Hypertension After Kidney Transplantation

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Hypertension After Kidney transplantation

- **Is a usual finding in this population**
- **One of the most common risk factors for CVD**
- **Occurs in patients with other metabolic diseases(DM, HLP ,Obesity)**
- **Pathogenesis is complex (interplay between immunological and non-immunological factors)**

EPIDEMIOLOGY

- **Depending on the definition and methods of blood pressure measurement , has been widely reported**
- **The great incidence maybe related to the introduction of cyclosporine**
- **Overall prevalence has ranged from 24 to 90%**

EPIDEMIOLOGY

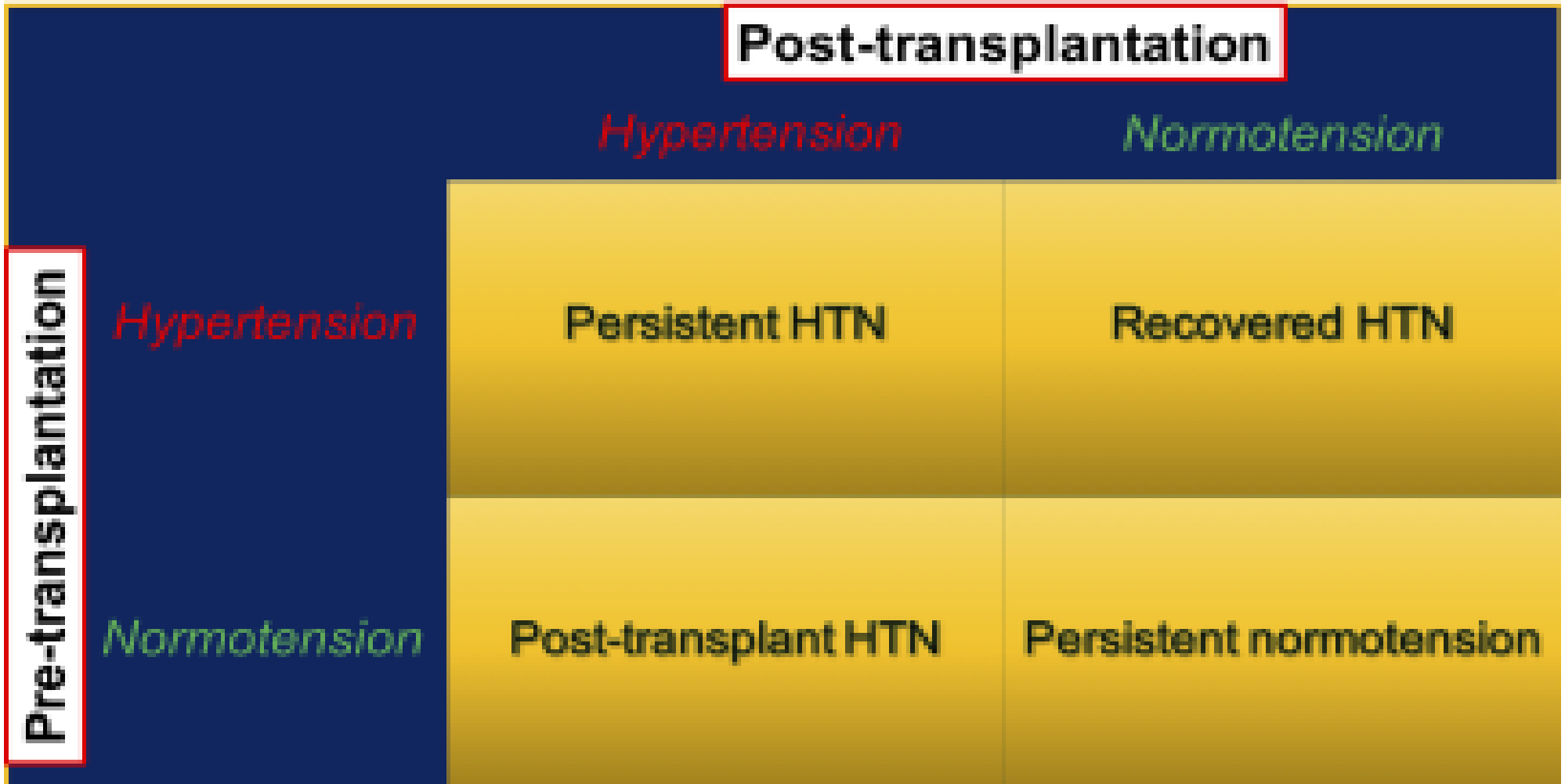
TABLE 1 | Summarized definitions of post-transplant hypertension from studies specifically examining the prevalence of post-transplant hypertension.

