

No significant differences between medical and surgical management were identified for hypertension remission. However, a meta-analysis (53) of 20 observational studies, including 3209 individuals with PA, showed an association of *lower* long-term efficacy in achieving BP control with PA-specific medical therapy compared with surgical therapy (odds ratio [OR]: 0.333; 95% CI: 0.202-0.550). Additionally, long-term SBP levels were higher with medical management in an analysis of 42 observational studies (53) of 10 286 persons with PA mean difference (MD: 4.811; 95% CI: 3.327-6.294).

Observational studies also indicate that medical treatment for PA is associated with a higher number of antihypertensive agents (21 studies, 4998 individuals) and higher dosage of antihypertensive agents (8 studies, 1409 individuals) compared with surgical intervention (MD: 1.339; 95% CI: 1.136-1.542; MD: 1.855; 95% CI: 1.400-2.309, respectively) (53). The higher number of antihypertensive agents with medical treatment was supported by a review of clinical trials including 425 persons with PA (MD: 1.348; 95% CI: 0.866-1.830) (115-117), and the higher dosage of antihypertensive agents associated with medical vs surgical management persisted in an analysis based on lateralizing disease only (MD: 1.733; 95% CI: 1.160-2.306).

The systematic review (53) assessed the comparative efficacy of medical vs surgical management for cardiovascular risk. No statistically significant differences were found between the 2 treatment modalities for ischemic heart disease, atrial fibrillation, MACEs, and cardiovascular mortality. However, compared with surgical therapy, review of observational studies indicated medical management had an increased risk of stroke (OR: 1.821; 95% CI: 1.144-2.898). The increased risk for heart failure and all-cause mortality persisted in a review of metadata based on lateralizing PA only (OR: 2.182; 95% CI: 1.38-3.452 and OR: 2.082; 95% CI: 1.124-3.855, respectively). One cohort study reported that MRA therapy compared with adrenalectomy had a higher risk of mortality, major cardiac or cardiovascular events, and combined new-onset atrial fibrillation with mortality (118). However, this increased risk might be mitigated with adequate mineralocorticoid receptor blockade based on unsuppressed renin activity (9).

Due to off-target androgen receptor antagonism and progesterone receptor agonism, spironolactone has dose-dependent side effects of gynecomastia and sexual dysfunction in men and menstrual irregularities in women (116, 119-121). The meta-analysis of a systematic review of 2 observational studies estimated significantly higher medication-related adverse events with medical therapy compared to surgical therapy (OR: 29.853; 95% CI: 3.726-239.166) (123). Of note, fewer side effects were associated with eplerenone than spironolactone, consistent with eplerenone's greater specificity for the mineralocorticoid receptor (122). While the antihypertensive efficacy of eplerenone was lower than that of spironolactone, the eplerenone doses studied were about one-third less potent than the spironolactone doses.

Therefore, the panel concluded that the balance of effects favor surgery, depending on lateralization of aldosterone hypersecretion, individual choice, and suitability for surgery. Refer to Question 6 for a definition of lateralization.

Evidence to Decision Factors

- Medical treatment is cheaper and requires fewer resources (124). However, in an individual with PA and a remaining

life expectancy of 25.4 years or more, surgery was estimated as the least costly strategy in the long-term due to the decreased risk of PA-associated adverse events (125).

- MRAs are readily available, including in resource-poor settings, whereas surgery requires additional resources.
- MRA treatment is equitable and independent of socioeconomic status with no significant inequality of outcomes (126).
- MRA therapy is often preferred by health care clinicians due to its accessibility and low cost. However, individual adherence to spironolactone is lower compared with other antihypertensive medications, possibly related to its anti-androgen and progestogenic side effects.
- Adherence may improve with the use of more selective MRAs, such as eplerenone and potentially finerenone (127-129).
- Adrenalectomy appeals to individuals seeking a definitive cure for hypertension.

Justification for the Recommendation

Based on the systematic review and indirect evidence, the panel provided a recommendation for either medical therapy or surgical intervention for the treatment of PA. This recommendation is based on the observed benefits of surgical treatment, including lower SBP, more effective BP control, reduced risk of stroke, fewer MACEs, lower incidence of heart failure, decreased need for antihypertensive medications, improved quality of life (QOL), and lower all-cause mortality. While medical therapy with MRAs showed less favorable outcomes overall, the excess risk of hard outcomes might be mitigated by monitoring treatment response based on an increase in renin rather than the BP response alone (9) (refer to Question 7). However, individuals often favor surgical therapy due to the possibility of avoiding lifelong medical therapy, overall QOL improvements, limited pharmacologic treatment options, and side effects of some MRAs (eg, spironolactone). Thus, surgical treatment is generally preferred by individuals with lateralizing PA and may offer superior outcomes, but the choice between surgical and medical management should be based on individual characteristics, preferences, and the specific presentation of the disease.

For a definition of lateralization, refer to Question 6.

Comments

Individuals managed either medically or surgically should be monitored according to clinical and biochemical outcomes and to ensure clinical safety as recommended by international expert consensus and in Questions 7 and 9 (85, 86).

Postsurgical outcomes partly depend on successful AVS and the availability of skilled adrenal surgeons, which might be limited outside specialized centers. Preoperative morbidity and length of stay are more favorable in high-volume centers (130).

Adrenalectomy is mainly performed by a laparoscopic approach, but open adrenalectomy can be considered under specific conditions (eg, in individuals who have had multiple prior laparotomies).

Individuals with bilateral PA in whom medical therapy is not well-tolerated or effective can be considered for unilateral adrenalectomy although evidence regarding clinical effectiveness in those situations is limited (131-133).