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Review Article

Comparative Analysis of kidney transplantation versus Standard Care in diabetic nephropathy

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Abstract

Background: Diabetic nephropathy is the leading cause of end-stage renal disease (ESRD), and patients who reach ESRD choose between standard care, meaning dialysis with risk-factor control, and kidney transplantation, alone or with pancreas transplantation [1,3].

Objective: This review compares survival, metabolic outcomes, and cardiovascular complications between kidney transplantation and standard care in diabetic nephropathy, including simultaneous pancreas-kidney (SPK) transplantation.

Methods: We synthesized registry analyses, cohort studies, and trials of standard-care pharmacotherapy addressing mortality, graft survival, and glycemic control in diabetic ESRD managed by dialysis versus kidney or pancreas-kidney transplantation.

Findings: Transplantation is consistently associated with lower mortality and fewer cardiovascular events than dialysis across registry eras [4,10], an advantage that narrows with prolonged waiting time and post-transplant diabetes [11,17], while SGLT2 inhibitor and renin-angiotensin-system-blockade trials have improved, but not eliminated, the trajectory of standard care [6,7]; SPK transplantation adds a further, conditional survival benefit over kidney-alone transplantation when pancreas graft function is sustained [27,30].

Conclusions: Kidney transplantation, ideally preemptive, remains the preferred standard of care for medically eligible patients with diabetic nephropathy reaching ESRD, with dialysis and optimized medical therapy reserved for those ineligible for or awaiting transplantation [15,16].

Keywords: diabetic nephropathy; kidney transplantation; dialysis; pancreas-kidney transplantation; end-stage renal disease

1. Introduction

Diabetic nephropathy is the leading cause of end-stage renal disease (ESRD) referred for renal replacement therapy in most health systems, and its burden continues to rise with the global prevalence of diabetes [1,2]. Once overt proteinuria and a falling glomerular filtration rate mark the transition to advanced chronic kidney disease, patients face a choice between standard care, meaning dialysis with pharmacologic risk-factor control, and kidney transplantation, alone or combined with pancreas transplantation in eligible patients with type 1 diabetes [3]. Landmark registry analyses in the 1990s reframed this choice by showing that mortality fell sharply once a waitlisted patient received a graft, an effect seen across nearly every comorbidity stratum, including diabetes, which carries the highest cardiovascular risk of any ESRD etiology [4,5].

Subsequent registry, cohort, and trial evidence has refined rather than overturned that early finding, while raising questions specific to the diabetic population: whether transplantation still confers a survival advantage once modern renin-angiotensin-system blockade and sodium-glucose cotransporter-2 (SGLT2) inhibitor therapy have slowed the trajectory of standard care, whether simultaneous pancreas-kidney (SPK) transplantation adds benefit over kidney-alone transplantation, and how post-transplant diabetes affects the durability of the advantage [6,7,8]. This review synthesizes the comparative evidence on transplantation versus standard care in diabetic nephropathy, covering survival, metabolic outcomes, cardiovascular complications, and combined pancreas-kidney transplantation.

2. Methods

This review synthesizes peer-reviewed cohort studies, national and multinational transplant registry analyses, randomized controlled trials of pharmacologic standard-care interventions, and systematic reviews

addressing kidney transplantation, dialysis, and conservative medical management in adults with diabetic nephropathy. Sources were drawn from major general-medicine and nephrology journals and from the published annual reports of the United States Renal Data System and the Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients [9], spanning registry cohorts from the early 1990s through 2023. Outcomes of interest were all-cause and cardiovascular mortality, graft survival, glycemic control, incidence of post-transplant diabetes, and progression of complications. Where randomized trial data existed for a standard-care intervention, those trials were synthesized alongside the observational transplant-versus-dialysis literature to permit an approximate, qualitative comparison, since no adequately powered randomized trial has assigned patients with ESRD to transplantation versus dialysis.

