

ABO-Incompatible Kidney Transplantation as a Strategic Expansion Tool in Low- and Middle-Income Countries

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Abstract

The persistent disparity between organ supply and demand remains the principal limitation to kidney transplantation worldwide. ABO-incompatible kidney transplant has progressively evolved from an experimental procedure to an established strategy for expanding the living donor pool. This review critically evaluated whether ABO-incompatible kidney transplant represents a justified, effective, and feasible solution in low- and middle-income countries. We conducted a structured review of international registry data, meta-analyses, and major cohort studies to assess epidemiology, historical evolution, immunologic principles, clinical outcomes, desensitization protocols, economic implications, and complication profiles associated with ABO-incompatible kidney transplant. Our results showed that global transplant activity fulfills <10% of estimated needs. ABO-incompatible kidney transplant procedures have increased living donor availability by approximately 25% to 33% in countries adopting this strategy. Contemporary data showed that graft and patient survival rates approached rates of compatible transplant, although early risks of antibody-mediated rejection, infection, and bleeding remain higher. Advances in B-cell depletion

therapy, immunoadsorption techniques, and modern immunosuppressive regimens have markedly improved outcomes. The primary limitation in low- and middle-income settings is financial cost, particularly related to antibody removal technologies; however, validated cost-reduction strategies exist. ABO-incompatible kidney transplantation is no longer experimental and should be considered a mature, evidence-supported strategy. When implemented in experienced centers with appropriate protocols and cost-adaptation measures, this method constitutes a reasonable and potentially transformative approach to mitigating organ shortages in selected low- and middle-income countries.

Key words: Blood group incompatibility, Desensitization, Living donor transplantation, Renal transplant, Resource-limited settings

Introduction

The global shortage of organ donors remains the central challenge of modern transplantation medicine. According to the 2024 International Report on Organ Donation and Transplantation Activities, more than 173 000 solid organ transplants were performed worldwide in 2024, yet this number represents less than 10% of global need.¹ Even in highly developed systems such as the United States, the imbalance between supply and demand persists, with approximately 100 000 candidates remaining on the waiting list in 2020 despite substantial annual transplant activity.²

Prolonged wait times translate into excess mortality among patients with end-stage kidney disease (ESKD) who are maintained on dialysis.³ Consequently, expansion of the donor pool is not merely desirable but ethically imperative. Traditional strategies, including marginal donor utilization, presumed

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consent legislation, paired exchange programs, and altruistic donation, have improved access but remain insufficient.

Within this context, ABO-incompatible kidney transplant (ABOi-KT) represents one of the most conceptually transformative strategies; this strategy converts previously excluded donor-recipient pairs into viable transplant opportunities.⁴ The central question is not whether this approach works in highly specialized centers, but whether this approach is justified, effective, feasible, and safe enough to be adopted in low- and middle-income countries (LMICs).

Is ABO-Incompatible Transplantation Justified?

The justification for ABOi-KT rests on epidemiologic necessity. Organ shortage is universal and disproportionately severe in LMICs, where deceased donor programs are often underdeveloped.¹

Simulation studies and clinical implementation data have demonstrated that ABOi-KT increases the effective living donor pool by approximately 25% to 33%.⁵⁻⁷ This magnitude of expansion is not incremental; it is transformative. In regions that rely predominantly on living donation, this increase may represent the difference between stagnation and growth of transplant programs.

Survival after kidney transplant is superior compared with remaining on dialysis.³ Even if incompatible transplant carries moderately increased early risk, the relevant comparison is not compatible transplantation but continued dialysis. When framed in this manner, the ethical justification becomes compelling.

Is the Strategy Supported by Sufficient Experience?

The immunologic barrier of ABO incompatibility was historically considered absolute. After the discovery of the ABO system by Landsteiner⁸ and early demonstrations of catastrophic rejection by Starzl and colleagues,⁹ incompatibility was deemed prohibitive.

The first successful ABOi-KT in 1981 in Belgium, followed by structured protocols incorporating splenectomy and plasma exchange, demonstrated feasibility.^{10,11} Japan subsequently refined and expanded this strategy, driven by limited deceased donations.^{6,7}

Over 4 decades, ABO-incompatible transplantation has transitioned from anecdotal rescue therapy to a structured, protocol-driven practice supported by multicenter registries involving thousands of patients.¹² Such cumulative experience clearly exceeds the threshold required to consider a technique mature rather than experimental.

Is ABO-Incompatible Transplantation Effective?

Graft survival

Progressive improvement has been documented over time. Single-center analyses have shown that contemporary graft survival with incompatible transplant closely approximates rates with compatible transplant (Table 1).^{13,14} A systematic review and meta-analysis reported higher graft loss at 1 and 3 years, with convergence of survival curves thereafter.¹⁵ Large registry data, which included 1420 cases from 101 centers, confirmed acceptable 3-year outcomes following antibody reduction.¹² Thus, although early immunologic risk remains elevated, long-term graft survival is increasingly comparable in experienced centers.

