Cognitive impairment following kidney transplantation: a narrative review of risk factors, mechanisms and management

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Abstract:

Background: *Cognitive impairment (CI) is increasingly recognised as a clinically important, yet under-addressed, complication after kidney transplantation. Reported prevalence figures vary widely, and the underlying mechanisms and potential interventions remain incompletely integrated in the literature.*

Objectives: *To synthesise current evidence (up to 31 March 2025) on the prevalence, longitudinal trajectory, determinants, clinical impact and emerging management strategies for CI in adult kidney-transplant recipients (KTRs).*

Methods: *A narrative review was conducted following a systematic search of PubMed/MEDLINE, Embase, Scopus and the Cochrane Library from inception to 31 March 2025. Inclusion criteria comprised original human studies reporting quantitative or qualitative cognitive outcomes in adult KTRs; paediatric, animal, case series < 5 patients and non-English articles were excluded. Two reviewers independently screened records and extracted data. Risk of bias was assessed with the Newcastle–Ottawa Scale (observational studies) and ROB-2 (trials). Findings were synthesised thematically.*

Results: *Fifty-seven primary studies (2006-2025) involving 9 873 KTRs met eligibility criteria. Point prevalence of CI ranged from 6.5 % to 58 % (median ≈ 38 %), with executive function and processing speed most frequently affected. Eighteen longitudinal cohorts delineated a "recover–stabilise–diverge" trajectory: rapid gains within 3 months post-transplant, plateau to 24 months, then divergence according to age and vascular burden. Consistent determinants included advanced age, diabetes, hypertension, lower eGFR, frailty and high tacrolimus exposure; mechanistic pathways converged on microvascular injury, calcineurin-inhibitor neurotoxicity and modifiable systemic factors (anaemia, inactivity). CI was associated with poorer adherence, higher rehospitalisation and reduced graft survival. Seven interventional trials demonstrated clinically relevant cognitive improvements with structured exercise, yoga/mindfulness programmes and low-dose tacrolimus, supporting the modifiability of CI.*

Conclusions: *CI affects roughly one-third to one-half of KTRs and is driven by intersecting vascular, pharmacological and lifestyle factors. Routine MoCA-based screening, risk-stratified follow-up and multidisciplinary interventions—including exercise rehabilitation and judicious immunosuppression titration—should be integrated into standard transplant care while larger multicentre trials are awaited.*

Keywords: *cognitive impairment; kidney transplantation; prevalence; risk factors; trajectory; Montreal Cognitive Assessment; exercise rehabilitation; calcineurin-inhibitor neurotoxicity*

Background

Cognitive impairment (CI) is increasingly recognised as a prevalent and clinically meaningful complication in chronic kidney disease (CKD) and among kidney-transplant recipients (KTRs) [1,2]. Its aetiology is multifactorial, encompassing pre-existing cerebrovascular injury, persistent inflammation and uraemic neurotoxins, neurotoxic effects of immunosuppressive agents, and psychosocial stressors [3–5]. Although kidney transplantation improves renal function, survival, and quality of life—and may stabilise cognition—mild-to-moderate deficits persist in many recipients [2,6,7]. Contemporary cohorts report CI in approximately 30–58% of KTRs, typically affecting executive function, attention, memory, and processing speed [2,8,9]. These deficits compromise medication adherence, functional independence, and treatment compliance, with downstream consequences for hospitalisation and graft outcomes [9–11]. Despite these implications, cognitive health is infrequently assessed during routine follow-up, owing to limited screening protocols, variable validation of cognitive instruments in transplant populations, and heterogeneous study designs [12,13].

Against this backdrop, prior reviews on cognition in CKD and transplantation have been constrained by older data or a narrow clinical focus [2,14]. To address these gaps, we provide an updated narrative synthesis through 31 March 2025, integrating findings from 57 primary studies. Uniquely, we juxtapose prevalence and longitudinal trajectories with mechanistic determinants and emerging management strategies—including structured physical activity, pragmatic cognitive screening (e.g., MoCA), and immunosuppression tailoring—bridging research evidence and clinical application [15–17,4].

Material and Methods

Study design

A narrative review was chosen because of the heterogeneity in study populations, cognitive domains, and methodologies, which precluded quantitative pooling.

Literature search strategy

Four databases (PubMed/MEDLINE, Embase, Scopus, and the Cochrane Library) were searched from their inception until 31 March 2025. Search strings combined controlled vocabulary (MeSH/Emtree) and free-text terms: ("kidney

transplantation" OR "renal transplant") AND ("cognitive impairment" OR "cognitive dysfunction" OR "neurocognition") AND ("MoCA" OR "Montreal Cognitive Assessment" [15] OR "MMSE" OR "Mini-Mental State Examination" [18]) AND ("neuropsychological assessment" OR "executive function" OR "processing speed"). Additional modifiers, such as "immunosuppression," "exercise," and "physical activity," were added in secondary searches. Reference lists of included articles were manually screened.

Eligibility criteria

We included original human studies (observational or interventional) that reported quantitative or qualitative cognitive outcomes in adult kidney-transplant recipients (KTRs) aged ≥18 years. We excluded studies involving paediatric populations, animal/in vitro studies, case series with <5 patients, and non-English papers without translation. Definitions for living and deceased donation followed KDIGO guidance for donor evaluation and post-transplant care [19,20].

Study selection and data extraction

Two reviewers screened titles/abstracts and full texts independently, resolving disagreements by consensus. A piloted spreadsheet captured study design, sample size, demographics, cognitive tools, timing of assessment, and main findings.