References	Incidence or prevalence	Definition	Study design	*n*	Mean time since transplantation (range)
Budde et al. (16)	Incidence 77.3% [81.6% persistent HTN (HTN both pre- and post-transplantation) and 18.4% post-transplant HTN (normotension during pre-transplantation but HTN post-transplantation)]	>150/90 or using antihypertensive medications except the single use of diuretics	A single-center cross-sectional study of patients with stable graft function (>3 months) Mean of ≥5 consecutive BP records Sphygmomanometer in the sitting position	409 patients (64.5% had pre-KTx HTN and 35.5% had pre-KTx normotension) Mean age 47 ± 1 (19–68) years	45 ± 2 months (3–204)
Malek-Hosseini et al. (17)	Incidence 60% [68% persistent HTN (HTN both pre- and post-transplantation) and 32% post-transplant HTN (normotension during pre-transplantation but HTN post-transplantation)]	145/95 or required antihypertensive medication	A single-center study	84 patients (67.9% had pre-KTx HTN and 32.1% had pre-KTx normotension) Mean age at transplantation was 33.5 ± 11.3 years (range 11–58)	34 ± 22.6 months (3–93)
Zeier et al. (8)	Prevalence 90%	>140/90 mmHg or antihypertensive treatment	150 kidney transplants recipients in outpatient clinic with a median follow-up of 3.8 years		
Kasiske et al. (18)	Incidence 50–80%	≥140/90 mmHg	Clinical Practice Guidelines by searches conducted using Medline and pertinent bibliographies and an electronic database used to collate references, but no systematic data extraction or synthesis Experts' opinions		
Campistol et al. (9)	≥80% 3 years post-KTx 85% 5 years post-KTx	SBP ≥140 and/or DSP ≥90 and/or treated with antihypertensive medications	Data from the Spanish Chronic Allograft Nephropathy Study	3,365 adult kidney transplant recipients	

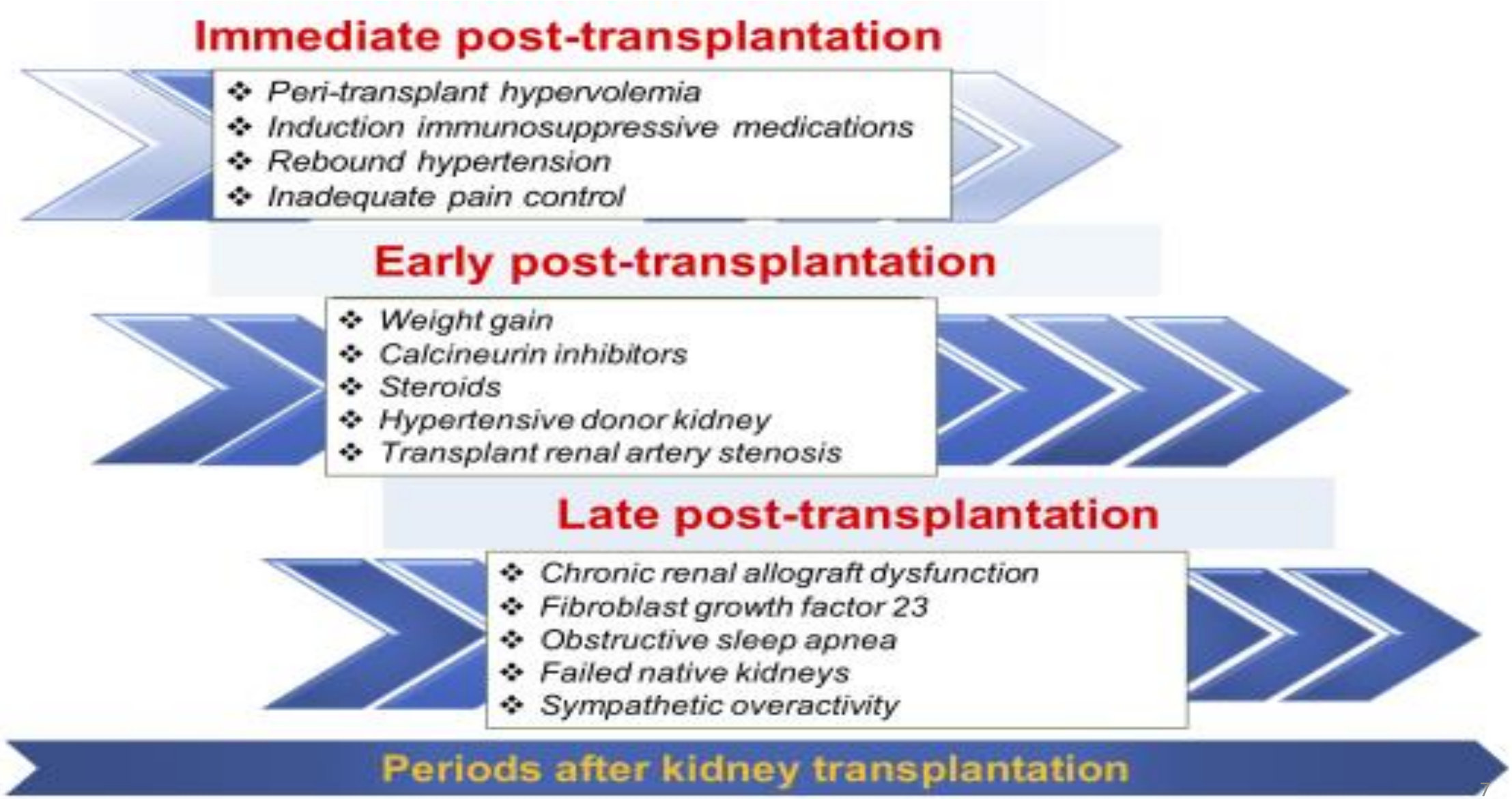
DEFINITION OF POST-TRANSPLANT HYPERTENSION

