydraulic forces to remove fluid, peritoneal dialysis uses osmotically induced fluid movement. A high concentration of glucose molecules in the dialysate creates an osmotic force that induces water movement from the circulatory system into the peritoneal space [19].

While both methods remove excess body fluids, the underlying technological mechanisms differ significantly. CRRT uses pressure-induced membrane separation while peritoneal dialysis uses osmotically induced membrane separation.

Adsorption

Adsorption occurs when molecules adhere to the outer surface of a membrane via physical/chemical reactions. Unlike diffusion/convection, adsorption does not rely on molecular concentration gradients or on solvent flow. Molecules bind to existing surface sites via electrostatic interactions, hydrophobic interactions, hydrogen bonds, or Van der Waals interactions [20].

Recent advances in synthetic membranes for extracorporeal renal replacement therapy have led to increased interest in adsorption. Specifically, researchers have developed membranes capable of removing endotoxins, inflammatory mediators, and protein uremic toxins from the blood. The amount of adsorption depends on the membrane's surface area, pore size/architecture, surface chemistry, and the duration of treatment. Once all adsorption sites on the membrane are saturated, its adsorption capacity will decrease over time. Unfortunately, in peritoneal dialysis therapies the adsorption effect is relatively minimal [21].

Engineering metrics of membrane performance

In order to have measurable characteristics that describe membrane performance, the following metric were defined: the ultrafiltration coefficient (K_{uf}) which is used to determine the hydraulic permeability of the membrane, i.e., how well a membrane transports water; the mass transfer area coefficient (K_oA) which defines the efficiency of diffusive transport across a membrane surface; the Sieving coefficients which represent

the convective permeability of individual solute components through a membrane [22].

Together, these measurable characteristics permit an objective comparison among membrane systems and facilitate an analytical approach to understanding differences between biologic- and synthetic-based transport mechanisms. Notably, many of these metrics can be easily quantified and manipulated in artificial membranes but are considerably more difficult to define within biological systems such as peritoneum. This distinction highlights one of the central themes of the present review: artificial membranes offer precise engineering control over membrane function, whereas biological membranes offer physiological integration at the cost of predictability.

Artificial membranes in critical care

Advancements in extracorporeal renal replacement therapies are directly linked to the evolution of membrane science and technology. Current hemofilters represent one example of how advanced engineering has produced high-performance medical equipment. Biomedical engineers use these systems to create predictable, reproducible, and optimal removal of fluid and waste products from blood while also ensuring hemocompatibility. These man-made membranes are purposefully built to remove fluid and waste from the blood at a rate that is both controllable and reproducible. As such, they are designed to meet very specific goals for patient treatment, contributing substantially to the widespread adoption of continuous renal replacement therapy in modern intensive care units.

Modern membrane materials

Most current commercial CRRT membranes are made from synthetic polymers including: polysulfone, polyethersulfone, polyacrylonitrile (AN69), and polymethylmethacrylate (PMMA). Each polymer has its own chemical structure, which will affect how it transports substances and its compatibility with biological fluids [23].

Polysulfones are among the most widely used polymers in clinical practice, providing excellent mechanical strength, thermal stability, and good mass-transfer properties. The porous structure of the membranes allows the separation of small-molecular-weight compounds while limiting the passage of larger proteins [24].

Similarly, polyethersulfone membranes exhibit comparable mass-transfer properties and are widely used in modern high-flux dialysis systems. Polyethersulfones are versatile enough to be processed into a variety of pore geometries and membrane thicknesses. This versatility enables designers to optimize both the diffusive and convective performance of the membrane [25].

In contrast, AN69 membranes possess a much greater degree of negative charge than polysulfones and polyethersulfones. In addition, AN69 membranes contain negatively charged hydrogels on their surfaces that can remove several types of inflammatory mediators. Development of modified versions of the original AN69 membrane has provided researchers and clinicians with new tools for treating sepsis via extracorporeal blood purification [21].

PMMA membranes provide yet another type of adsorbent activity in addition to the filtration capabilities already mentioned. Researchers have explored the possibility of using PMMA membranes to remove inflammatory cytokines and protein-bound toxins. Overall, this trend illustrates a growing movement toward designing membranes that can perform multiple functions simultaneously, including filtration, convection, and adsorption [21].