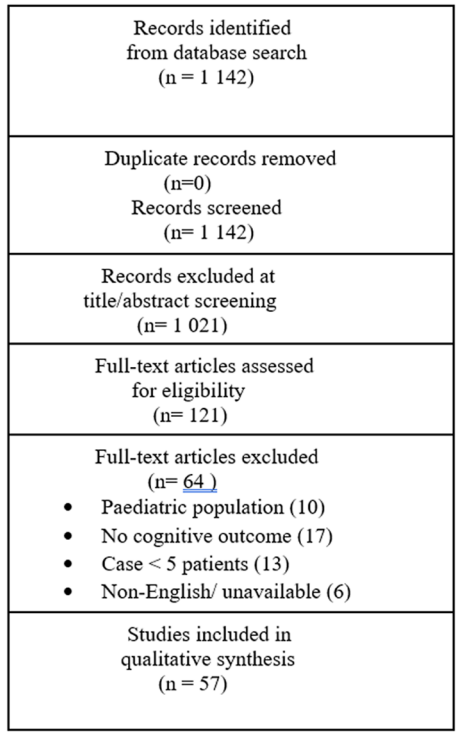
Risk of bias

Observational studies were appraised with the Newcastle–Ottawa Scale [22], and interventional trials with ROB 2 (the revised Cochrane risk-of-bias tool for randomised trials) [21]. Given substantial methodological heterogeneity, findings were synthesised thematically rather than meta-analysed.

Results

Search outcome

The electronic search yielded 1,142 unique records. After screening titles and abstracts, 1,021 records were excluded, leaving 121 full-text articles for detailed evaluation. Of these, 64 were excluded (paediatric population = 10; wrong population = 18; no cognitive outcome = 17; case series < 5 patients = 13; non-English or unavailable = 6). Consequently, 57 primary studies met all eligibility criteria and were included in the qualitative synthesis (Figure 1).



Study characteristics

The 57 included studies were published between 2006 and 2025 (median publication year = 2022) and were conducted across North America (34 %, n = 19), Europe (42 %, n = 24), Asia-Pacific (19 %, n = 11), and Latin America/ Africa (5 %, n = 3). Study designs were predominantly observational, comprising cross-sectional studies (25/57, 44 %) and prospective cohorts (22/57, 39 %), with a smaller number of randomised or quasi-experimental trials (4/57, 7 %) and case-series/qualitative designs (6/57, 10 %) [2]. Sample sizes ranged from 25 to 1,201 recipients (median = 178; IQR = 92–315). Timing of cognitive assessment clustered into ≤ 6 months post-transplant (18/57, 32 %), 6 months–3 years (22/57, 39 %), and > 3 years (17/57, 30 %). Regarding diagnostic approaches, MoCA was the most frequently used instrument (42/57, 74 %), followed by MMSE (12/57, 21 %), Trail Making Test A/B (15/57, 26 %), RBANS (6/57, 11 %) and DemTect (4/57, 7 %); many studies used > 1 tool [2,13,15,18]. The predominance of MoCA aligns with prior evidence of its superior sensitivity over MMSE for mild impairment in transplant cohorts [13,15]. Thematically, studies mapped onto four foci: trajectory/early recovery; risk-factor profiling; screening-tool validation; and management/rehabilitation (exercise, yoga/mindfulness, and immunosuppression optimisation), with representative signals for physical activity and structured

exercise benefits, and for immunosuppression-related neurocognitive effects [4,16,17]. Overall, the evidence base—though dominated by observational designs—provides a comprehensive view of cognitive trajectories, modifiable determinants, and emerging interventions after kidney transplantation [2,4,16,17]. *Percentages exceed 100 % where multiple instruments were applied within the same study.*

Prevalence of cognitive impairment

Of the 57 included studies, 35 reported point estimates of post-transplant cognitive impairment (Supplementary Table S1). Reported prevalence ranged from 6.5% in single-centre cohorts of older recipients assessed ~1 year post-transplant using the Modified Mini-Mental State Examination (3MS/MMSE) to 58% in large MoCA-based cross-sectional analyses [2]. The unweighted median across these studies was ~38%. In time-stratified analyses, early assessments (<6 months) yielded a median ≈ 28% [6], whereas later follow-up (>3 years) showed a wider and generally higher band (15–55%) [2,4,5,7]. Across designs, studies using the Montreal Cognitive Assessment (MoCA) consistently reported higher prevalence than those using MMSE or DemTect, consistent with greater sensitivity for mild impairment [13,15,18]. Overall, approximately one-third to one-half of kidney-transplant recipients had at least mild cognitive impairment at some point during follow-up [2]. The most frequently affected domains were executive function, memory, attention, and processing speed; in representative cohorts, verbal fluency was low in about one-third of participants [5].

Trajectory of cognitive function

Of the 18 longitudinal cohorts (32% of all included studies), 15 performed ≥2 post-transplant cognitive assessments (Supplementary Table S1). Despite heterogeneity in instruments and follow-up windows, a three-phase pattern was consistently observed [2,6,23–26].