- **Persistently elevated BP or normotension with use of antihypertensive medications after successful kidney transplantation**

DEFINITION OF POST-TRANSPLANT HYPERTENSION



PATHOGENESIS



Immediate Post-transplant Period

- **Peri-transplant Hypervolemia**
  - **prevalence was 30%, and up to 5% had severe hypervolemia**
- **High-Dose Steroids**
  - **The mechanism is unclear**
  - **May result from alterations in intrinsic pressor response**
  - **More than 20 mg of prednisone/day is the threshold for having HTN**
- **Rebound Hypertension**
  - **Abrupt discontinuation of drugs**
  - **B.Blockers , clonidine**
  - **ACC/AHA guidelines (class I with B level evidence for the continuation of beta-blockers during the peri-operative period in whom chronically use them)**
- **Inappropriate Pain Management**

Early Post-transplant Period

There is no classical definition as the early post-transplant period ,May consider 26–50 weeks after kidney transplantation

- **Weight Gain**
  - ✓**Between 6- and 12-months post-transplantation occur**
  - ✓**weight gain & increase in BMI at 1 year is 6.2 ± 10.7 kg and 2.1 ± 3.8 kg/m2**

Early Post-transplant Period

- **Calcineurin Inhibitors**

Altered vascular tone

- **Renal vasoconstriction mediated by endothelin**
- **local effect on smooth muscle cells by increasing the number of angiotensin II type 1 receptors**
- **Renal vasodilation Impairment (reduction of nitric oxide)**

Increased renal sodium transport handling

- **Sympathetic nervous system activation**
- **Salt-sensitive HTN via activation of NCC similar to Gordon syndrome (hyperkalemia/non-anion gap metabolic acidosis / hypercalciuria)**
- **Thiazide diuretics should be effective for CNI-induced HTN**

Early Post-transplant Period

Steroids

- **HTN decreased in patients taking alternate day steroid therapy**
- **In one RCT no difference between them**
- **Steroid avoidance or withdrawal significantly decreases CV outcomes including HTN**

Hypertensive Donor Kidney

- **Patients receiving kidneys from donors with family history of HTN required 10 times greater antihypertensive medication requirement as compared to those who receive kidneys from donors without a family history of HTN**

Early Post-transplant Period

Transplant Renal Artery Stenosis (TRAS)

