# HYPERTENSION

## Pretransplant

→ **Beta-adrenergic agonists, clonidine** and beta-blockers are commonly associated with this rebound hypertension , particularly when abruptly stopped.

→ Sympathetic overactivity without renin angiotensin system mediation plays a major role in the mechanism of rebound HTN from clonidine .

→ Similar to clonidine, **rebound HTN** from beta-blockers **causes elevated BP and heart rate. It also leads to cardiac events including angina, myocardial infarction, or sudden cardiac death in patients with underlying coronary artery disease (CAD)** .

→ .Given the cardiac risk with peri-operative beta-blocker withdrawal the 2014 ACC/AHA guidelines give a class I **recommendation** with B level evidence for the **continuation of beta-blockers during the peri-operative period in patients who chronically use them(3)**

# Post Renal transplant management

**TABLE 2 |** Common interventions for post-kidney transplant hypertension.

| Blood pressure managements | Interventions | Comments |
|---|---|---|
| Lifestyle modifications | Diet<br>Exercise<br>Stress reduction | Required for all patients |
| Pharmacological therapy | Antihypertensive medication<br>• Diuretics<br>- Loop<br>- Thiazides<br>• Calcium channel blockers<br>• Beta-blockers<br>• Renin-Angiotensin-Aldosterone System blockade<br>- Angiotensin-converting enzyme inhibitors<br>- ARB, angiotensin II receptor blockers<br>- Mineralocorticoid receptor antagonists<br>• $Alpha_1$ antagonists<br>• $Alpha_2$ agonists | Choice of medications depending on:<br>• Patients' characteristics,<br>• Tolerability<br>• Medication side effect profiles |
| Procedural or surgical interventions | Specific treatment modalities<br>• Transplant renal artery angioplasty ± stenting<br>• Continuous positive airway pressure (CPAP)<br>• Bilateral native nephrectomy<br>• Native renal denervation | Etiologies of resistant hypertension<br>• Transplant renal artery stenosis<br>• Obstructive sleep apnea (OSA)<br>• Failed native kidney<br>• Sympathetic overactivity |

→ glucocorticoid-induced hypertension.
→ The optimal regimen is certainly **not clear** given the potential impact of glucocorticoids on several hypertensive pathways, including increased vascular tone, increased sodium reabsorption, and centrally mediated mechanisms.
→ It is proposed that using **calcium channel blockers** or other vascular relaxants if hypertension is manifest within the first few days of glucocorticoid administration with the eventual addition of a **diuretic** if the hypertension persists or worsens.
→ There is potentially a role for centrally acting agents such as **clonidine**, either in addition to other pharmacotherapy or independently, although this is less clear[2]

→ High-dose IV steroids as more than 20 mg of prednisone per dah can contribute to HTN during immediate post-transplant period.
→ **steroid avoidance or withdrawal (SAW)** maintenance immunosuppressive medication regimens can be considered.

→ However, the **effect of SAW** on post-transplant HTN has yielded conflicting data.
→ A systematic review and meta-analysis revealed that steroid avoidance or withdrawal significantly decreases CV outcomes including HTN but increases risk of acute rejection .
→ It is common for steroids to be reintroduced after a diagnosis of acute rejection in recipients who were initially managed with a SAW regimen.
→ A randomized control trial, however, demonstrated no difference in blood pressure change between alternative day and daily prednisone .
→ So **SAW protocols** should be considered in select patients, specifically those who would be at greater risk for CV outcomes but be immunologically lower risk of rejection

