

Age Adapted Immunosuppression For Elderly Kidney Allograft Recipients: Balancing Risks For Cancer Versus Rejection

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Introduction:

Cancer is a significant cause of morbidity and mortality after kidney transplantation^{1,2,3,4,5}, driven by the milieu of immunosuppression^{6,7}. Age is one of the strongest risk factors for developing cancer after transplantation² and, with immunosenescence in the elderly well documented, age-adapted immunosuppression may be warranted for older adults to reduce overall immunosuppression burden but this requires further investigation.

Aims:

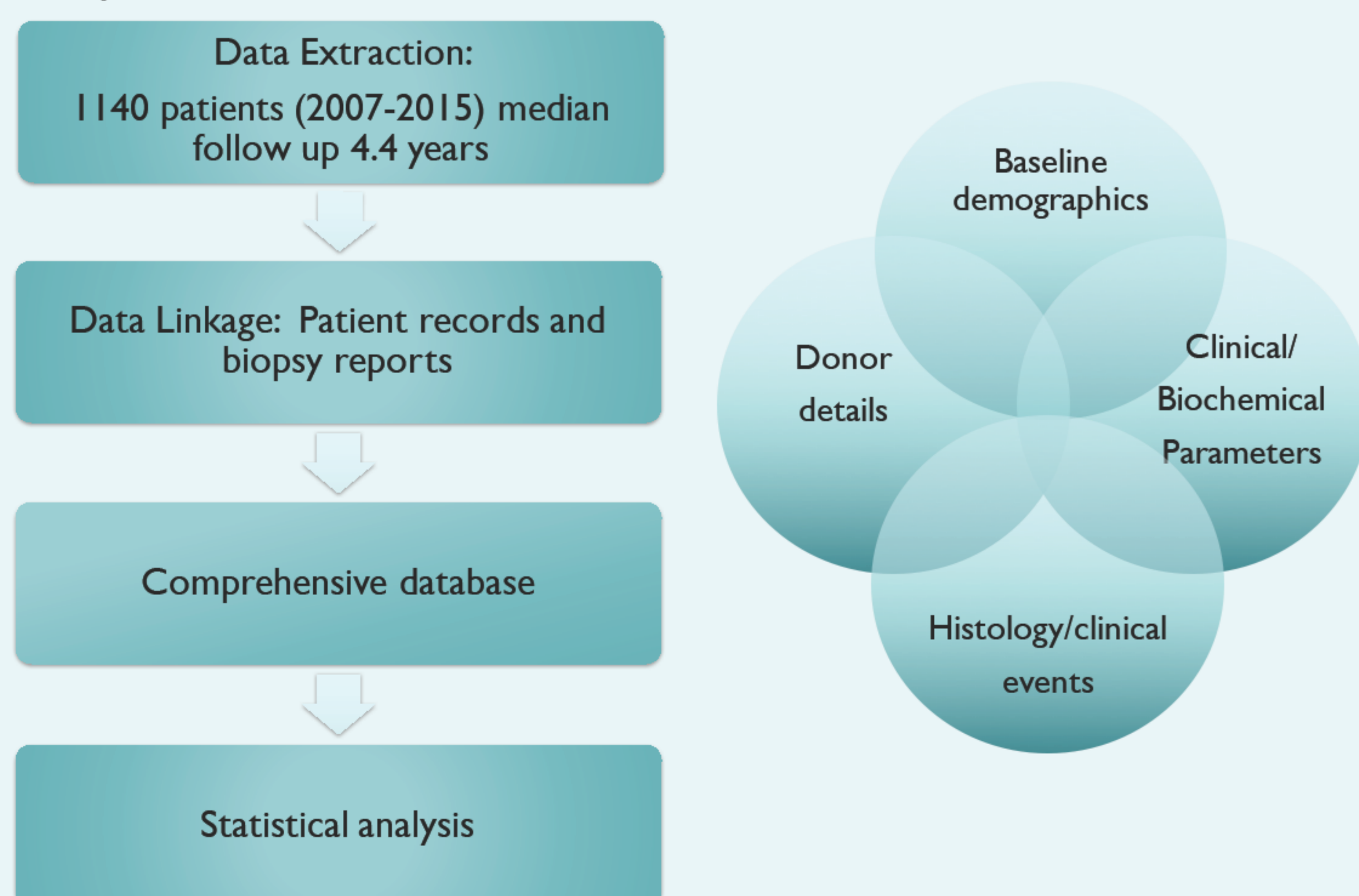
- To see if the elderly allograft recipients in our cohort have:
 - A more senescent immune response (and lower rates of rejection).
 - A reduced risk for allograft rejection
 - More immunosuppression related complications (i.e. cancer).
- To see if our local data supports current discussion for age-adapted immunosuppression.

Methods:

Retrospective single centre analysis of all adult patients receiving a kidney transplant between January 2007 and January 2015 at the Queen Elizabeth Hospital, Birmingham.

Data was extracted by the University Hospitals Birmingham informatics team. Electronic patient records were then manually searched to facilitate data linkage between various sources to create a comprehensive database of baseline demographics, donor details, clinical/biochemical parameters, histology and clinical events.

Data was extracted for 1,140 patients who received a kidney allograft, with median follow up 4.4 years post-transplantation. Median age for the study cohort was 47 and we classified older at this dichotomised age of 47 and over compared to younger recipients aged under 47. SPSS version 22 was utilised for all statistical analysis. STATA version 14 was used to conduct cox regression analysis for various outcomes, adjusting for age as an independent factor.



Results: Older vs. Younger recipients:

1) Incidence of Death /Death-Censored Graft Loss:

- Older recipients have an increased risk of Death post-transplantation, compared to younger recipients (10.6% vs. 3.3%, $p < 0.001$), but not Death Censored Graft Loss (9.1% vs 11.3%, $p = 0.130$).

2) Cancer Incidence and Mortality:

- Older recipients have increased rates of Cancer (9.0% vs. 3.1%, $p < 0.001$) and Cancer Related Mortality (12.9% vs. 5.9%, $p < 0.001$) post transplantation.

3) Rates of Rejection:

- Older recipients have same risk for Cellular Rejection
- Older vs. younger have reduced risk for Antibody-Mediated Rejection (2.7% versus 4.7% respectively, $p = 0.047$).

	Cellular rejection	Antibody-mediated rejection	Mixed rejection
Younger (<47 years)	12.6%	4.7%	3.5%
Older ≥ (47 years)	13.7%	2.7%	1.4%
P value	0.324	0.047	0.015

4) Adjusted analysis (with age as a factor for outcomes):

Outcome	Odds Ratio	P-Value
All Cancer	2.88 (1.61-5.15)	<0.001
Skin cancer	1.13 (0.099-2.613)	0.032
Non-skin cancer	2.88 (1.61-5.15)	<0.001
Any Rejection	0.98 (0.69-1.38)	0.897
Cellular Rejection	0.97 (0.678-1.40)	0.890
Antibody Mediated Rejection	0.54 (0.275-1.05)	0.072
Time to Death	3.17 (1.82-5.52)	<0.001
Time to Rejection	1.00 (0.72-1.39)	0.984

Discussion:

Older kidney allograft recipients have increased risk for **death** and **immunosuppression-related complications** including **cancer**, cardiac and cerebrovascular events but **reduced risk for rejection**. Our data supports the rationale that **older recipients** may benefit from **tailored immunosuppression** to reduce risk from related complications⁸ but this requires targeted clinical trials to investigate further.

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