- Approximately 1–5% of post-transplant HTN is secondary to TRAS
- Incidence of TRAS was reported to increase from 1 to 23%
- May occur at any time after kidney transplantation
- Generally diagnosed between 3 and 24 months post transplantation

pathogenesis of TRAS

- Non-immunological
- Immunological
- Cytomegalovirus infection
- Atherosclerosis

Symptoms and signs

- Non-specific
- Unexplained worsening renal allograft function
- Uncontrolled HTN
- Peripheral edema
- Congestive heart failure
- Flash pulmonary edema

Early Post-transplant Period

Transplant Renal Artery Stenosis (TRAS)

Diagnosis

- Ultrasonography
- Computed tomography (CT) or MRA should be utilized to confirm
- Renal artery angiography remains the gold standard
- Carbon dioxide (CO2) angiography can mitigate some of the risk of CIN

Treatment

- Pharmacological therapy alone
- Pharmacologic + renal artery angioplasty with stenting
- Surgical revascularization

Late Post-transplant Period

Chronic Renal Allograft Dysfunction

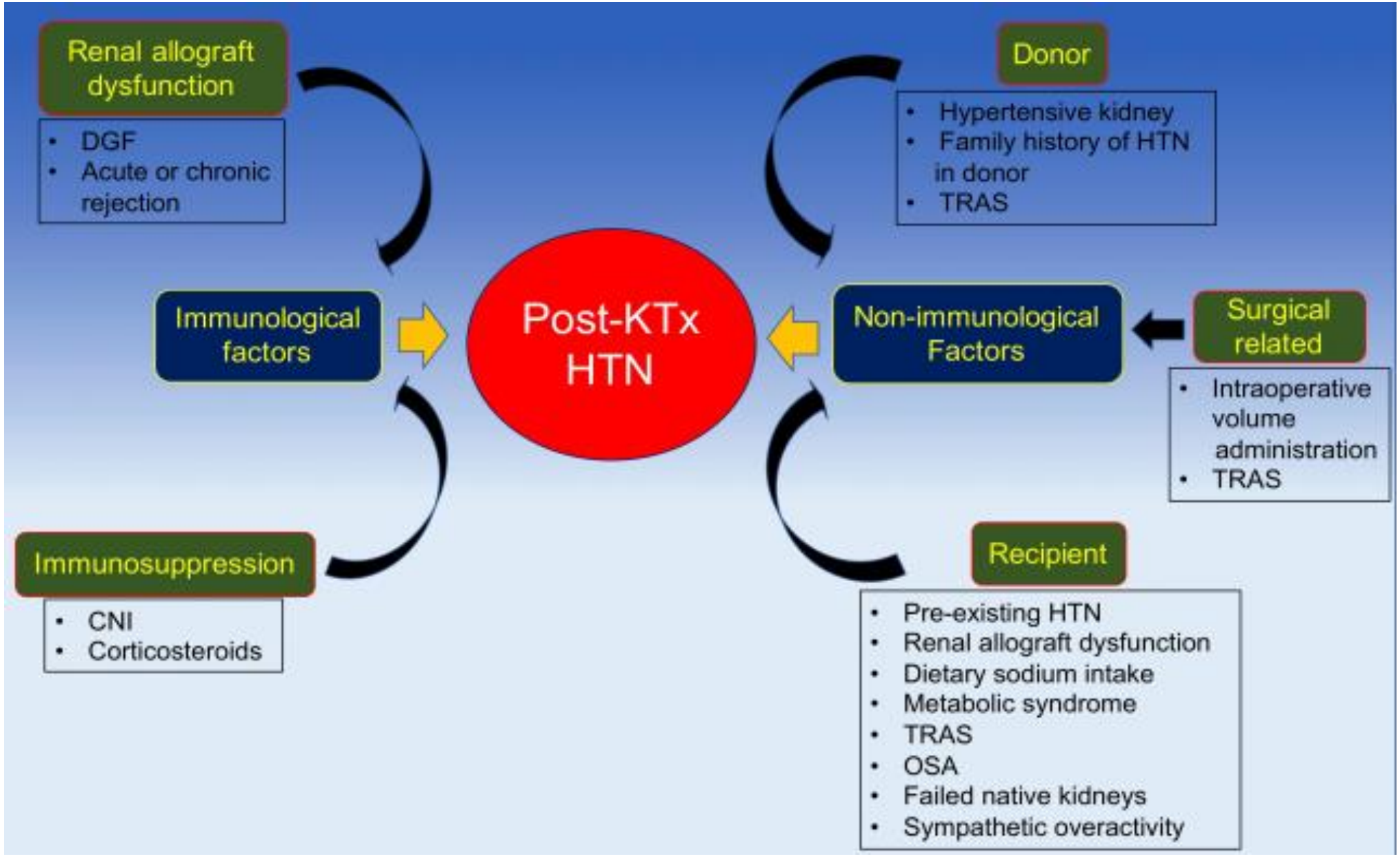
Fibroblast Growth Factor (FGF) 23

- **higher level of FGF23 is associated with increased SBP and DBP**

Obstructive Sleep Apnea

- **Increased sympathetic activity**
- **Endothelial dysfunction**
- **Increased inflammatory markers**
- **hyperaldosteronism**
- **Chronic volume overload**

Hypertension After Kidney transplantation



OUTCOMES OF HYPERTENSION AFTER KIDNEY TRANSPLANTATION

Cardiovascular Outcomes

- **Heart failure , with preserved EF &LVH**
- **Renal insufficiency is involved in the pathogenesis of HFpEF**
- **Vicious cycle of cardio-renal dysfunction**

BLOOD PRESSURE MEASUREMENT

<u>BP measurement in clinical practice an be standardized with the following definitions</u>

Office blood pressure (OBP):

- **The mean of three non-invasive BP measurements**

Home blood pressure monitoring (HBPM) :

- **Recording at least twice the daily average of two home blood pressure readings over a minimum of 4 days**

24-h ambulatory blood pressure monitoring (24-h ABPM)

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BLOOD PRESSURE MEASUREMENT

A 24-h ABPM

- **Provides the average of day and night BP**
- **Can assist with the common misclassification of HTN diagnosed traditionally by OBP or HBPM**
