IS STEROID PROFILING USING LC-MS/MS USEFUL IN THE DIAGNOSTIC WORK-UP OF PRIMARY ALDOSTERONISM?

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OBJECTIVES

To select those patients with a high probability of having an aldosterone producing adenoma (APA) to potentially circumvent adrenal venous sampling (AVS) in those patients with bilateral adrenal hyperplasia (BAH)

INTRODUCTION

Primary aldosteronism (PA) is mainly caused by unilateral aldosterone-producing adenomas (APA) or bilateral adrenal hyperplasia (BAH) (**figure 1**). Subtype differentiation relies on the invasive and technically challenging adrenal venous sampling (AVS). We recently demonstrated the potential utility of peripheral plasma steroid profiling by LC-MS/MS to distinguish APA and BAH (1,2). We tested the following hypotheses: first, if steroid profiling in combination with AVS, effectively identifies patients with unilateral disease who are candidates for surgery and second, if steroid profiling identifies those patients with a high likelihood for BAH in whom AVS may be avoided.

METHODS

208 confirmed PA patients underwent computed tomography, AVS and steroid profiling of peripheral plasma by LC-MS/MS analysis of 12 adrenal steroids (3). Long-term outcome of adrenalectomy was assessed by clinical and biochemical re-evaluation in all subjects. The diagnostic accuracy for subtyping PA patients was calculated based on different strategies for subtype differentiation and compared to the gold standard of AVS.
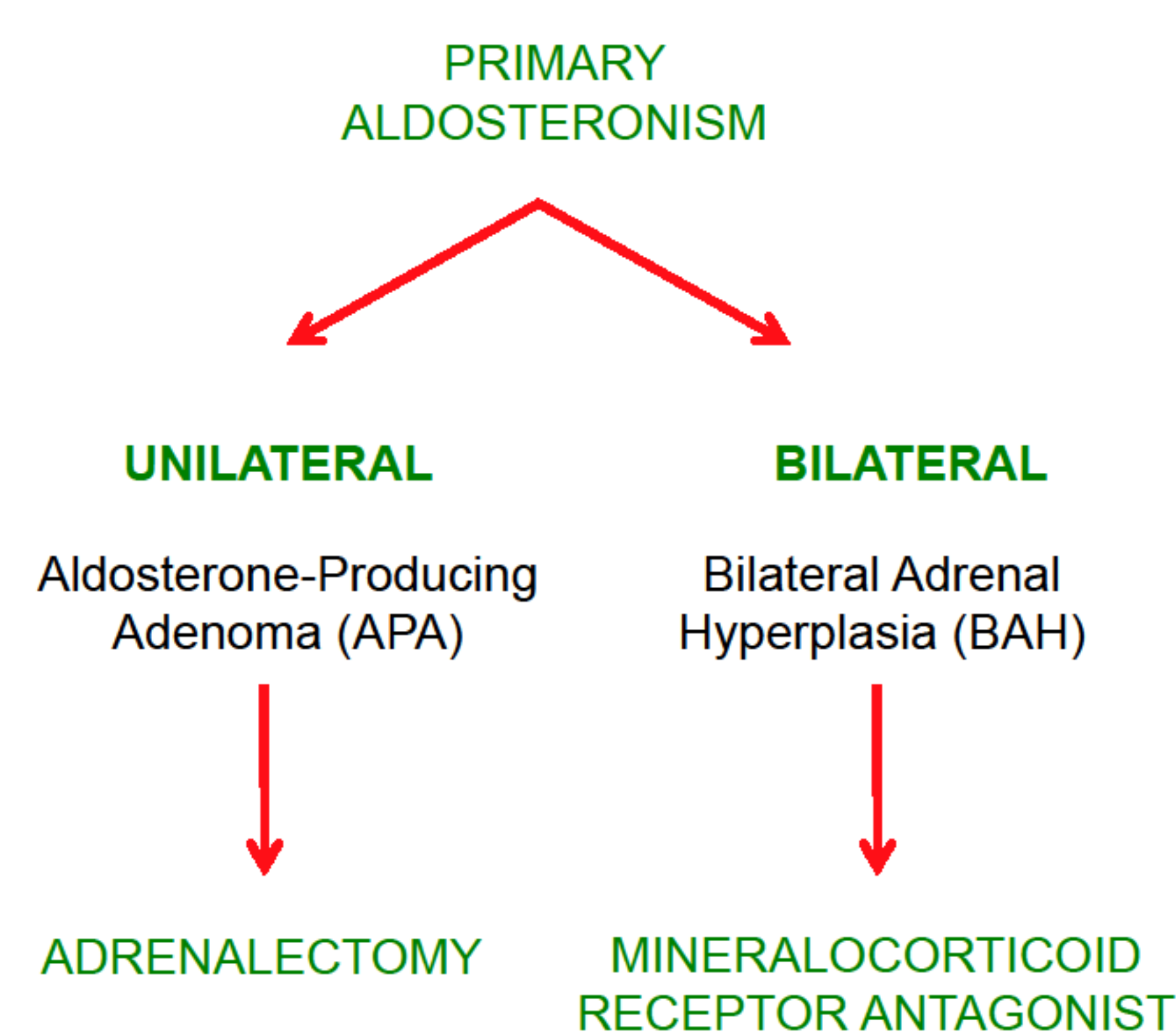
Figure 1
Subtype differentiation is essential to target the patient with PA to the correct therapeutic strategy
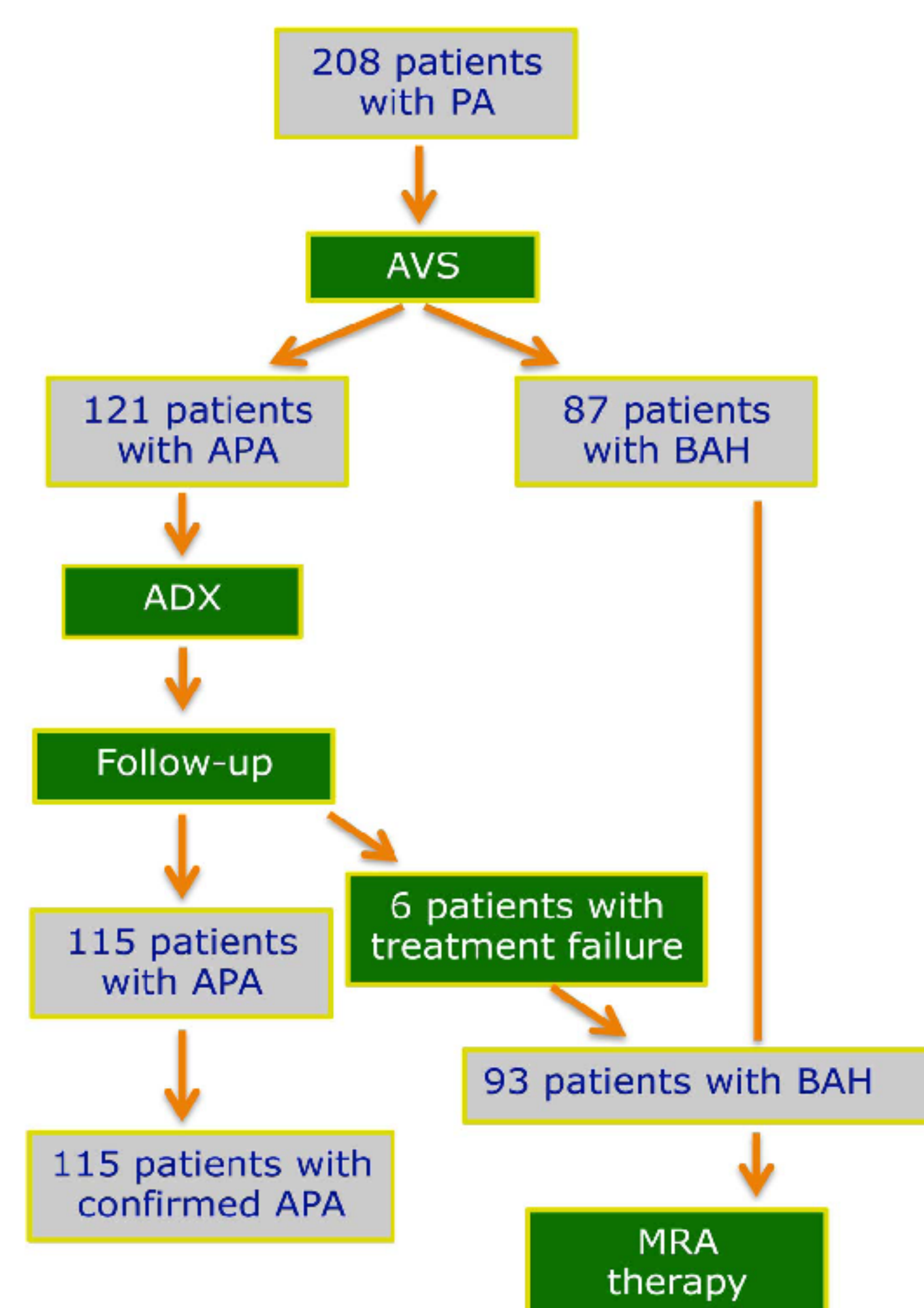
Figure 2
Decision for ADX based on AVS