Patient survival

Data from meta-analyses have shown modestly higher mortality within the first 5 years (Table 1).¹⁵ However, infection-related mortality appears closely linked to intensity of immunosuppression and center experience.¹² Of note, the alternative, prolonged dialysis, carries substantial mortality risk.³ Therefore, effectiveness must be interpreted within clinical context rather than isolated comparative statistics.

Mechanistic advances underpinning success

The cornerstone of modern ABOi-KT includes (1) B-cell depletion, (2) antibody removal, (3) prevention of antibody rebound, and (4) induction of accommodation.¹⁶ The concept of accommodation, graft resistance despite circulating antibodies, was formally described in this context and is attributed to reduced antigen expression and protective endothelial adaptation.¹⁷

B-cell depletion

Splenectomy, once considered mandatory,¹⁸ has been replaced by rituximab-based protocols, eliminating the need for invasive surgery.¹⁹

Table 1. Comparative Outcomes of ABO-Compatible Versus ABO-Incompatible Kidney Transplant

Outcome	ABO-Compatible	ABO-Incompatible
1-year graft survival, %	95 to 97 ¹³	92 to 95 ^{14,15}
3-year graft survival, %	90 to 92 ¹³	88 to 91 ^{14,15}
1-year patient survival, %	96 to 98 ¹³	94 to 96 ^{14,15}
Antibody-mediated rejection, %	5 to 7	12 to 15 ¹⁵
Infection risk	Baseline	Increased ¹²
Bleeding complications	Baseline	Increased ³²

Antibody removal

Immunoadsorption techniques, particularly antigen-specific columns, have demonstrated superior graft outcomes compared with conventional plasma exchange.¹²

Modern immunosuppression

Replacement of cyclosporine and azathioprine with tacrolimus and mycophenolate mofetil have significantly reduced rejection rates.²⁰ Depleting polyclonal induction therapy has shown safety in high-risk settings.²¹ These advances collectively explain the improved outcomes observed over the past 2 decades.

Is Monitoring of ABO Antibody Titers a Feasible and Reliable Strategy in Low- and Middle-Income Countries?

Hemagglutination remains the most widely used antibody titration method, although standardization remains imperfect.^{22,23} Flow cytometry offers precision but is costly and less practical for frequent monitoring.²⁴ For LMICs, pragmatic standardization of hemagglutination techniques may represent a feasible compromise.

Are Economic Constraints a Limiting Barrier to ABO-Incompatible Kidney Transplantation in Resource-Limited Settings?

Cost represents the principal barrier to adoption. National cohort analyses have shown that incompatible transplant incurs additional expenses related to desensitization and monitoring.²⁵

The largest contributor to cost is immunoadsorption columns, which cost approximately €4000 per unit.²⁶ With 5 sessions, costs may approach €20 000. However, validated mitigation strategies exist, including safe reuse of immunoadsorption columns, reducing expenditure without compromising efficacy,²⁷ and individualized desensitization based on baseline titers, reducing unnecessary procedures.²⁸⁻³⁰ In selected tertiary centers, these measures may render implementation economically defensible.

Is the Safety Profile of ABO-Incompatible Kidney Transplantation Acceptable Compared With ABO-Compatible Transplantation?

A previous meta-analysis confirmed increased risk of antibody-mediated rejection, infectious complications, and bleeding events.^{31,32} Infections are associated with increased mortality.¹² These risks necessitate careful patient selection, optimized prophylaxis, and experienced management. However, the

existence of risk does not equate to unacceptability. Rather, it defines the need for structured implementation.

Should Low- and Middle-Income Adopt ABO-Incompatible Kidney Transplantation?

The answer is not universally affirmative. It depends on existing transplant infrastructure, laboratory capacity for antibody monitoring, access to modern immunosuppressive therapy, financial sustainability, and surgical and immunologic expertise. Where these prerequisites are met, ABOi-KT offers a rational and evidence-supported expansion strategy. Where they are absent, premature implementation may increase morbidity. Thus, adoption should be selective, centralized, and protocol-driven.

Conclusions

ABO-incompatible kidney transplant has evolved from experimental innovation to established clinical strategy supported by decades of cumulative evidence. Its use has expanded the living donor pool by approximately one-quarter to one-third, a magnitude highly relevant for regions with limited deceased donations. Although associated with increased early immunologic and infectious risks and additional costs, long-term graft and patient outcomes approach outcomes of compatible transplant procedures in experienced centers. For selected LMICs with established transplant programs and the capacity for structured implementation, ABOi-KT constitutes a reasonable and strategically important solution to organ shortages.

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