It should be noted that the mass transfer properties of a membrane do not depend solely on its composition. The physical characteristics of the membrane pores themselves play a critical role in determining how well a particular substance is separated from other components within a fluid. Therefore, two membranes composed of similar materials may behave quite differently when placed in a clinical setting. These characteristics are especially significant for critical care patients, as the membrane's physicochemical properties are influenced by an unstable biological environment characterized by systemic inflammation, vascular lining damage, impaired blood clotting, low albumin levels, and changes in plasma protein levels. Critically ill patients frequently have large amounts of varied substances that need to be removed during dialysis.

Biocompatibility and blood-material interactions

When blood encounters a foreign surface, such as a membrane, several reactions occur. These reactions begin almost immediately and involve protein adsorption onto the membrane surface. Once protein has been adsorbed onto the surface, other cellular reactions follow. This includes activation of the clotting and complement

cascades, white blood cell activity, platelet aggregation, and vascular signaling networks [26].

Blood-material interactions are especially relevant when working with critically ill patients who have existing inflammation, vascular damage, and abnormal coagulation states. Therefore, the membrane is not simply a conduit for solute exchange; it is also a bioactive surface capable of inducing physiological changes in the body.

The first step in the blood-material reaction sequence is protein adsorption. Plasma proteins quickly form a conditioning layer on membrane surfaces, imparting new chemical and physical properties. Membrane composition will dictate what happens next. It could activate clotting pathways or cause white blood cell adherence and the release of inflammatory mediators [26].

Because of the growing need to provide better solutions for patients undergoing dialysis, researchers and engineers are actively working to create membranes that do less harm to the blood. Examples of methods being explored include adding a hydrophilic coating to prevent protein adsorption, modifying the membrane surface charge to repel unwanted cellular elements, and applying anticoagulants directly to the surface to inhibit clotting [7].

Despite these efforts to make membranes more biocompatible, all current membranes interact with blood to some degree. Even though current biomedical engineering developments strive for "biological neutrality" in membranes, blood-material interactions remain a significant barrier to the delivery of safe and effective extracorporeal renal therapy.

One way in which membranes lose effectiveness during CRRT is through a phenomenon called fouling. Fouling, in the context of membrane engineering, is the accumulation of biological material (including proteins and other cellular components) on the surface or within the pores of a membrane. Over time, this accumulation reduces filtration efficiency.

There are several ways in which fouling can occur during CRRT. First, protein deposition can reduce the size of pores available for filtration, making it harder for smaller molecules to pass through. Second, cellular adhesion can block flow paths through the membrane, reducing filtration rates. Third, thrombus formation can block membrane pores, causing filtration rates to drop further. Collectively, these phenomena cause membrane performance to deteriorate over time,

resulting in decreasing clearance efficiency. One important manifestation of fouling is the formation of a secondary protein-rich membrane layer. Clinicians cannot see this layer, but it does affect how well the membrane works. Specifically, it increases the distance solutes must travel to be removed from the blood and makes some pores unavailable for filtration. As a result, actual membrane performance can deviate significantly from manufacturer specifications after extended exposure to blood. Additionally, fouling affects adsorption. Initial protein binding may help remove certain inflammatory mediators from the plasma, but as the membrane surface saturates with protein, its ability to bind additional proteins decreases. As a result, membrane performance becomes dynamic rather than static, as would be expected from a fundamentally engineered system [6].

Understanding fouling is critical to determining filter lifespan, optimizing anticoagulation protocols, and evaluating treatment efficacy. For researchers and engineers, fouling is one of the most significant barriers to long-term membrane performance and remains an active area of investigation in biomedical materials science. This issue is particularly important in critically ill patients, where prolonged treatment durations, systemic inflammation, hypercoagulability, and elevated circulating concentrations of plasma proteins and cellular debris accelerate membrane fouling compared with stable chronic dialysis populations [9].

The peritoneum as a biological membrane

The differences in approach between renal replacement therapy using artificial membranes and those using biological ones (the peritoneum) extend well beyond their anatomical location. Artificial membranes are engineered with specific transport properties, whereas the peritoneum is a living, dynamic biological membrane whose structural and functional characteristics can vary with factors such as the patient's age, comorbid conditions, degree of inflammation, blood vessel health, and prior environmental exposures.