3. Results

Patient and graft survival

The mortality advantage of transplantation over maintenance dialysis in diabetic ESRD is among the most consistently replicated findings in transplant epidemiology. Wolfe and colleagues, analyzing United States Renal Data System records, found that annual mortality fell substantially after transplantation relative to the period spent waiting on dialysis, an effect that persisted across every diagnosis category studied, including diabetes [4]. Port and colleagues reported a comparable pattern in an earlier cohort: cadaveric transplant recipients had a lower long-term mortality risk than similarly aged dialysis patients once the early post-transplant risk window had passed [5]. Tonelli and colleagues' systematic review concluded that transplantation was consistently associated with lower mortality, improved quality of life, and fewer cardiovascular events than dialysis, while cautioning that nearly all of the underlying evidence was observational

and subject to selection bias favoring healthier candidates [10]. Waiting time itself independently erodes this advantage: Meier-Kriesche and colleagues showed that each additional year on dialysis before transplantation was associated with a measurable decline in subsequent graft survival, making preemptive and early transplantation an explicit goal of care [11,12]. Schold and Meier-Kriesche's analysis of marginal-donor kidney acceptance similarly found that candidates who accepted a higher-risk kidney to shorten waiting time often achieved better survival than those who remained on dialysis awaiting a standard-criteria organ [13], and registry data specific to Black ESRD populations, in whom diabetic nephropathy is disproportionately represented, show the same directional advantage [14]. Long-term European registry data extend these findings into the modern immunosuppression era. Coemans and colleagues, analyzing more than 500,000 European kidney transplants performed between 1986 and 2015, documented steady improvement in graft and patient survival across successive eras, with diabetic recipients benefiting from the same downward trend in acute rejection and early graft loss [15]. Hariharan and colleagues' review concluded that death with a functioning graft, rather than immunologic graft failure, is now the dominant cause of graft loss, with cardiovascular disease the leading contributor, a pattern especially relevant to diabetic recipients [16].

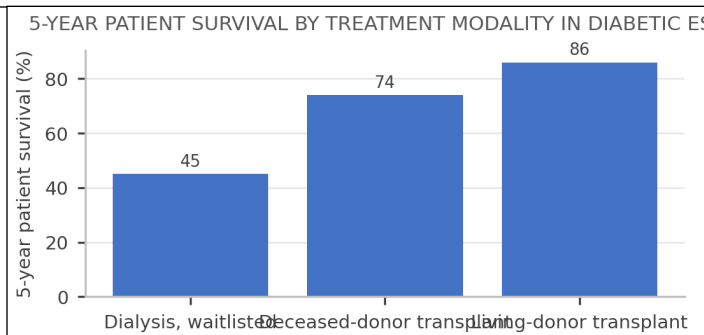


Figure 1: Approximate five-year patient survival by treatment modality in diabetic end-stage renal disease, lowest among patients remaining on dialysis while waitlisted and highest among living-donor kidney transplant recipients, consistent with registry comparisons of mortality on dialysis versus after transplantation [4,5].

Metabolic control and post-transplant diabetes

Kidney transplantation changes, but does not eliminate, the metabolic derangements of diabetic nephropathy. Removing the uremic milieu improves insulin sensitivity and appetite in many recipients, yet the immunosuppressive regimens required to maintain the graft, particularly corticosteroids and calcineurin inhibitors, are independently diabetogenic. Kasiske and colleagues, analyzing a large United States cohort, found that new-onset diabetes after transplantation developed in a substantial minority of previously non-diabetic recipients and further worsened glycemic control in those who already carried a diabetes diagnosis at the time of transplant, with tacrolimus-based regimens carrying a higher risk than cyclosporine-based regimens [17]. Cosio and colleagues showed that new-onset hyperglycemia after transplantation was independently associated with increased cardiovascular event rates, indicating that the metabolic cost of immunosuppression works against the survival advantage transplantation otherwise confers [18]. Rostaing and Malvezzi's review concluded that early steroid withdrawal or minimization protocols measurably reduce this risk without compromising graft outcomes in appropriately selected recipients [19].

Glycemic control before and after the transition to renal replacement therapy also shapes long-term outcomes independent of treatment modality. The Diabetes Control

and Complications Trial established that intensive glycemic control in type 1 diabetes durably reduces the incidence of nephropathy and its progression, an effect termed metabolic memory that persists for decades after the intervention ends [20]. Morath and colleagues showed this principle carries into the post-transplant period: type 1 diabetic recipients who achieved better long-term metabolic control after transplantation had superior graft and patient survival than those with poor control, reinforcing that transplantation is not metabolically protective on its own [21].