# PHARMACOLOGICAL MANAGEMENTS
## Use of Antihypertensive Medications

**TABLE 3 |** Summarized common antihypertensive medications used in kidney transplant patients.

| Antihypertensive classes | Pros | Comments | Cons | Comments |
|---|---|---|---|---|
| **Diuretics** | | | | |
| Loop | - Generally, not the first line antihypertensive medication Used in CsA treated recipients<br>- Used for volume control<br>- May use with ACEI or ARB in TRAS | - Renal sodium excretion defect in CsA-induced HTN (198) | - Loop diuretic may worsen renal allograft function from redistribution of decreased renal blood flow at juxtamedullary cortex and outer medulla (199) and ↓ oxygenation in medulla due to decreased cortical vascular resistance diverting medullary perfusion (200). | |
| | | | - Electrolyte disturbance | - Hyponatremia<br>- Hypomagnesemia<br>- Hyperuricemia |
| Thiazide | - May consider in hypomagnesemic patients who needs volume control from diuresis (154). | - Not the first line antihypertensive medication | - Potential volume depletion<br>- Hyperlipidemia | |
| | - May consider in salt-sensitive HTN from CNIs | - WNK-SPAK-NCC pathway | - Electrolyte disturbance | - Hyponatremia<br>- Hypomagnesemia |
| | - May use with ACEI or ARB in TRAS | | | - Hyperuricemia |
| CCB | - May improve renal allograft function (201) and lower DGF but inconclusive | - Afferent arteriolar vasodilatation (202) | - Non-dipyridamole CCB is CYP450 inhibitor and increases CNI level | - CYP450 3A4 enzyme inhibitor → ↑CNI and mTOR inhibitors level |
| ACEI/ARB | - Anti-proteinuric | | - Hyperkalemia | |
| | - Cardioprotection (203, 204) | | - Anemia | |
| | - May use with diuretic in TRAS | | - Elevated creatinine | - In the setting of volume depletion, TRAS |
| Beta-blockers | - For cardioprotection | | - Mask symptoms of hypoglycemia and thyrotoxicosis<br>- Worsening lipid profiles | |
| | | | - Hyperkalemia | - Especially with mTOR inhibitors |
| | | | - Potential rebound HTN | |
| Mineralocorticoid receptor antagonists | - Systolic dysfunction | - Safe with using ACEI and ARB | - Hyperkalemia | |
| Alpha$_1$ antagonist | - Comparable to ACEI for BP control<br>- Generally, not the first line antihypertensive agents | - May need to add other antihypertensive agents | | |
| Alpha$_2$ agonist | - Lower plasma renin activity that modulated renal vascular resistance and subsequently lower MAP (140).<br>- No change in GFR and effective renal plasma flow (141) | | - Potential rebound HTN | - Need to be slowly tapered off if medication discontinuation is needed. |

*ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; CNI, calcineurin inhibitor; CYP, cytochrome; DGF, delayed graft function; GFR, glomerular filtration rate; mTOR, mammalian target of rapamycin; TRAS, transplant renal artery stenosis; WNK-SPAK-NCC, WNK, With-No-K(Lys)—STE20/SPS1-related proline/alanine-rich kinase—Sodium Chloride Cotransporter.*

## OTHER MANAGEMENT FOR BLOOD PRESSURE FOR RENAL TRANSPLANT RECIPIENTS:

1.Native Nephrectomy and ACES

2.Native Renal Sympathetic Denervation

3.Surgical Renal Denervation by Bilateral Native Nephrectomy

→ ALL IN ALL There is no conclusive BP target for kidney transplant recipients and **therapy targets need to be individualized.** Further research is needed [1]

[1]- Tantisattamo, E., Molnar, M., Ho, B., Reddy, U., Dafoe, D., & Ichii, H. et al. (2020). Approach and Management of Hypertension After Kidney Transplantation. Frontiers In Medicine, 7. doi: 10.3389/fmed.2020.00229

[2]- Goodwin, J.E., Geller, D.S. Glucocorticoid-induced hypertension. Pediatr Nephrol 27, 1059–1066 (2012). https://doi.org/10.1007/s00467-011-1928-4

[3]- Tantisattamo, E., Molnar, M., Ho, B., Reddy, U., Dafoe, D., & Ichii, H. et al. (2020). Approach and Management of Hypertension After Kidney Transplantation. Frontiers In Medicine, 7. doi: 10.3389/fmed.2020.00229