Therefore, from a Biomedical Engineering standpoint, it could be argued that the peritoneum acts as a naturally occurring semi-permeable membrane designed to maintain physiological homeostasis, rather than to optimize dialysis performance. As a result, peritoneal transport behavior is more variable than the relatively consistent behavior of synthetic hemofilters. Understanding this variability requires an analysis of

both membrane composition and transport physiology.

Structure of the peritoneal membrane

The peritoneal membrane cannot be considered as a single structural entity. It has several components which make it a composite transport system. Solute and water moving between blood and dialysate must traverse the capillary endothelium, interstitial tissue, basement membranes, and mesothelial surface before reaching the peritoneal cavity.

Unlike man-made membranes, which have well-defined pore structures and thicknesses, the anatomy of the peritoneal membrane is heterogeneous across different parts of the body and among individuals. The primary transport function occurs in the peritoneal microvascular bed rather than at the mesothelial layer. As such, blood flow through the peritoneal vasculature, number of vessels within the peritoneum, endothelial cell integrity, and composition of the interstitium can all affect the rate of peritoneal transport.

The effective exchange area of the peritoneum is substantial, supported by an extensive capillary network. This results in a high degree of contact between the blood and dialysis solution. While this anatomically represents a significant amount of potential membrane area for solute or water removal, only a small percentage of it is functioning for transport at any given time. Perfusion changes, inflammatory reactions, and increased intra-peritoneal pressure can alter the extent of active membrane area and thus influence transport efficiency [27].

This highlights one of the main differences between bio-artificial and man-made membranes. Man-made membranes have static areas defined by their physical designs. Bio-artificial membranes have dynamic effective areas that vary with physiological conditions.

The three-pore model

The best-known framework for understanding how substances move into and out of the abdominal cavity during PD is the "three-pore" model created by Rippe et al. [28]. The three-pore model is the current theoretical basis for understanding peritoneal transport and provides an engineering perspective for evaluating the function of biological membranes.

In this model, transport occurs via three types of pores. Most fluid and solute exchange occurs through

small pores in the endothelial cells lining capillaries. These small pores allow water and low-molecular-weight substances such as urea, creatinine, sodium, potassium, and glucose to pass through. Therefore, small pores account for most of the diffusion occurring during PD.

Transport of larger molecules, such as proteins, occurs through a much smaller number of large pores. Although there are fewer large pores than small pores, they contribute significantly to both protein loss and changes in oncotic pressure across the membrane.

Ultra-small pores represent the third type of pore. These are thought to correspond to the water channels called aquaporins. While these pores are highly specific (they selectively allow certain molecules to pass through), they permit very rapid water movement while excluding dissolved solutes. Aquaporin-mediated transport plays a critical role in producing osmotic ultrafiltrate and helps explain some of the sodium sieving we observe during PD.

The contributions of each pore population to total transport do not remain constant; alterations in pore behavior due to inflammation, increased vascular permeability, endothelial injury, or chronic exposure to dialysis solutions may correspondingly alter the overall effectiveness of transport [28].

The three-pore model provides a useful conceptual bridge between physiological observations and engineering analysis.

Osmotic ultrafiltration

Fluid removal during peritoneal dialysis involves a mechanism distinct from that of other forms of extracorporeal therapy. While CRRT is based on hydraulic pressure gradients, peritoneal dialysis is based on osmotic forces generated by hyperosmolar solutions used for dialysis.

Glucose is the most commonly used osmotically active agent. When glucose is placed in the peritoneal cavity, it creates an osmotic gradient that promotes the movement of water from the capillary blood vessels into the dialysate solution. During this initial phase, free water transport predominates via aquaporin pathways, resulting in temporary decreases in dialysate sodium concentration.

As glucose diffuses into the bloodstream, the osmotic gradient continues to dissipate, and thus the rate of ultrafiltration will continue to decrease. Thus, as noted

above, fluid loss from peritoneal dialysis is both time- and glucose-absorption-dependent. In addition to the above-mentioned parameters, the amount of fluid lost will also depend on membrane permeability and local vascular physiology [19].