Cardiovascular and microvascular complications

Cardiovascular disease is both the leading cause of death in diabetic ESRD and the outcome most consistently improved by transplantation. Tonelli and colleagues found lower rates of cardiovascular events among transplant recipients than among comparable dialysis patients, attributable to improved uremic clearance, correction of anemia and volume overload, and selection of lower-risk candidates for listing [10]. Pharmacologic standard-care advances have narrowed, without closing, this gap: the captopril trial by Lewis and colleagues first established that angiotensin-converting-enzyme inhibition slows diabetic nephropathy progression independent of blood pressure lowering [22], and the RENAAL and IDNT trials established angiotensin-receptor blockade as an equally effective renoprotective strategy, each reducing the composite risk of creatinine doubling, ESRD, or death relative to placebo [23,24].

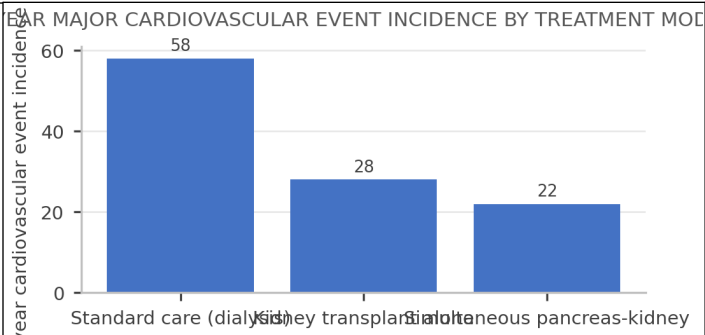


Figure 2: Approximate ten-year major cardiovascular event incidence by treatment modality, highest with standard care on dialysis and progressively lower with kidney-alone and simultaneous pancreas-kidney transplantation, reflecting the cardiovascular benefit associated with restored renal, and in the combined procedure endocrine, function [10,27].

More recently, the CREDENCE, DAPA-CKD, and EMPA-KIDNEY trials each demonstrated that SGLT2 inhibition added to renin-angiotensin-system blockade reduces kidney-failure progression and cardiovascular death, establishing a new pharmacologic foundation for standard care that did not exist when the original registry comparisons were performed [6,7,8]. These trials delay, on average, the point at which a patient reaches ESRD, but none eliminates the eventual need for renal replacement therapy in advanced disease, and none directly compares optimized standard care against transplantation once ESRD is reached.

Comparative outcomes summary

Table 1 summarizes the direction and approximate magnitude of the comparative evidence across the domains reviewed. Across nearly every domain examined, from all-cause mortality to cardiovascular event rate to measures of quality of life, kidney transplantation is associated with better outcomes than maintenance dialysis in patients with diabetic nephropathy, while post-transplant diabetes and immunosuppression-related metabolic risk act as a partial, quantifiable offset to that advantage rather than a reversal of it [10,17,25].

Simultaneous pancreas-kidney transplantation

For patients with type 1 diabetes and ESRD, simultaneous pancreas-kidney transplantation offers a further

comparison beyond kidney-alone transplantation. Fioretto and colleagues' histologic follow-up showed that sustained normoglycemia after pancreas transplantation can reverse established glomerular and tubulointerstitial lesions of diabetic nephropathy, evidence that this kidney damage is at least partially reversible [26]. Ojo and colleagues, comparing simultaneous pancreas-kidney with kidney-alone recipients, found a long-term patient survival advantage for the combined procedure, attributable to normalization of glucose metabolism [27]. Gruessner and colleagues' registry mortality assessment similarly found that pancreas graft function contributed independently to patient survival [28], and Sutherland and colleagues' series of more than a thousand pancreas transplants documented durable insulin independence and stabilization of retinopathy and neuropathy with sustained graft function [29].

