Malondialdehyde is a novel biomarker with potential prognostic utility for long-term graft function in kidney transplant recipients

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INTRODUCTION
- Chronic kidney disease is increasingly recognized as a global public health problem.
- Late failure of kidney transplants (KTx) is an important clinical problem and one of the leading causes of end-stage renal disease.
- Currently, available biomarkers lack sensitivity in predicting long-term graft function in renal transplant recipients.
- Oxidative stress and lipid peroxidation are now recognized to be prominent feature of various diseases and their progression. Malondialdehyde (MDA) is one of the most used lipid peroxidation markers and can be used as a marker of graft injury.

OBJECTIVES
- To assess the performance of MDA, singly or in combination with serum cystatin C (CysC) and serum creatinine (Scr), in predicting graft function throughout the 1st, 2nd and 3rd year following KTx.

STUDY DESIGN
- Prospective, longitudinal study

STUDY SAMPLE
- 40 adult patients with ESRD, undergoing deceased or living KTx

METHODS
- BIOMARKERS MEASURED:
  - Malondialdehyde (MDA)
  - Serum creatinine (Scr)
  - Serum cystatin C (CysC)
- TIMING OF BIOMARKERS MEASUREMENTS:
  - 2h before KTx (day0)
  - 1st, 2nd, 4th and 7th days post-KTx
- DEFINITIONS:
  - Delayed graft function (DGF): dialysis requirement during the first post-transplant week.
  - Graft function at 1st, 2nd and 3rd years evaluated by Scr level.
- STATISTICAL ANALYSIS:
  - Multivariable logistic regression to combine MDA with Scr and CysC at day-1 (Combined biomarker at day-1)
  - Combined biomarker = −12.062 + 0.152 × Scr + 1.429 × CysC + 16.789 × MDA
  - Multivariable linear regression
  - Software SPSS, version 23.0

REFERENCES:


RESULTS

40 KTx (11 from living donor and 29 from deceased donor)

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Age (years old, mean ± SD)</th>
<th>49 ± 15</th>
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</thead>
<tbody>
<tr>
<td>Gender (n, %)</td>
<td>26 (65)</td>
<td></td>
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<tr>
<td>Time on dialysis (years, mean ± SD)</td>
<td>4.4 ± 4.7</td>
<td></td>
</tr>
<tr>
<td>Post-KTx Delayed Graft Function (n, %)</td>
<td>18 (45)</td>
<td></td>
</tr>
<tr>
<td>Acute rejection (n, %)</td>
<td>10 (25)</td>
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- MDA: After KTx, mean MDA levels were consistently higher in DGF patients at all time points, compared to non-DGF recipients.
- Predictive value of single MDA levels on allograft function:
  - At 1-year:
    - Time on dialysis (ng/mL) | 0.05 (0.02 - 0.07) <0.001 |
    - MDA measured on day-7 (µmol/L) | 1.34 (0.47 - 2.20) 0.003 |
    - Rehospitalizations (yes vs. no) | 0.36 (0.10 - 0.62) 0.007 |
  - At 2-years:
    - MDA measured on day-7 (µmol/L) | 1.48 (0.64 – 2.31) 0.001 |
    - Rehospitalizations (yes vs. no) | 0.35 (0.12 - 0.59) 0.005 |
  - At 3-years:
    - MDA measured on day-7 (µmol/L) | 1.22 (0.46 – 1.98) 0.003 |
    - Rehospitalizations (yes vs. no) | 0.25 (0.04 - 0.46) 0.02 |

Results are given by multiple linear regression (stepwise method) after including donor status, recipient and donor age, gender, diabetes mellitus, hospitalizations, and acute rejection episodes throughout the first year, serum creatinine (Scr) level at 1st, 2nd and 3rd years after transplant as the dependent variable.

*Single MDA levels before KTx and on 1st, 2nd and 4th days were not predictive of 1st, 2nd, and 3rd year allograft function

- Predictive value of combined biomarker on allograft function:
  - At 1-year:
    - Combined biomarker at day-1 (µmol/L) | 0.30 (0.03 - 0.58) 0.03 |
    - Rehospitalizations (yes vs. no) | 0.36 (0.10 - 0.62) 0.007 |
    - Donor age | 0.01 (0.01 - 0.02) 0.021 |
    - Acute rejection | 0.27 (0.03 - 0.51) 0.031 |
  - At 2-years:
    - Combined biomarker at day-1 (µmol/L) | 0.26 (0.10 - 0.51) 0.042 |
    - Donor age | 0.01 (0.04 – 0.02) 0.005 |
    - Acute rejection | 0.27 (0.04 – 0.51) 0.025 |
  - At 3-years:
    - Combined biomarker at day-1 (µmol/L) | >0.05 |

CONCLUSIONS
- Levels of MDA appears to reflect the oxidative stress status and a significant improvement, but not normalization, was observed after successful renal transplantation.
- MDA can be used, individually or in combination, as and early biomarker of long-term graft function.