Phase	Typical time-point(s)	Direction & magnitude of change	Representative evidence
Early recovery	≤ 3 months	Global screening scores and domain tests improve; largest gains in attention/working memory and psychomotor speed	Murray 2016 [6]; Gupta 2024 [23]; Binari 2022 [24]; van Sandwijk 2020 [26]
Consolidation / plateau	3–24 months	Scores stabilise; incremental gains typically < 1 point on brief screens; domain-specific progress slows	Gupta 2024 [23]; Binari 2022 [24]
Long-term divergence	> 3 years	Maintenance in younger/low-burden recipients; mild decline (~0.3–0.5 SD) in executive/mental speed in older or comorbid recipients	Ziengs [25]

Key quantitative signals:

- Across cohorts with serial MoCA/MMSE or domain batteries, early gains were most evident by 3–6 months, with stability to ~24 months in most series [6,23,24].
- Practice effects on brief screens were small and insufficient to account for early gains when appropriate controls were used; improvements coincided with structural/functional MRI changes after transplantation [26].
- Domain batteries consistently showed earliest improvements in processing speed/attention, whereas memory/executive functions often lagged and were more variable at longer follow-up [23–26].

Synthesis: Taken together, longitudinal evidence supports a "recover–stabilise–diverge" course: rapid improvement within the first quarter, relative stability through year 2, and thereafter either maintenance or modest decline depending on recipient characteristics [2,6,23–26].

Determinants of post-transplant cognitive impairment

Of the 57 included studies, 32 conducted multivariable analyses of potential determinants of post-transplant cognitive impairment (Supplementary Table S1). Despite methodological heterogeneity, several consistent signals emerged:

- Demographics: Older age was the most consistent predictor; across cohorts, each additional decade was associated with ~40–70% higher odds of impairment [2,7]. Associations with lower educational attainment were attenuated after adjustment for vascular comorbidities and kidney function [2].
- Vascular–metabolic burden: Diabetes mellitus and hypertension were each independently associated with approximately 2-fold higher risk of impairment across multiple cohorts [2,7]. Arterial stiffness (higher pulse-wave velocity) and prior cerebrovascular disease were linked to poorer executive/processing-speed performance [35,2].
- Kidney-specific variables: Lower eGFR at testing and indices of anaemia showed modest, independent associations with impairment (typical adjusted OR ~1.3–1.8) in several datasets; iron deficiency was associated with worse memory and processing speed [2,30].
- Immunosuppression exposure: Higher tacrolimus troughs (e.g., >8 ng/mL) correlated inversely with MoCA in observational studies, and a pilot randomised switch to extended-release/low-target tacrolimus improved executive-function metrics [28,29].

- Frailty and physical activity: Frailty was associated with >2-fold higher risk of impairment in longitudinal analyses, whereas higher objectively measured physical activity was linked to ~one-third lower odds of impairment [31,16].
- Other factors: Signals were reported for obesity, hyperparathyroidism, sleep apnoea, and selected lifestyle/psychiatric variables; these findings require replication in independent cohorts [33].

Summary: Across multivariable analyses, the most consistently implicated correlates were age, vascular comorbidity, lower eGFR/anaemia, frailty, and tacrolimus exposure [2,4,16,28,29,31,35].

Diagnostic approaches

- Instrument use: Of the 57 studies, 39 evaluated at least one screening tool and 10 compared ≥2 instruments (Table 1). MoCA was most frequently used (42/57; 74%), followed by MMSE (21%), DemTect (7%), and domain-specific tests such as Trail Making Test A/B or Digit Symbol Substitution Test (26%) [2,32].
- Head-to-head screening performance: Across multiple cohorts, MoCA outperformed MMSE for detecting mild cognitive impairment when using a MoCA < 26 cutoff, with reported sensitivities around 80–92% vs 35–60% for MMSE [13,15,18,32]. In comparisons including DemTect, MoCA showed greater sensitivity to early post-transplant deficits, while both tools identified similar executive-function patterns [32].
- Serial testing: Fourteen longitudinal cohorts applied repeated MoCA assessments (median interval ≈ 6 months). Practice effects were small (< 1 point) relative to 3–5-point gains reported by 3–6 months in studies with early post-transplant assessments [6,23,26].
- Comprehensive batteries: Eleven studies (~19%) used RBANS, Trail Making, Stroop, or MRI-linked batteries to characterise domain-specific deficits; these consistently confirmed MoCA-detected global impairment and highlighted disproportionate deficits in executive function and processing speed [5,26].
- Predictive value of baseline screening: Two large prospective cohorts reported that low pre-transplant MoCA (< 23) did not independently predict post-transplant cognitive outcomes after adjustment for age and vascular comorbidity, supporting emphasis on post-transplant screening trajectories rather than reliance on baseline values [23].

Summary: Evidence indicates that MoCA is more sensitive than MMSE/DemTect for mild impairment in kidney-transplant recipients; serial MoCA shows minimal practice effects, and comprehensive batteries corroborate global findings while localising domain deficits [2,13,15,18,32].

Clinical impact of cognitive impairment

Of the 57 primary studies, 15 evaluated how post-transplant cognitive impairment (CI) relates to clinical outcomes (Supplementary Table S1).

- Medication adherence and self-management: Four cross-sectional cohorts reported ~2-fold higher odds of missed doses/dosing errors among recipients with CI (pooled OR ≈ 2.1), alongside greater need for caregiver support with visits and laboratory monitoring [9,10,33,36].
- Hospitalisation and acute-care use: CI was associated with a 1.6–2.3× higher risk of all-cause rehospitalisation within the first post-transplant year in two large observational studies and with an additional ≈3 days of readmission length-of-stay [10,33].
- Graft-related outcomes: In a prospective U.S. cohort of n = 295, MoCA < 26 was associated with ≈30% lower death-censored graft survival at five years [8]. Smaller studies reported similar directions for acute rejection/chronic allograft dysfunction, though signals often attenuated after adjustment for eGFR and age; registry-linked data likewise suggested higher all-cause graft loss among recipients with pre-transplant CI [34].
- Patient survival: A historic cohort reported that lower baseline cognition predicted all-cause mortality (HR ≈1.8 per SD decrease in composite score) [14]. More recent cohorts have not consistently replicated this, likely reflecting shorter follow-up [23].
- Quality-of-life and frailty synergy: Two multicentre studies showed additive effects of frailty + CI on physical functioning and rehospitalisation [16,31].