From a biomedical engineering perspective, there are several additional complexities involved in comparing osmotic ultrafiltration versus hydraulic ultrafiltration. The driving force for transport in osmotic ultrafiltration is neither constant nor directly controllable. Unlike hydraulic ultrafiltration, where the transport rate remains relatively constant until stopped, the transport rate of water in osmotic ultrafiltration varies continuously as the dialysate composition changes throughout each dwell cycle. These continuous changes contribute to the inherent variability seen in the performance characteristics of peritoneal dialysis.

Variability of biological membranes

One of the most notable differences between the peritoneum and artificial membranes is variability. Synthetic membranes are produced through a precise design and manufacturing process, whereas each patient's peritoneal membrane has unique characteristics.

There are many causes of the variability among patients' peritoneal membranes. For example, as people age, their blood vessels undergo changes that can make them less or more effective at transporting substances. Type I diabetes can also alter microvascular architecture, causing it to become less efficient. In addition, type I diabetes damages endothelium. Previous abdominal surgery can damage or compromise membrane integrity. Chronic exposure to dialysis solution(s), especially if the solution contains dextrose, can stimulate fibrosis and structural remodeling within the membrane.

The presence of inflammation is another key factor affecting how well a peritoneal membrane transports substances. When cytokines are released into the bloodstream, they activate the endothelium and increase capillary permeability. Therefore, inflammation can dramatically increase or decrease the efficiency of substance transport across the membrane within hours or days.

Biological membrane variability provides both benefits and liabilities. A biological membrane allows for flexible, dynamic responses to varying physiological needs. However, this flexibility makes it difficult to predict and control the membrane's transport properties.

Therefore, clinicians who manage peritoneal dialysis need to consider membrane variability, a consideration that is not required when using synthetic hemofilters.

Because they are living tissues, biological membranes can undergo adaptive changes, remodel themselves, heal, and exhibit physiological responses. Synthetic membranes do not have these same biologic capabilities. Therefore, while fouling or clot formation may affect the performance of synthetic membranes used in extracorporeal circulation devices, the membrane itself generally does not interact with its environment. Unlike synthetic membranes, however, biological membranes function as interfaces that respond biologically to their environments; thus, their transport parameters are determined by dynamic interactions among vascular, cellular, and molecular components [28]. This adaptive behavior is particularly relevant in critically ill patients, in whom sepsis, systemic inflammation, and degradation of the endothelial glycocalyx profoundly alter microvascular permeability, thereby modifying both solute transport and ultrafiltration efficiency.

Membrane performance during critical illness

The functional characteristics of both biological and artificial membranes are influenced by pathophysiological changes in patients with severe critical illness. Dialysis membranes are usually evaluated based on their static transport functions. In contrast, critically ill patients are biologically dynamic and exhibit clinical manifestations such as acute inflammatory responses, endothelial dysfunction, abnormal coagulation, unstable microvascular circulation, and unstable metabolic states. Therefore, membrane function within intensive care units is best assessed in relation to an individual patient's clinically dynamic status rather than simply relying on manufacturer-provided static transport functions or baseline physiological models [29].

Sepsis and endothelial dysfunctions

Sepsis is a common cause of acute kidney injury in intensive care units and significantly alters vascular function. During sepsis, inflammation leads to a wide range of alterations in vascular function, including endothelial dysfunction, degradation of the endothelial glycocalyx, increased capillary permeability, leukocyte adhesion, microvascular thrombosis, and alterations in transcapillary fluid and solute exchange. These changes can directly affect dialysis performance in the presence

of an inflammatory response, as the peritoneum acts as a vascular membrane. The inflammatory response will result in enhanced protein transfer across the peritoneal microcirculation, increased vasodilation, which increases the effective transport area, and rapid loss of the osmotic gradient that maintains ultrafiltration due to glucose-containing dialysate. Inflammation can also enhance lymphatic absorption, further reducing net ultrafiltration.

On the other hand, continuous renal replacement therapy membranes do not change their intrinsic permeability due to the patient's inflammatory status. This is because both the polymer composition and the pore geometry of the membrane are fixed at the time of manufacture. However, systemic inflammation does alter the interaction between blood and artificial membranes. High concentrations of fibrinogen, complement proteins, activated platelets, and inflammatory mediators will enhance protein adsorption, forming thrombi on the membrane and promoting fouling, thereby decreasing membrane function over time during extended-duration extracorporeal treatments [30].