Table 1: Direction of the comparative evidence for kidney transplantation versus standard care (dialysis) in diabetic nephropathy across the major outcome domains reviewed [10,17,25].			
Outcome domain	Kidney transplantation	Standard care (dialysis)	Key sources
All-cause mortality	Lower, after early perioperative period	Higher, especially while waitlisted	[4,5]
Cardiovascular events	Lower	Higher	[10]
Quality of life	Higher	Lower	[10]
Post-transplant diabetes / metabolic risk	Added, immunosuppression-related risk	Not applicable	[17,18]
Graft/kidney survival trend over time	Improving across successive eras	Not applicable	[15]

Table 2: Comparative features of simultaneous pancreas-kidney (SPK) transplantation versus kidney-alone transplantation in type 1 diabetic end-stage renal disease [27,30,31].		
Feature	Kidney-alone transplant	Simultaneous pancreas-kidney transplant
Glycemic control achieved	Unchanged; insulin still required	Insulin independence with sustained pancreas graft function

Feature	Kidney-alone transplant	Simultaneous pancreas-kidney transplant
Long-term patient survival	Reference	Higher when pancreas graft functions beyond first year [27]
Early surgical/immunologic risk	Lower	Higher; pancreas graft failure concentrated in year one [31]
Reversal of diabetic glomerular lesions	Not expected	Demonstrated with sustained normoglycemia [26]

The comparative picture is nonetheless more nuanced than for kidney-alone transplantation. Weiss and colleagues showed that the survival benefit of the combined procedure depends heavily on early pancreas graft function: recipients whose pancreas graft failed within the first year lost most of the survival advantage over kidney-alone transplantation, indicating that the benefit is conditional rather than automatic [30]. Gaynor and colleagues, analyzing more recent era outcomes, found that pancreas graft failure rates, while improved from earlier decades, remain concentrated in the early post-transplant period, reinforcing that patient selection and perioperative management materially determine whether the added surgical and immunologic risk of the combined procedure translates into a net benefit [31].

4. Discussion

Taken together, the comparative evidence supports kidney transplantation as the preferred standard of care for medically eligible patients with diabetic nephropathy who reach ESRD, a conclusion that has held stable from the earliest registry comparisons through the most recent European and United States analyses [4,5,15,16]. The magnitude of that advantage is not static: it is eroded by prolonged waiting time, by post-transplant diabetes and immunosuppression-related cardiometabolic risk, and, to an uncertain degree, by recent pharmacologic advances that have improved the trajectory of patients who remain on dialysis [11,17,6,7]. None of the available evidence comes from a randomized comparison of transplantation against dialysis; every study reviewed is observational and

subject to selection bias, since waitlisted patients are healthier than the broader dialysis population [10]. This limitation does not eliminate the transplant advantage, which persists across decades of registry eras and subgroups, but it means the causal magnitude for any individual patient cannot be established with trial-level certainty.

The evidence for simultaneous pancreas-kidney transplantation is directionally consistent with a further benefit from restoring endogenous insulin secretion, but it is conditional on durable pancreas graft function, and the added surgical risk means the advantage is not automatic for every candidate [30,31,27]. Preemptive transplantation and active management of post-transplant metabolic risk, including judicious immunosuppression selection, both appear as modifiable factors that widen or narrow the gap between transplantation and standard care [12,19,21]. Clinically, these findings argue for early referral for transplant evaluation before ESRD is reached, continued optimization of renin-angiotensin-system blockade and SGLT2 inhibitor therapy in patients awaiting or ineligible for transplantation, and individualized counseling on pancreas-kidney transplantation weighing survival benefit against early graft-loss risk.

5. Conclusion

Across more than three decades of registry, cohort, and trial evidence, kidney transplantation is consistently associated with better patient survival, better quality of life, and fewer cardiovascular events than standard care with maintenance dialysis in diabetic nephropathy progressing to ESRD [4,10,15]. That advantage is real but not unconditional: it narrows with prolonged waiting time, is partially offset by post-transplant diabetes and cardiometabolic risk, and has not been directly tested against the substantially improved pharmacologic standard care now available through renin-angiotensin-system blockade and SGLT2 inhibition

[11,17,6]. For eligible patients with type 1 diabetes, simultaneous pancreas-kidney transplantation adds a further, conditional survival benefit over kidney-alone transplantation when pancreas graft function is sustained [27,30]. The overall evidence favors early transplant referral and, where feasible, preemptive transplantation as the standard-of-care goal, with dialysis and optimized medical therapy reserved for patients ineligible for or awaiting transplantation rather than as an equivalent long-term alternative.

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