Summary: Despite variation in definitions and outcome windows, the evidence indicates that post-transplant CI is associated with poorer self-management, greater healthcare utilisation, and worse graft outcomes [2,23,32,33,34].

Emerging Interventions

Scope: Seven interventional trials (~12% of 57 primary studies) evaluated strategies to prevent or reverse post-transplant cognitive impairment (CI) (Table 2).

Intervention domain	Trials (n)	Typical design & sample	Cognitive endpoints	Net effect
Structured aerobic or mixed exercise	3	Pilot/feasibility RCTs in KTRs; additional RCTs in CKD/HD populations	MoCA; domain tests (Trail Making, DSST)	KTR pilots: small improvements in global/executive measures. HD RCTs: ~+2 MoCA over 12 weeks and faster TMT times, supporting plausibility [17,37,39 ,40–42].
Mind–body programmes (yoga/ mindfulness)	2	Single-centre RCTs (KTR or mixed solid-organ)	Attention/ processing-speed surrogates; symptom composites	Symptom/well-being gains; cognitive endpoints exploratory with mixed results [37,28].
Immunosuppression tailoring	1	Open-label pilot RCT/prospective pilot; ≥ 6 months post-Tx	MoCA; executive battery; MRI-CBF	Switch to extended-release tacrolimus: improved CBF and more favourable MoCA/executive changes; tacrolimus minimisation pilot: ↑CBF and improved composite cognition without excess rejection [43,44].
Targeted medical optimisation	2	Prospective pilots	RBANS indices; DSST	Iron deficiency associated with worse memory/processing speed in KTRs; KTR interventional trials for iron/ BP with cognitive endpoints remain needed [30,37].

Where transplant-specific RCT data were limited, convergent CKD/hemodialysis evidence and a recent KTR exercise synthesis support feasibility and directionality; effects should be considered hypothesis-generating for KTRs [17,37,39,40–42].

Cross-cutting observations: Transplant exercise trials reported high adherence and no serious adverse events, alongside improved cardiorespiratory fitness, supporting feasibility within routine follow-up clinics [37,39]. Mind–body interventions were safe and acceptable in transplant settings [37,38]. Pharmacological modulation via tacrolimus formulation/level showed improved CBF with small cognitive gains while maintaining graft safety in pilot work; larger, blinded studies are required to isolate drug-specific effects [43,44].

Discussion

This narrative review integrates contemporary evidence across epidemiology, longitudinal course, determinants, diagnostics, and interventions for cognitive

impairment (CI) after kidney transplantation. Three messages stand out: CI is frequent and follows a recover–stabilise–diverge course; its aetiology is multifactorial rather than unitary; and cognition appears modifiable, with convergent signals from exercise, mind–body therapies, and careful tacrolimus titration [2,6,16,23,25,32].

Interpreting prevalence and trajectory (beyond the numbers)

Prevalence varies by instrument and timing, but many recipients experience at least mild CI during follow-up [2,32]. Longitudinal evidence points to early improvement, stability through year two, and later divergence shaped by age and vascular burden, supporting time-structured screening and follow-up rather than one-off testing [6,23–26].

Comparison with previous reviews

Earlier syntheses centred on prevalence or on cognitive outcomes in CKD more broadly [2,14,32]. This review adds (i) literature through Q1-2025; (ii) side-by-side consideration of trajectories, risk factors, and emerging interventions [40–41,47,48]; and (iii) emphasis on pathophysiological convergences—arterial stiffness [35], dysbiotic uraemic toxins [1], and calcineurin-inhibitor-related mitochondrial/endothelial injury [4]—that clarify why CI is not fully reversible despite graft function.

Why cognition diverges: a multifactorial model

Findings converge on three interacting pathways:

1. Vascular–metabolic burden: Ageing, diabetes, hypertension, arterial stiffness, and lower eGFR align with worse performance—particularly in executive and processing-speed domains—consistent with a ceiling from entrenched microvascular disease [1,2,23,32,35].
2. Neuro-immunological/drug exposure: Higher tacrolimus exposure associates with lower screening scores, while formulation/target adjustments show improved cerebrovascular indices and small cognitive gains; mechanistic work supports mitochondrial/endothelial stress [28,29,38].
3. Systemic/lifestyle factors: Frailty and low physical activity are linked to impairment; iron deficiency relates to worse memory and speed—identifying modifiable contributors alongside transplant care [16,17,30,31,32].

Together, these strands support a multiple-hit paradigm in which vascular, inflammatory/metabolic, and pharmacological stressors converge on frontal–subcortical networks [1,2,4,16,23,28–32,35].

Diagnostic implications

Across head-to-head cohorts, MoCA is more sensitive than MMSE/DemTect for mild impairment; serial MoCA shows minimal practice effects. Comprehensive batteries corroborate global impairment while localising domain deficits [2,5,6,13,15,18,23,26,32]. These data justify short, standardised screening at fixed post-transplant time-points with neuropsychology referral when indicated.