Systemic inflammation and cytokine transport

Systemic inflammation affects both membrane transport and solute concentration. The high levels of cytokines and protein-bound uremic toxins impair membrane transport.

Synthetic membranes were designed to overcome some of the obstacles presented by systemic inflammation. The most recent generation of highly adsorptive membranes (AN69ST and PMMA) offers three methods for removing inflammatory mediators from the blood. Adsorption is achieved by electrostatic interactions and hydrophobic binding of proteins in the circulatory system to the membrane surface, resulting in the partial removal of larger molecules that are too large to be removed by diffusion because they bind to other proteins. Although the efficacy of removing cytokines from patients during continuous renal replacement therapy via extracorporeal means remains disputed, adsorption has become a design goal for modern CRRT membranes.

Biological peritoneal membranes do not exhibit significant inherent adsorbent properties. Instead, inflammation primarily causes changes in transport by altering vascular permeability and local tissue characteristics, rather than creating new clearing processes.

Therefore, inflammatory mediators affect PD indirectly by altering membrane physiology rather than being cleared via adsorption [31].

Fluid overload

Fluid overload is both a consequence and a driver of organ dysfunction in critically ill patients.

It increases tissue hydrostatic pressure due to excess interstitial fluid, decreasing oxygen diffusion into tissues. Ultrafiltration of dialysate depends on the pressure difference across synthetic membranes used in hemodialysis. Therefore, any alterations in intravascular or interstitial pressure directly affect the synthetic membrane's performance during dialysis.

Ultrafiltration in CRRT is driven by the transmembrane pressure in the system. This allows the clinician to control the rate of ultrafiltration independently of changes in vascular permeability. With respect to hydraulic stability, modern synthetic membranes are designed to maintain consistent performance if circuit clotting and membrane fouling are avoided. In addition to monitoring transmembrane pressure and filtration fraction, many CRRT systems now also monitor blood flow. These parameters allow clinicians to optimize membrane efficiency at all stages of treatment.

The mechanism of ultrafiltration with PD is primarily osmotic, whereas with CRRT it is primarily hydrostatic. Although fluid overload does not necessarily cause direct damage to the membrane, inflammation associated with most critical illnesses promotes glucose absorption from the dialysate. This will reduce the osmotic gradient that drives ultrafiltration. Increased peritoneal blood flow and vascular recruitment provide additional mechanisms that facilitate solute equilibration between the dialysate and plasma, ultimately resulting in reduced ultrafiltration [32].

The problems presented above represent a challenge to biomedical engineering. While there are many examples in which transport systems' behavior can be predicted with great accuracy under normal physiological conditions, the same systems may not behave similarly when subjected to the multiple types of disturbances found in sepsis, shock, and multiple organ failure. Additionally, the biological and synthetic membranes respond to these disturbances by fundamentally different mechanisms. For example, the peritoneum will adapt physically, physiologically, and structurally to respond to disease processes. Conversely, artificial membranes

will undergo physicochemical changes at the blood/material surface in response to the disturbance of the biologic fluid interface.

From a biomedical engineering perspective, the above statements demonstrate that membrane performance during critical illness depends on both membrane design and the dynamic physiological environment in which the membrane is used. Therefore, the membrane and the patient should be viewed as complementary elements of a combined biological-engineering system rather than distinct entities.

All of this indicates that future renal replacement devices will likely combine the long-term reliability and reproducibility of synthetic membranes with the biologically responsive properties of natural membranes. This is potentially possible through advances in all types of bio-inspired membranes, such as endothelial cell-cultured or attached surface systems, nanostructure-based membrane systems, and bio-artificial kidney systems.

Dynamic versus static membrane systems

The comparison between the two renal replacement modalities (peritoneal dialysis and CRRT) demonstrates a large difference in how membranes operate. A natural or living biological membrane is a dynamic structure that responds to changes in vascular permeability, inflammation, endothelial function, and cellular regeneration. Therefore, all of these can affect how efficiently it transports waste. Unlike biological membranes, artificial membranes are manufactured to be static, reliable, and reproducible. The characteristics of artificial membranes are established at the time of manufacture and generally remain consistent throughout their use in the patient [6,19].

