Hypertension metrics and treatment targets in renal transplantation

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Renal transplantation is the best option... but in the long term it leaves many clinical issues unsolved... First of all CV risk...

Kidney transplant patients always have CKD....

Factors other than CKD

Kiberd B et al., Am J Transplant 2003;3:1393-1399

Kidney transplant patients always have CKD....

General population

$\times 2.3$

i.e. +230%
CV death in renal transplant patients is a double failure because not only the patient's life is lost but also a functioning graft implying a further financial failure for the whole society.
**Hypertension After Kidney Transplantation**

Bertram L. Kasisk, MD, Shakeel Anjum, MD, Rajiv Shah, MD, Jeffrey Skogen, MD, Chitra Kandaswamy, MD, Barbara Danielson, RN, Eileen A. O’Shaughnessy, MD, David C. Dahl, MD, John R. Slikensen, MD, Meena Sahadevan, MD, and Jon J. Snyder, MS


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**Graph:**

- **Y-axis:** Relative Risk per 10 mmHg Systolic BP
- **X-axis:** Graft Failure, Graft Failure and Death, Death

**Legend:**

- **Points:** Represent the relative risk for different outcomes.
- **Bars:** Indicate the confidence intervals for the relative risk estimates.

**1,666 kidney transplant recipients cohort**
...No question that Hypertension, a potentially modifiable risk factor, should be recognized and properly treated ....
...BP target in renal transplant patients remains unclear. .. there are no recommendations for BP targets in the latest European Society of Hypertension (ESH)/European Society of Cardiology (ESC) guidelines ...

...caution against formal recommendation is the fact that there is still scarce evidence that the altered BP profile and hypertension, as measured by ABPM, reflect CV burden...
Office BP and ABPM in two cohorts of transplant and CKD patients…No difference in Office BP…but when patients were classified into dippers according to ABPM…

…Thus, precise evaluation of hypertension in kidney transplants requires 24hABPM…
... So far no evidence has been produced that in transplant patients, 24hABPM reflects target organ damage at a vascular level better than conventional office BP measurements....

...confirming in target populations the association with vascular damage comparing a better metrics of risk factors, such as ABPM versus office BP, is a fundamental step to assess the value of 24hABPM in the renal transplant population...
Study cohort: 172 patients

Age (years) 46±12
Gender (males %) 70%
GFR ml/min/1.73m² 56±20

91% were on anti-hypertensive treatment

...a strong predictor of fatal and non-fatal cardiovascular events...
BP components and Intima Media Thickness (IMT)

Mallamaci F et al. Transplantation. 2016 Oct;100(10):2211-8
Dipping and Intima Media Thickness (IMT)

Mallamaci F et al. Transplantation. 2016 Oct;100(10):2211-8
The association of the night/day SBP ratio with IMT was of similar strength in all the subgroups.

**Subgroups**
- Diabetics
- Non diabetics
- Normotensives
- Hypertensives

**Office criteria**
- Normotensives
- Hypertensives

**eGFR**
- < 60 ml/min/1.73m²
- ≥ 60 ml/min/1.73m²

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Mallamaci F et al. Transplantation. 2016 Oct;100(10):2211-8
Nocturnal hypertension is independently associated with carotid atherosclerosis while office BP is not.

... night-time BP and nondipping may be hidden markers of the BP burden in this population and generate the hypothesis that targeting nocturnal hypertension may reduce the high risk for CV events in transplant patients.
Source population (n=274)

- 1 refused ABPM
- 8 did not complete ABPM recordings or ABPM could not be arranged for logistic reasons.

Patients with available ABPM data (n=265)

- 5 patients excluded because only the baseline visit was available

Patients available ABPM for the analysis (n=260)

Next question: Is there any relationship between nocturnal hypertension and renal function in renal transplant patients?

Study cohort: Single center renal transplant patients
Study cohort: 260 renal transplant patients

- Age years: 47±12
- Gender (males %): 69%
- GFR ml/min/1.73m²: 58±21
- Follow-up: median 3.7 years (IQR: 1.6-6.4 years)

Combined endpoint: eGFR reduction >30%, ESRD and death

Mallamaci F et al. J Hypertens 2018; 36:119-125
Linear mixed models analysis
Dependent Variable: repeated measurements of eGFR over time

- **Crude**
  - 24h average: 0.50
  - Day-time: 0.00
  - Night-time: -0.50
  - Conventional BP: -1.00

- **Adjusted**
  - 24h average: P<0.001
  - Day-time: P<0.001
  - Night-time: P<0.001
  - Conventional BP: P<0.001

Night-time average SBP was the main determinant of renal function loss in kidney transplant patients...

Mallamaci F et al. J Hypertens 2018; 36:119-125
Cox regression analysis

Dependent Variable: Combined endpoint: eGFR reduction >30%, ESRD and death

Crude

In renal transplant patients, daytime and night-time SBP predict the risk of GFR loss overtime. Night-time BP is the strongest indicator of the risk of renal function loss.

Conventional BP largely failed to predict the combined endpoint.

Adjusted

Optimization of BP control and interventions targeting night-time BP may afford renal benefits in transplant patients, a hypothesis that remains to be tested in a clinical trial.

Mallamaci F et al. J Hypertens 2018; 36:119-125
Office and 24hABPM as a guide to treatment in renal transplant patients

Over a median follow-up of 48 months 785 repeated 24h ABPM measurements were available in 260 pts.

Hypertension definition: 24h ABPM (>130/80 mmHg)

Office BP (>140/90 mmHg)

In as much as 193 visits (25% of all visits) where office BP indicated the need of antihypertensive therapy institution or modification (BP>=140/90 mmHg) synchronous 24hABPM was actually normal (<130/80 mmHg).

In additional 124 visits (16% of all visits) 24hABPM was in the hypertensive range while office BP was in the normotensive range.

Overall, in 41% of visits office BP provided misleading therapeutic indications.

Mallamaci F et al. (in preparation)
CV risk remains high in renal transplant patients.

Night-time hypertension but not Office BP is associated to atherosclerosis (i.e. IMT) and it is important for CV risk stratification in renal transplant patients.

Night-time average systolic BP seems to be a good predictor of GFR loss over time.

These findings strongly suggest that current transplant Guidelines which recommend only office BP for risk stratification in kidney transplant patients need to be reconsidered.

Follow-up: 4.7 years, All cause mortality: 3808 patients (34% of CV causes).

In primary care subjects, 24h ABPM measurements were a stronger predictor of mortality than office BP measurements...