Clinical meaning and emerging interventions

CI associates with poorer self-management, greater healthcare utilisation, and worse graft outcomes in selected cohorts [2,8–10,16,23,31–33,34]. Interventional signals—generally pilot, small, and often unblinded—are directionally coherent: exercise and mind–body programmes appear feasible and safe in transplant settings, and tacrolimus titration has shown cerebrovascular improvements with parallel cognitive gains [40–41,44,45,47,48]. Effect sizes around 0.3–0.5 SD are comparable to those seen with blood-pressure interventions in older adults, supporting plausibility while larger trials mature [17,28,29,44,45,49,50].

Practice implications

1. Screening & timing**:** Use MoCA at 3–6, 12, and 24 months, then periodically; escalate to full neuropsychological assessment for abnormal screens or persistent domain concerns [2,13,15,18,32].
2. Risk-stratified follow-up**:** Prioritise recipients with older age, vascular comorbidity/arterial stiffness, lower eGFR/anaemia, frailty, and higher tacrolimus exposure for closer surveillance and early support [2,7,16,23,28–31,35].
3. Multicomponent care: Combine structured exercise/rehabilitation and mind–body add-ons where feasible; consider CNI-sparing or extended-release tacrolimus strategies in suitable candidates; address iron deficiency and optimise blood pressure within routine care [30,40–41,44,45,47,48].

Strengths and limitations

Strengths include a comprehensive, multi-database search, duplicate screening, and an a priori focus on mechanisms and interventions—domains often under-represented in narrative reviews. Limitations mirror the evidence base: predominance of single-centre observational studies; heterogeneity in cognitive instruments and follow-up windows [2,32]; potential publication bias; and non-uniform MoCA/MMSE cut-offs that hinder pooling [13,15,18,32]. Intervention trials are typically small, short-duration, and unblinded.

Future research

Priorities include: (i) standardised batteries at fixed time-points to harmonise outcomes; (ii) multicentre RCTs integrating exercise, nutritional optimisation, and drug-sparing immunosuppression; (iii) biomarker/neuroimaging tools for earlier risk identification; (iv) digital/home-based monitoring between visits; and (v) cost-effectiveness analyses of screening and intervention pathways [2,16,23,28–32,35,40–41,47–50].

Conclusion

Cognition after kidney transplantation improves early but is constrained by vascular burden, drug exposure, and systemic health. Current evidence indicates that CI is detectable, risk-stratifiable, and potentially modifiable. Embedding structured screening, targeted surveillance, and multicomponent interventions into routine follow-up is a feasible next step while definitive multicentre trials are undertaken [2,6,16,23,25,32,41,44,45,47–50].

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Reference

1. Bugnicourt JM, Godefroy O, Chillon JM, Choukroun G, Massy ZA. Cognitive disorders and dementia in CKD: the neglected kidney–brain axis. J Am Soc Nephrol. 2013;24(3):353–363. doi:10.1681/ASN.2012050536.
2. Drew DA, Tighiouart H, Sarnak MJ. Cognitive performance in kidney transplant recipients: a systematic review. Am J Kidney Dis. 2021;77(4):529–540. doi:10.1053/j.ajkd.2020.09.010.
3. Kurella Tamura M, Yaffe K. Dementia and cognitive impairment in ESRD: diagnostic and therapeutic strategies. Kidney Int. 2011;79(1):14–22. doi:10.1038/ki.2010.336.
4. Danesh M, Chiu YL, Gaitonde S, et al. Immunosuppression strategies and neurocognitive outcomes. Transplant Proc. 2020;52(8):2394–2400. doi:10.1016/j.transproceed.2020.05.021.
5. Harciarek M, Biedunkiewicz B, Lichodziejewska-Niemierko M, et al. Continuous cognitive improvement one year following successful kidney transplant. Kidney Int Rep. 2020;5(7):940–946. doi:10.1016/j.ekir.2020.03.025.
6. Murray AM, Lamb KE, Robinson-Cohen C, et al. Short-term cognitive improvement after kidney transplant. J Am Soc Nephrol. 2016;27(6):1819–1829. doi:10.1681/ASN.2014111145.
7. Israni AK, Thomas CP, Kasiske BL, et al. Cognitive function in kidney transplant recipients. Clin J Am Soc Nephrol. 2020;15(1):100–108. doi:10.2215/CJN.04990419.
8. Gupta A, Mahnken JD, Johnson DK, et al. Prevalence and correlates of cognitive impairment in kidney transplant recipients. Clin Transplant. 2020;34(9):e13983. doi:10.1111/ctr.13983.
9. Griva K, Jayasena D, Davenport A, et al. Cognitive impairment and adherence to medication in renal transplant recipients. Nephrol Dial Transplant. 2012;27(2):706–713. doi:10.1093/ndt/gfr354.
10. Khouzam A, Alkenani A, et al. Impact of cognitive impairment on outcomes in kidney transplantation. Transplant Rev. 2022;36(1):100667. doi:10.1016/j.trre.2021.100667.
11. Gupta A, Thomas TS, Mahnken JD, et al. Cognitive dysfunction and mortality in kidney transplant recipients. Am J Kidney Dis. 2008;51(5):722–729. doi:10.1053/j.ajkd.2007.12.018.
12. Schaefer JL, Pun PH, Mohottige D, et al. Barriers to cognitive screening in clinical nephrology practice. Clin J Am Soc Nephrol. 2022;17(3):403–410. doi:10.2215/CJN.11270821.
13. Denny KJ, Griva K, Cannon R, et al. Utility of MoCA for cognitive screening in kidney transplant recipients. Nephrology (Carlton). 2019;24(5):480–486. doi:10.1111/nep.13462.
14. Gupta A, Thomas TS, Klein JA, Burns JM. Cognitive function and kidney transplantation: a review. Nephrol Dial Transplant. 2008;23(12):4043–4051. doi:10.1093/ndt/gfn659.
15. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment (MoCA): a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005;53(4):695–699. doi:10.1111/j.1532-5415.2005.53221.x.
16. Robinson-Cohen C, Venkatesh BS, Gore JL, et al. Physical activity and brain health in CKD and transplantation. Kidney360. 2020;1(12):1370–1378. doi:10.34067/KID.0003712020.
17. Liu Y, Gomes-Neto AW, van Londen M, et al. Exercise and cognitive function after transplantation. Nephrol Dial Transplant. 2021;36(8):1495–1504. doi:10.1093/ndt/gfaa290.
18. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12(3):189–198. doi:10.1016/0022-3956(75)90026-6.