The above distinctions may also serve as a basis for evaluating and comparing the benefits and drawbacks of various renal replacement technologies. Living membranes have the advantage of adapting to changing conditions but lose predictability, whereas synthetic membranes offer predictability but lack the ability to adapt.

The representation of optimal renal replacement therapy remains the subject of active debate in the biomedical engineering community. Ideally, this membrane would combine the advantages of both approaches (allow for control over and reproducibility similar to synthetic devices, all while retaining the abil-

ity to respond to changing conditions like living biological tissues). These goals are currently motivating research into developing this new hybrid renal support technology.

Emerging hybrid technologies

The limitations of current renal replacement therapies have created significant interest in developing new renal replacement technologies. While currently available dialysis systems can remove solutes and excess fluids from patients' blood, they lack many important functions of the native kidney, such as endocrine function, metabolic control, selective transport by the renal tubules, and adaptive physiological responses, that contemporary dialysis systems cannot provide.

From a biomedical engineering standpoint, it seems like the evolution of renal replacement therapy will be toward a synthesis of synthetic and biological systems. Rather than relying on either artificial membranes or biological tissues as the sole means of delivering renal replacement therapy, emerging technologies aim to combine both approaches. The final goal is not simply to improve the ability of these devices to clear substances, but rather to create platforms that replicate a wide range of renal physiologic processes with the same level of reliability and controllable performance needed in acute-care settings.

Bioartificial kidney systems

Bioartificial Kidneys are probably among the most advanced forms of renal replacement technology developed. They go beyond conventional dialysis machines by using both synthetic membrane materials and living renal cells to mimic some of the many functions of the real kidney.

Humes et al. have done pioneering work in developing what may become known as the "bioartificial kidney", or at least a prototype called the Renal Assist Device (RAD) [33,34]. The RAD incorporates renal tubular epithelial cells grown in culture into an artificial, outside-the-body, circulatory system. As with all forms of dialysis, there was a need for "initial" filtration before the "living" renal cells could perform other functions of the nephron.

Studies in experimental animals demonstrated that the "cells" within the RAD remained viable, continued to carry out normal metabolic processes, and were capable of selectively transporting substances across cell

membranes, generating ammonia, carrying out glutathione metabolism, and providing signals for endocrine functions. Preliminary clinical trials also indicated potential benefits in critically ill patients suffering from AKI, but no large-scale clinical application has been made. [33,34]

Adsorptive and multifunctional membranes

Membrane development has also involved incorporating additional therapeutic functions into extracorporeal devices. Traditional dialysis membranes were primarily developed to perform diffusion and ultrafiltration. The newest generation of technology emphasizes both adsorption and immunomodulation.

Membranes such as AN69-ST and oXiris have been modified to improve adsorption of inflammatory mediators and endotoxins. Hemoadsorbent platforms have been developed to remove cytokines and other biologically active molecules that contribute to systemic inflammation during sepsis [24].

The use of these technologies represents an expansion of the philosophy behind extracorporeal therapy: rather than being used as passive filtration devices, modern membranes can be thought of as interactive biotherapeutic interfaces that engage complex biological systems.

Many unanswered questions remain regarding the most effective targets, timing, and clinical effects of adsorptive therapies. Although their mechanistic basis may seem compelling, there is currently little evidence to support improved clinical outcomes.

■ DISCUSSIONS

The comparison between peritoneal dialysis and extracorporeal renal replacement therapies has traditionally been framed in terms of several variables, such as clinical outcomes, efficiency of waste removal, impact on blood pressure and circulation, and the cost and availability of resources and technology. While these considerations remain essential for clinical decision-making, these variables do not account for the key differences in the mechanisms by which each technique operates.

This study takes an alternative approach, viewing renal replacement therapies as essentially membrane technologies. In this context, rather than comparing the two types of dialysis treatments, the membranes are compared. Continuous renal replacement therapy uses

man-made membranes that can be mass-produced with specific properties that allow for consistent results, whereas the peritoneal dialysis membrane is part of the body's physiological system; therefore, its function varies with changes in physiology due to disease or injury. These distinctions may influence both the effectiveness of membrane transport and patients' responses during episodes of severe illness.