Figure 3
Decision for ADX based on steroid profiling and AVS

PA, primary aldosteronism; AVS, adrenal venous sampling; APA, aldosterone-producing adenoma; BAH, bilateral adrenal hyperplasia; ADX, adrenalectomy; MRA, mineralocortiod receptor antagonist
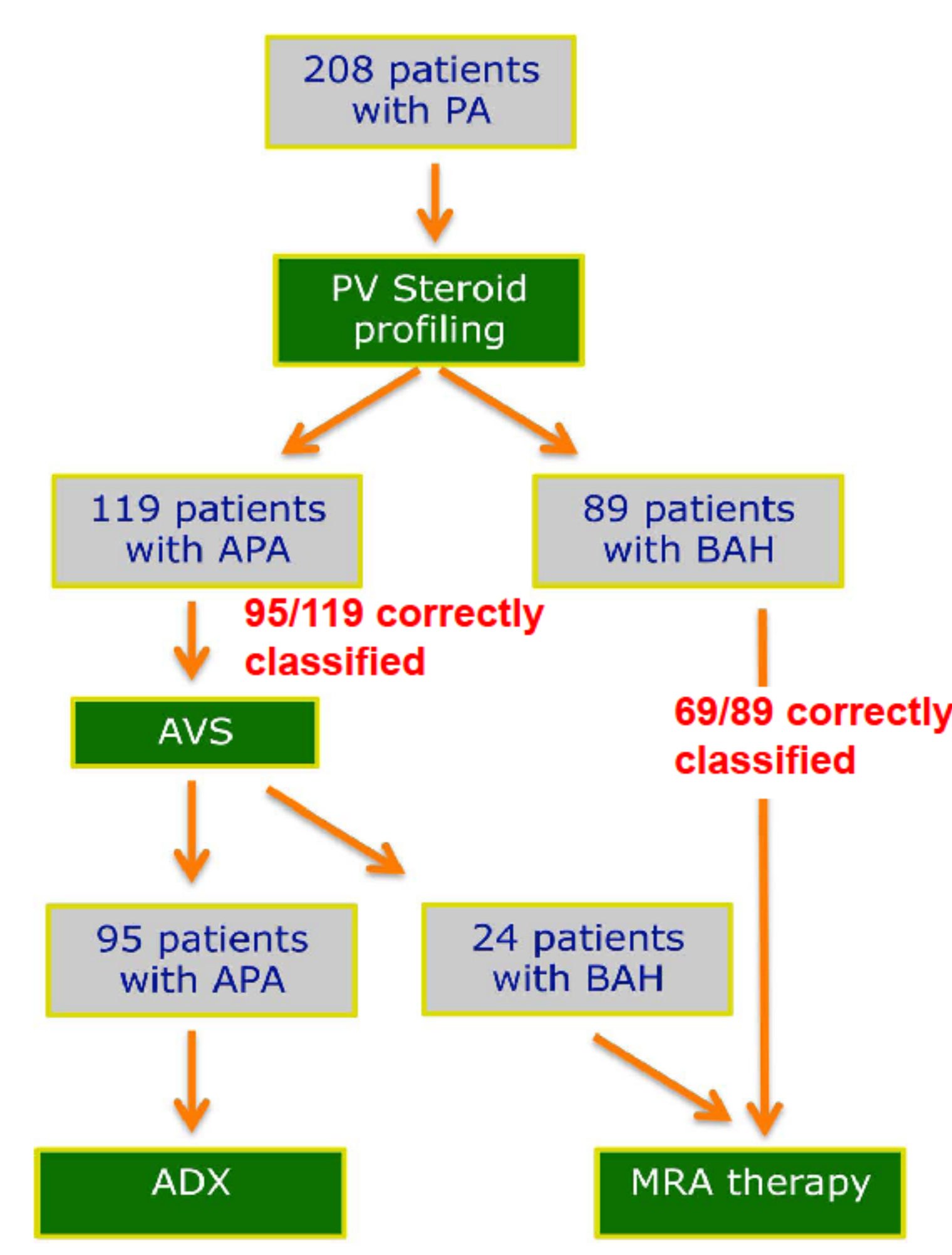
	FAILURE (n=6)	CURE (n=115)	P VALUE		FAILURE (n=6)	BAH (n=85)	P VALUE
Dominant AV plasma				**Right AV plasma**			
Aldosterone/Cortisol	4.3 (3.4-12.1)	32.1 (11.0-97.1)	0-003	Aldosterone/Cortisol	1.82 (0.19-6.07)	0.87 (0.53-2.01)	0.963
18-Oxocortisol/Cortisol	3.2 (1.2-6.6)	10.4 (3.7-34.6)	0.019	18-Oxocortisol/Cortisol	2.18 (0.24-6.33)	1.03 (0.51-1.66)	0.434
18-Hydroxycortisol/Cortisol	1.4 (0.7-2.2)	2.1 (1.2-4.7)	0.071	18-Hydroxycortisol/Cortisol	1.11 (0.69-3.50)	1.09 (0.77-1.33)	0.650
Non dominant AV plasma				**Left AV plasma**			
Aldosterone/Cortisol	0.23 (0.08-0.29)	0.03 (0.01-0.09)	0.003	Aldosterone/Cortisol	1.87 (0.20-6.54)	1.15 (0.50-1.87)	0.969
18-Oxocortisol/Cortisol	0.32 (0.15-2.14)	0.10 (0.03-0.27)	0.019	18-Oxocortisol/Cortisol	0.50 (0.16-4.64)	0.98 (0.60-1.96)	0.421
18-Hydroxycortisol/Cortisol	0.74 (0.46-2.52)	0.47 (0.21-0.86)	0.074	18-Hydroxycortisol/Cortisol	0.96 (0.34-1.50)	0.91 (0.75-1.31)	0.633