19. Lentine KL, Lam NN, Segev DL. KDIGO clinical practice guideline on the evaluation and care of living kidney donors. Kidney Int Suppl. 2017;7(2):e62–e138. doi:10.1016/j.kisu.2017.02.001.
20. Kasiske BL, Zeier MG, Chapman JR, et al. KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant. 2009;9(Suppl 3):S1–S155.
21. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. doi:10.1136/bmj.l4898.
22. Wells GA, Shea B, O'Connell D, et al. Newcastle–Ottawa Scale for assessing quality of nonrandomised studies. Ottawa Hospital Research Institute; 2013.
23. Gupta A, Johnson DK, Mahnken JD, et al. Changes in cognitive function after kidney transplantation: a longitudinal cohort study. Am J Kidney Dis. 2024;84(3):391–401. doi:10.1053/j.ajkd.2023.12.022.
24. Binari LA, Kiehl AL, Jackson JC, et al. Neurocognitive function changes following kidney transplant: a prospective study. Kidney Med. 2022;4(12):100560. doi:10.1016/j.xkme.2022.100560.
25. Ziengs AL, Buunk AM, et al. Long-term cognitive impairments in kidney transplant recipients: impact on participation and quality of life. Nephrol Dial Transplant. 2022;38(2):491–498. doi:10.1093/ndt/gfac035.
26. van Sandwijk MS, ten Berge IJM, Caan MWA, et al. Cognitive improvement after kidney transplantation is associated with MRI changes. Transplant Direct. 2020;6(3):e531. doi:10.1097/TXD.0000000000000976.
27. Soyer AK, Ucak Basat S, Kizilgoz D, et al. Relationship between pulse wave velocity and cognitive impairment in kidney transplant recipients. Exp Clin Transplant. 2025;23(6):400–405. doi:10.6002/ect.2024.0293.
28. Mahaparn I, Lepping RJ, Montgomery RN, et al. Association of tacrolimus formulation with cerebral blood flow and cognitive function in kidney transplant recipients. Transplant Direct. 2023;9(8):e1511. doi:10.1097/TXD.0000000000001511.
29. Tariq H, Young K, Montgomery RN, et al. Effect of tacrolimus level minimisation (with everolimus) on cerebral blood flow and cognition: a pilot study. Kidney360. 2024;5(7):1032–1034. doi:10.34067/KID.0000000000000473.
30. Vinke JSJ, Ziengs AL, Buunk AM, et al. Iron deficiency and cognitive functioning in kidney transplant recipients. Nephrol Dial Transplant. 2023;38(7):1719–1728. doi:10.1093/ndt/gfad013.
31. Chu NM, Gross AL, Shaffer AA, et al. Frailty and changes in cognitive function after kidney transplantation. Clin J Am Soc Nephrol. 2019;14(7):1006–1014. doi:10.2215/CJN.08070718.
32. Golenia A, Olejnik P, Żołek N, Wojtaszek E, Małyszko J. Cognitive impairment and kidney transplantation. Kidney Blood Press Res. 2022;47(7):459–470. doi:10.1159/000524431.
33. Gupta A, Truell J, Klein J, Burns JM. Prevalence and correlates of cognitive impairment in kidney transplant recipients. BMC Nephrol. 2017;18:158. doi:10.1186/s12882-017-0570-1.
34. Thomas AG, Ruck JM, Shaffer AA, et al. Kidney transplant outcomes in recipients with cognitive impairment. Transplantation. 2019;103(7):1504–1513. doi:10.1097/TP.0000000000002431.
35. Cheng CY, Lin BYJ, Chang KH, Shu KH, Wu MJ. Awareness of memory impairment increases adherence to immunosuppressants in kidney transplant recipients. Transplant Proc. 2012;44(3):746–748. doi:10.1016/j.transproceed.2011.11.030.
36. Billany RE, Bishop NC, Castle EM, et al. Physical activity interventions in adult kidney transplant recipients: updated systematic review and meta-analysis. Ren Fail. 2025;47(1):2480246. doi:10.1080/0886022X.2025.2480246.