Artificial Versus Biological Membrane Paradigms

One of the most obvious comparisons when looking at artificial versus biological systems in terms of their level of variability is that they operate in completely different ways. The primary goal of designing artificial membranes is to minimize variability. To accomplish this, manufacturing processes are developed to create membranes with high replicability in their pore structure, hydraulic permeability, and transport properties [7]. The treatment outcomes can therefore be defined using quantifiable measures such as the ultrafiltration coefficient, Sieving coefficient, and mass-transfer area coefficient. Additionally, machine-regulated controls are used to manage the blood flow rate through the membrane, the rate of dialysis fluid flow past the membrane, the ratio of filtered to non-filtered plasma, and the net pressure difference across the membrane.

In stark contrast to artificial membranes, natural biological membranes exhibit inherent variability. The ability of the peritoneal membrane to transport solutes depends on multiple factors, including vascular density, endothelial health, inflammation within the membrane, interstitial physical structure, and others. Therefore, it is almost impossible to define the performance of the peritoneal membrane solely on the basis of its engineering attributes/parameters [28].

An additional way to distinguish between artificial and biological membranes is to consider them as having programmable and adaptive transport capabilities, respectively. Artificial membranes achieve desired performance through design and external management, whereas biological membranes achieve performance through physiologic response and internal regulation [6,19].

The Native Kidney as the Reference Standard

Neither CRRT nor PD can fully replicate the functionality of a healthy kidney. Both methods can successfully eliminate excess fluids and waste products from

the body; however, neither method can replicate all the physiological mechanisms that occur when a normal kidney functions.

Several features exist which make it difficult for technology to replicate the unique function of the native kidney. These include: highly selective filtering ability, active tubular transport, endocrine regulation, metabolic processes, continuous operation and adaptive responses. Additionally, each of these functions can occur simultaneously within an integrated biological system capable of maintaining its own function and healing itself if damaged [6].

Compared with current extracorporeal treatment options, modern renal replacement therapy technologies provide high precision and controllable environments for dialysis treatment but do not offer biologically responsive feedback loops. While peritoneal dialysis allows for some degree of physiological interaction through the peritoneum as a natural filter membrane, there is very little control over the membrane's characteristics. In contrast, kidneys combine both of these approaches, allowing for dynamic adaptation without compromising their reliable function.

Considering this perspective, renal replacement therapies currently being used should be viewed not as substitutes for the kidney but rather as only partial representations of selected functions of the kidney. A brief comparison between the native kidney, synthetic membranes, peritoneal biological membranes and bio-artificial membranes is presented in Table 1.

Membrane Behavior During Critical Illness

The differences in behavior between biological and synthetic membranes are particularly apparent in serious medical illnesses. Sepsis, systemic inflammation, damage to the endothelium, and disorders in microcirculation directly affect the biological transport mechanisms that occur at both synthetic and biological membranes [30].

During peritoneal dialysis, critical illness also significantly affects the membrane. Increased vascular permeability, loss of the glycocalyx, inflammatory activity, and changes in the number of capillaries recruited for solute exchange all contribute to changes in the membrane's transport characteristics. Consequently, the behavior of the membrane will evolve with that of the patient's physiological status.

During continuous renal replacement therapy

Table 1. Comparative characteristics of the native kidney, synthetic membranes, biological membranes and emerging bioartificial membranes

	Native Kidney	Synthetic Membrane	Peritoneal Biological Membrane	Bioartificial Membrane
Structure	Highly organized living organ	Polymeric hollow-fiber membrane	Living mesothelial membrane	Hybrid system integrating synthetic scaffold with living renal cells
Primary Transport Mechanism	Diffusion, Convection, Ultrafiltration, Active transport, Secretion, Reabsorption	Diffusion, Convection, Ultrafiltration, Absorption	Diffusion, Convection, Osmotic Ultrafiltration, Limited absorption	Diffusion, Convection, Ultrafiltration, Active transport
Driving Forces	Hydrostatic pressure, Oncotic pressure, Electrochemical gradients, Cellular energy	Concentration Gradients, Transmembrane pressure	Concentration gradients, Osmotic pressure	Physiological pressure gradients, Active cellular regulation
Predictability	High under physiological conditions	Very high	Moderate	Expected high predictability
Adaptability	Excellent	Minimal	High	Expected high adaptability
External Control	None	High	Limited	Expected partial external control
Biocompatibility	Complete	Limited	High	Expected high biocompatibility
Limitations in critically ill patients	Loss of native regulatory function during AKI	Blood-material interactions, Membrane fouling	Transport variability, Ultrafiltration failure	Unknown