Values are in ng/mL and indicate the median with lower and upper quartiles in parenthesis. P values calculated by Mann-Whitney U test. AV= adrenal venous.

Table 1 Steroid concentrations in dominant and nondominant adrenal venous plasma: failure *vs* cure

Table 2 Steroid concentrations in adrenal venous plasma: failure *vs* BAH

RESULTS

- The diagnostic accuracy of AVS was 97%, with 6 out of 121 APA patients incorrectly classified on the basis of persistent PA following adrenalectomy (**figure 2**).
- Steroid profiling correctly classified 79% of PA patients but this does not identify the adrenal source of aldosterone excess for the APA group (**figure 3**).
- The most effective strategy in our model was steroid profiling followed by selective AVS in those patients designated by peripheral steroid profiling to have a high likelihood of an APA (**figure 3**).
- 20 patients would have been falsely classified and treated as BAH (**figure 3**) while the 6 patients falsely classified as APA by AVS would have been spared unnecessary adrenalectomy.
- Notably, the requirements for AVS would have been reduced by 43% (AVS in 119 patients *vs* 208 patients).
- Aldosterone and 18-oxocortisol concentrations in AV plasma samples indicate the similarity of the failure group with the BAH group and the difference from the APA group (**tables 1-2**)

CONCLUSIONS

Subtype differentiation in PA by peripheral venous steroid profiling followed by AVS in the APA group could provide an alternative to AVS alone and significantly reduce the need for AVS

REFERENCES

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Adrenal 1
Tracy A.

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