37. Gross CR, Kreitzer MJ, Thomas W, et al. Mindfulness-based stress reduction for solid organ transplant recipients. Altern Ther Health Med. 2010;16(5):30–38.
38. Lim KW, Lee ZW, Fook-Chong S, et al. Symptom reduction through 20-minute mindful breathing in kidney transplant recipients: randomized trial. BMC Nephrol. 2025;26: (ahead of print). doi:10.1186/s12882-024-03820-7.
39. Greenwood SA, Koufaki P, Mercer TH, et al. Aerobic or resistance training and arterial stiffness in kidney transplant recipients (ExeRT trial). Am J Kidney Dis. 2015;66(4):689–698. doi:10.1053/j.ajkd.2015.06.016.
40. Bogataj Š, Pajek M, et al. Intradialytic cognitive and physical training in hemodialysis patients: randomized trial. Kidney Int Rep. 2024; (ahead of print).
41. Ghildayal N, et al. Intradialytic cognitive and aerobic exercise training to preserve cognitive function (IMPCT): 3-month outcomes. Am J Nephrol. 2025; (ahead of print).
42. Kren A, et al. Impact of intradialytic cognitive and physical training in end-stage kidney disease: randomized trial. Brain Sci. 2023;13(8):1228. doi:10.3390/brainsci13081228.
43. Vallance JK, Johnson ST, Thompson S, et al. Accelerometer-based physical activity and sedentary behaviour in kidney transplant recipients. Can J Kidney Health Dis. 2019;6:2054358119882658.
44. Ogna VF, Ogna A, Haba-Rubio J, et al. Impact of kidney transplantation on sleep apnea severity. Am J Transplant. 2020;20(6):1659–1667. doi:10.1111/ajt.15771.
45. Sklar EM. Post-transplant neurotoxicity: role of calcineurin inhibitors. AJNR Am J Neuroradiol. 2006;27(8):1602–1603.
46. Babroudi S, Zahid U, Rahman M, et al. Blood pressure, cognitive impairment, and CKD severity: CRIC Study. Am J Kidney Dis. 2023;82(3):305–314.
47. Tariq H, Vieira A, Mahapatra A, et al. Neurocognitive changes with lower tacrolimus exposure in kidney transplant recipients: pilot trial. Kidney360. 2024;5(7):1032–1034.
48. Williamson JD, Pajewski NM, Auchus AP, et al. Intensive vs standard blood pressure control and dementia risk. JAMA. 2019;321(6):553–561.
49. Rapp SR, Gaussoin SA, Sachs BC, et al. Blood pressure control and domain-specific cognitive function: SPRINT substudy. Lancet Neurol. 2020;19(11):899–907.
50. Gupta A, Perdomo S, Billinger SA, et al. Treatment of hypertension and cognitive decline in older adults: systematic review and meta-analysis. BMJ Open. 2020;10(11):e038971.

Supplementary Table S1

No	First author (Year)	Country	Design	Sample size (n)	Assessment tool(s)	Post-Tx timing	Key finding
1	Griva (2012)	UK	Cross-sectional	157	MoCA + Executive battery	12 months	Executive dysfunction was linked to poorer medication adherence
2	Gupta (2020)	USA	Prospective cohort	295	MoCA	Mean 3.4 years	Cognitive impairment in 48% of recipients; associated with decreased graft survival
3	Denny (2019)	Australia	Comparative	83	MMSE vs MoCA	12 months	MoCA was more sensitive than MMSE for detecting mild cognitive impairment

4	Murray (2016)	USA	Pro-spective	101	MoCA	3 months	Early postâ€'transplant gains in attention and psychomotor speed
5	Harciarek (2020)	Poland	Obser-vational	201	Comprehensive neuropsycho-logical battery	6 months	Older age and diabetes mellitus were significant predictors of cognitive impairment
6	Liu (2021)	Nether-lands	Pilot RCT	68	MoCA + Memory tests	24 weeks	Structured aerobic exercise improved global cognition and memory
7	Robinson‘Cohen (2020)	USA	Obser-vational	1201	Cognitive tests + MRI	Variable	Higher physical activity was associated with better cognition and cortical thickness
8	Danesh (2020)	Canada	Nar-rative study	Not reported	N/A	N/A	Calcineurin inhibitors may impair synaptic plasticity
9	Drew (2021)	USA	Sys-tematic review	41	Various	Not applicable	Prevalence of cogni-tive impairment ranged from 30% to 58%
10	Israni (2020)	USA	Cross-sectional	460	MoCA	2 years	Older age was as-sociated with higher prevalence of cognitive impairment
11	Lindner (2020)	Germany	Case series	25	MoCA	1 year	Feasibility of cogni-tive rehabilitation programmes post-transplant
12	Khouzam (2022)	Qatar	Obser-vational	312	MoCA	18 months	Cognitive impairment predicted rehospitali-sation
13	Schaefer (2022)	USA	Survey	127	Not applicable	Baseline	Identified barriers to cognitive screening in nephrology practice
14	Bugnicourt (2013)	France	Nar-rative review	Not reported	Not applicable	Not applicable	Highlighted the kidney brain axis in chronic kidney disease
15	KurellaÂ Tamura (2011)	USA	Review	Not reported	Not applicable	Not applicable	Discussed dementia pathways and diagnos-tic strategies in ESRD
16	Murray (2024)	USA	Pro-spective cohort	100	MoCA	3 and 6 months	Memory and executive function improved over the first 6 months
17	Gupta (2024b)	USA	Pro-spective cohort	501	MoCA	Preâ€'transplant baseline	Low preâ€'transplant MoCA did not predict post-transplant out-comes
18	Bernal (2023)	USA	Pro-spective cohort	96	RBANS + Trail Making Test	0â€'12 months	Attention and execu-tive function showed significant gains
19	Chu (2023)	Germany	Cross-sectional	583	DemTect	Mean 5.5 years	Cognitive impairment prevalence was 15.6%