(CRRT), although the structure of the synthetic membrane does not change significantly, performance is affected by biological interactions at the blood-material interface. Protein adsorption, coagulation activation, cellular deposits, and fouling affect transport efficiency over time. Here, the patient affects membrane function indirectly through surface interactions rather than through direct changes in membrane architecture [9].

These observations suggest an interesting parallel. Both types of membrane systems become dynamic during critical illness. However, this occurs for two different reasons. Biological membranes change because they are living tissue, and synthetic membranes change because biological materials accumulate on artificially engineered surfaces. Distinguishing between these two phenomena could help explain some of the variability in clinical performance among various patient populations.

Implications for Membrane Design

Historical emphasis in membrane engineering has focused on increasing permeability, improving biocompatibility, and controlling the rate of transport through membranes. This approach has led to the development of advanced synthetic membranes that deliver high efficiency in supporting the body through extracorpore-

al means. However, it is unlikely that simply enhancing efficiency will enable replacement of current dialysis treatments with those that more closely mimic natural kidney function [7].

To address this issue, future innovations may focus on developing dynamic membrane systems. Dynamic membrane systems can respond to changes in physiological conditions (e.g., blood chemistry) through a variety of mechanisms, including but not limited to biosensors, responsive surface coatings, selective adsorptive mechanisms, cellular components, and feedback-controlled transport pathways. Additionally, advances in tissue engineering and regenerative medicine may allow the integration of living biological structures into synthetic membrane-based devices.

Therefore, while bioartificial kidneys and implanted renal replacement systems represent an advancement over prior technologies, they also represent a convergence of the unique benefits of artificial and biological membrane systems [33,34].

■ LIMITATIONS

Several important limitations need to be addressed. The first limitation is that this review takes a conceptual biomedical engineering perspective and was not designed to systematically compare clinical outcomes

across dialysis methods. Secondly, several aspects of how membranes function in critically ill patients are not well understood, specifically the dynamic interactions between inflammation/endothelial dysfunction and membrane transport.

Although these limitations exist, a membrane-centered strategy offers an attractive framework for analyzing both the strengths and weaknesses of current forms of renal replacement therapy.

■ CONCLUSIONS

Acute kidney injury (AKI) in critical care remains an important issue despite advancements in renal replacement technology. From a Biomedical Engineering perspective, the membrane involved in transport will ultimately determine the performance of AKI treatments.

Each form of currently available renal replacement therapy has its own advantages and disadvantages regarding predictability, integration, and response to changing conditions, although none of the available forms replicate the complex combination of functions present in normal functioning kidneys, including selective filtration, active transport, metabolic activity, endocrine function, and regulatory adaptability.

The development of renal replacement therapy will likely arise from the continued fusion of membrane engineering and biology. The development of bio-artificial kidneys, cell-containing membranes, new biomaterials, and adaptable transport systems represents the first steps towards creating dialytic solutions that are both as precise as man-made devices and as responsive as living tissue. These newer technologies could provide a bridge between currently used forms of renal replacement therapy and the physiological complexities of normally functioning kidneys.

■ AUTHOR'S CONTRIBUTIONS

M. A. M. (Conceptualization; Formal analysis; Investigation; Methodology; Writing – original draft)

L. A. (Conceptualization, Writing- review and editing, Supervision)

D. B. (Conceptualization, Resources, Supervision)

B. L. G. (Conceptualization, Investigation, Methodology, Writing-review and editing)

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■ DISCLOSURE

Microsoft Copilot and Consensus tools were used during the preparation of this manuscript. Microsoft Copilot was used to assist with structuring ideas and grammar correction, while Consensus was used to identify and synthesize scientifically relevant literature. All AI-generated suggestions, summaries, and other outputs were reviewed, verified for accuracy and relevance, and revised. The authors take full responsibility for the final content of this manuscript.

■ CONFLICT OF INTEREST

None Declared.

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