Appendix A. Full Search Strategy

A systematic search was conducted across MEDLINE (via PubMed), Embase, Cochrane Library, and Web of Science from inception to May 2025. Both controlled vocabulary (MeSH/Emtree) and free-text keywords were used.
Example Boolean syntax (PubMed):
("heart transplantation"[MeSH Terms] OR "cardiac transplant" OR "mechanical circulatory support") AND ("mitochondrial diseases"[MeSH Terms] OR "mitochondrial cardiomyopathy" OR "oxidative phosphorylation disorder" OR "metabolic syndrome" OR "primary mitochondrial disorder").
Filters: Humans; English language; publication types including case report, case series, cohort, or observational study. Reference lists of included papers were screened manually to identify additional studies.

Appendix B. Joanna Briggs Institute (JBI) Quality Appraisal Framework

All studies were appraised using JBI critical-appraisal tools appropriate to design (case report, case series, or cohort). Assessment domains included:
1. Confirmation of mitochondrial diagnosis (genetic or histologic)
2. Patient description and baseline characteristics
3. Clarity of intervention (transplant technique, perioperative management)
4. Outcome measurement and follow-up completeness
5. Overall internal validity and reporting transparency.
Quality outcomes are summarised in Table 4 of the main manuscript.

Appendix C. Frequency of Cardiac Involvement Across Major Mitochondrial Syndromes

Table 13. Frequency of Cardiac Involvement Across Major Mitochondrial Syndromes*

Mitochondrial Disease Name	General Frequency (per birth)	Cardiac Involvement frequency (%)	Reference
Leber hereditary optic neuropathy (LHON)	1/25,000*	33	(8,25)
MELAS	1/4,000	38	(1,26)
MERRF	9/1,000,000	53	(27)
NARP	1/12,000	50	(47)

Leigh syndrome (MDLS)	1/32,000	21	(27)
Kearns-Sayre syndrome (KSS)	1/33,000	57	(29)
Barth syndrome (BS)	1/300,000	94	(27)
MNGIE	1-9/1,000,000	**	(30)
MIDD	6/100,000	55	(27)
Friedreich's ataxia (FA)	1/20,000 to 1/725,000	35	(48)

*Estimates based on UK population data. Abbreviations: MELAS = mitochondrial encephalopathy, lactic acidosis and stroke-like episodes; KSS = Kearns–Sayre syndrome; MDLS = mitochondrial DNA–associated Leigh syndrome; BS = Barth syndrome; LHON = Leber hereditary optic neuropathy; FA = Friedreich's ataxia; MERRF = myoclonic epilepsy with ragged red fibres; NARP = neuropathy–ataxia–retinitis pigmentosa; MNGIE = mitochondrial neurogastrointestinal encephalopathy; MIDD = maternally inherited diabetes and deafness.

Appendix D. Perioperative and Long-Term Management Framework

Table 14. Perioperative and Long-Term Management Framework for Heart Transplantation in Mitochondrial Cardiomyopathy

Phase	Key Measures	Rationale
Preoperative	Optimise metabolic stability (lactate <3 mmol/L); avoid fasting; involve neurology and metabolic teams.	Reduces perioperative metabolic risk.
Intraoperative	Continuous glucose infusion (5–10%); minimise corticosteroid boluses; maintain normothermia.	Supports oxidative metabolism.

Early Postoperative	Early feeding (<12 h); daily lactate/ammonia/CK; taper steroids by 3 months.	Prevents catabolic decompensation.
Follow-Up	1, 3, 6, 12 months, then annually; cardiac imaging, metabolic and neurologic review.	Enables early detection of systemic progression.

Appendix E. Proposed Registry Data Template for Future Multicentre Collaboration

Table 15. Proposed Registry Data Template for Heart Transplantation in Mitochondrial Cardiomyopathy

Domain	Data Elements
Demographics	Age, sex, country, ethnicity
Genetic Diagnosis	Mutation (mtDNA/nDNA), heteroplasmy level, genotype–phenotype correlation
Pre-Transplant Status	NYHA class, LVEF, metabolic profile, extracardiac involvement
Transplant Procedure	Donor type (DCD/DBD), graft ischaemic time, operative technique, immunosuppression
Postoperative Course	ICU stay, metabolic crises, neurological events, acute rejection
Follow-Up	Survival (30-day, 1-year, 5-year); graft function; metabolic outcomes
Patient-Reported Outcomes	Quality of life, return to work/education, independence

Appendix F. Ethical and Practical Considerations

Ethical decision-making in mitochondrial cardiomyopathy transplantation should integrate four guiding principles:

1. Autonomy – transparent counselling regarding uncertain systemic prognosis;
2. Beneficence – proceed only where cardiac recovery confers meaningful benefit;
3. Non-maleficence – avoid interventions likely to accelerate metabolic decline;

4. Justice – ensure equitable allocation of donor organs through multidisciplinary consensus.

Future development of international registries will enhance ethically grounded, data-driven selection frameworks.