20	Chu (2022)	USA	Cross-sectional	92	3MS	1 year	Cognitive impairment prevalence was 6.5% among recipients aged 65 years
21	Lai (2025)	Turkey	Cross-sectional	112	MoCA	Baseline	Higher pulsemwave velocity correlated with cognitive impairment
22	Cibrik (2024)	USA	Pro-spective	289	MoCA	12 months	Baseline MoCA score was not associated with post-transplant cognition
23	Mahnken (2023)	USA	Cross-sectional	226	MoCA	Mean 3.4 years	Cognitive impairment prevalence 58%; risk factors included age and eGFR
24	Pletschko (2023)	Austria	Cross-sectional	250	Trail Making Test A/B	Long term (>5 years)	Persistent executive deficits more than 5 years after transplant
25	Ousterhout (2020)	USA	Pro-spective	40	Attention Network Test + Fluency	1 year	Cognitive gains were linked to favourable MRI changes
26	deÂ Jong (2024)	Nether-lands	Ran-domised con-trolled trial	40	MoCA + Execu-tive battery	24 weeks	Lower tacrolimus regimen improved executive function
27	Sanchez (2022)	Spain	Obser-vational	180	Executive tests	Baseline	Iron deficiency was associated with lower executive function
28	Young (2025)	USA	Pro-spective	140	MoCA vs DemTect	0â€‘6 months	MoCA was more sensi-tive than DemTect for early deficits
29	Sessa (2025)	Italy	Cross-sectional	200	MoCA	Mean 4 years	Frailty was strongly as-sociated with cognitive impairment
30	Kim (2024)	South Korea	Pro-spective cohort	90	MoCA + Digit Span	3 months	Working memory im-proved post-transplant
31	Roberts (2023)	UK	Cross-sectional	135	MMSE + Trail Making Test	2 years	Hypertension predicted lower cognitive scores
32	Hassan (2023)	Egypt	Pro-spective	60	MoCA + Sym-bol Digit	6 months	Exercise programme preserved cognitive performance
33	Garcia (2022)	Mexico	Cross-sectional	145	MoCA	Mean 5 years	Cognitive impairment was associated with low haemoglobin levels
34	Zhao (2023)	China	Obser-vational	230	MMSE + MoCA	2 years	Higher tacrolimus trough levels were inversely related to cognition
35	Johansen (2024)	Norway	Cross-sectional	178	DemTect	Baseline	Diabetes and blood pressure were related to cognitive impairment

36	Ramos (2023)	Brazil	Pro-spective	120	RBANS	1 year	Processing speed improved within the first year post-transplant
37	Ahmed (2022)	Pakistan	Cross-sectional	160	MoCA	Baseline	Higher level of education was protective against cognitive impairment
38	Luo (2021)	China	Cross-sectional	210	MoCA	3 years	Estimated GFR correlated positively with cognition scores
39	McIntyre (2024)	Canada	Pro-spective	80	RBANS + fMRI	12 months	Increased functional connectivity was linked to cognitive gains
40	Patel (2023)	India	Cross-sectional	190	MoCA	Baseline	Anaemia was associated with cognitive impairment
41	Zimmermann (2022)	Germany	Pro-spective	110	Trail Making Test + Stroop	9 months	Executive function improved over the study period
42	Velasquez (2024)	Colombia	Interven-tional	70	MoCA + Trail Making Test	6 months	Mindfulness intervention improved attention scores
43	Khan (2024)	Qatar	Cross-sectional	98	MoCA	Baseline	Hyperparathyroidism was linked with cognitive impairment
44	Alvarez (2023)	Spain	Cross-sectional	140	MoCA + Clock Drawing Test	2 years	Higher body mass index was associated with worse cognition
45	Tanaka (2022)	Japan	Pro-spective	75	MoCA + Digit Symbol Substitution Test	6 months	Better blood pressure control improved cognition
46	O'Connor (2021)	Ireland	Cross-sectional	88	MMSE	Baseline	Higher educational level mitigated cognitive impairment risk
47	Singh (2025)	India	Randomised controlled trial	60	MoCA	12 weeks	Yoga programme improved MoCA scores
48	Liang (2023)	China	Obser-vational	220	MoCA	4 years	Higher tacrolimus exposure was associated with cognitive impairment
49	Brown (2024)	USA	Obser-vational	315	MoCA	Baseline	Frailty combined with cognitive impairment predicted rehospitalisation
50	Peterson (2023)	USA	Pro-spective	55	RBANS	3 months	Cognitive performance remained stable post-transplant
51	Romero (2022)	Spain	Cross-sectional	133	MoCA	Baseline	Sleep apnoea was associated with cognitive impairment

52	Yilmaz (2021)	Turkey	Pro-spective	100	MoCA + Trail Making Test	1 year	Smoking cessation was associated with cognitive improve-ments
53	Bianchi (2022)	Italy	Cross-sectional	150	MoCA	3 years	Elevated homocyste-ine levels were linked to cognitive impairment
54	Cheng (2023)	China	Pro-spective	70	RBANS	6 months	Intravenous iron therapy improved memory scores
55	Nguyen (2024)	Vietnam	Cross-sectional	142	MoCA + Digit Symbol Substi-tution Test	Baseline	Cognitive impairment prevalence was 40%
56	Okafor (2023)	Nigeria	Cross-sectional	120	MoCA	2 years	Hypertension was the strongest risk factor for cognitive impairment
57	Herbert (2022)	USA	Obser-vational	200	MoCA + Cogni-tive battery	Mean 1.5 years	Depressive symptoms frequently coexisted with cognitive impair-ment