- **Compared with OBP, led to 61% disagreement in diagnosis (58% and 3% due to masked and white-coat HTN, respectively)**
- **HBPM appears to be a common utilized method**
- **Higher correlation between a 24-h ABPM and HBPM**

BLOOD PRESSURE MANAGEMENT

Non-pharmacologic interventions

- **Diet**
- **Exercise**
- **Stress reduction**

Pharmacological managements

- **Data from transplant recipients from 2001,2006, 2011, and 2014**

Beta-blockers were the most common antihypertensive medication followed by calcium channel blockers

POINTS IN DRUG SELECTION

Loop Diuretics

- **Increased risk of UTI during the first 5 years after kidney transplantation**
- **Because there use depletes medullary NaCl gradient**

Thiazides

- **Metabolic side effects(hyperglycemia,hyperuricemia ,hypercalcemia, hyponatremia)**
- **Prevent magnesium loss**

Mineralocorticoid Receptor Antagonists

- **Decrease proteinuria (in some study by 50%)**

Beta-Blockers

- **metabolic side effects, (proteinuria,masking of hypoglycemic symptoms, hyperkalemia specially with mTOR inhibitors)**

POINTS IN DRUG SELECTION

Calcium Channel Blockers

- Appropriate agent for post-transplant HTN
- Vasodilatory effect (counteract the vasoconstrictive effect of CNIs)
- Lower incidence of ATI
- Higher GFR with primary function
- Can result in peripheral edema and muscle weakness especially with steroids

POINTS IN DRUG SELECTION

ACEI&ARB

- **Decrease in proteinuria, eGFR , and hematocrit**
- **Insufficient data regarding the benefits of ACEI or ARB in terms of patient or renal allograft survival**
- **Can lead to regression of LVH**
- **Not choice during the immediate and early post-transplant periods**

Alpha1-Antagonists

- **An adjunctive therapy rather than first line antihypertensive agent in transplant recipients.**

POINTS IN DRUG SELECTION

Alpha2 Agonists

- **Antihypertensive tolerance, edema, and weight gain**
  Sodium and water retention

DRUG OF CHOICE

In summary

- **There is no drug of choice for BP control after kidney transplantation.**
- **Several factors are involved in selecting the appropriate antihypertensive medications include immunologic and non-immunologic factors as well as the time after kidney transplantation**

OTHER TREATMENT

- **Native kidney Nephrectomy**
- **Native Renal Sympathetic Denervation**