THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

"A 48-year-old female with morbid obesity, diabetes, and hypertension"

Dr. Doycheva does not have any relevant financial relationships with any commercial interests.

OBJECTIVES

- Review effects of metabolic surgery on glycemic control and hypertension
- Discuss approaches for diagnosis of hyperaldosteronism
- Review outcomes after adrenalectomy

HPI -02/2016

- 48yo female with h/o morbid obesity (BMI 45), T2DM, and HTN presents for initial evaluation and diabetes optimization before bariatric surgery
- Diagnosed with gestational diabetes in 2002, treated with diet, then lost to follow up, and in 2015 presented to PCP and diagnosed with T2DM; started on glimepiride 4 mg bid
- Weight has been a problem since mid 20s with highest weight of 390 lbs at the age of 28 and lowest 150 lbs at age 18.

Other history and medications

- Past Medical History: HTN diagnosed during pregnancy, not on treatment until age of 40
- Past Surgical History: none
- Medications: ASA 81 mg, Glimepiride 4 mg bid, Amlodipine/Valsartan 10/320, KCl 20 Eq/d
- SH: never smoked, no alcohol, works 3pm -1am
- FH: Obesity- mother and sisters; T2DM- mother, HTN- mother and sister, breast cancer - sister

Physical exam and labs

- Wt 348 lbs, Ht 6'2", BMI 44.7, HR 68 bpm; BP 144/92
- PE: Central obesity, no striae, EOMI, No thyromegaly; Lungs: CTA, CVD: RRR, Abdomen: soft, nontender, Extremities: no pedal edema
- **LABS**

	2/10/16
Sodium	136
Potassium	3.1
Chloride	92
Bicarbonate	29
BUN	22
Creatinine	1.3
GFR	53
Glucose	305
HbA1C	12.2

	2/10/16
Urine alb/Cr	93.7
TSH	0.86
PTH	61
25-OH Vit D	34
Vit B12	376

How to optimize diabetes treatment: what to use? What should be my goal for HbA1C before surgery?

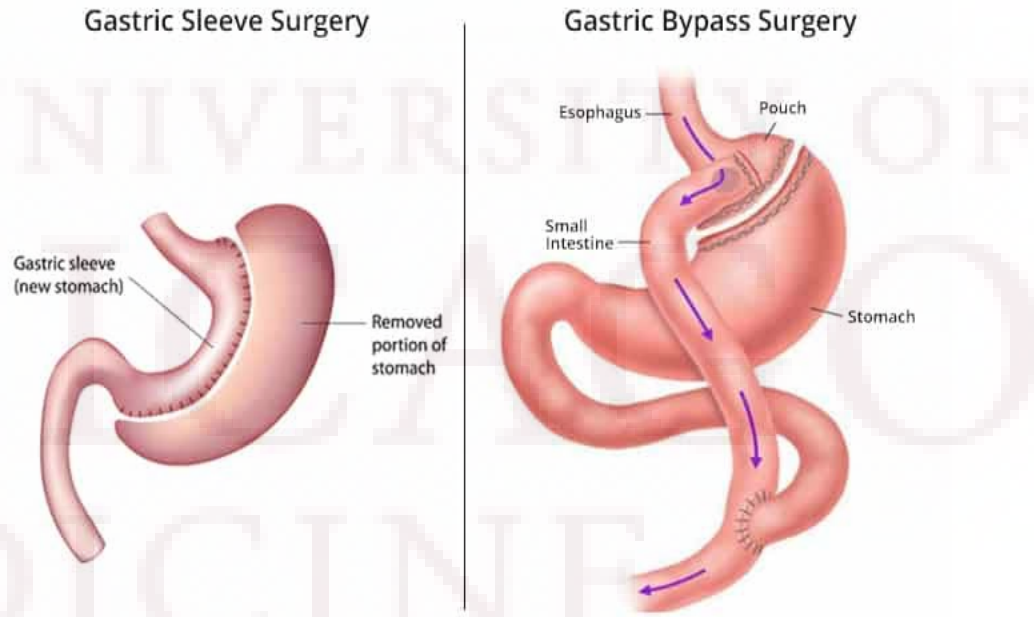
Impact of glycemic control on bariatric surgery outcomes

- Retrospective analysis of MBSAQIP cohort (30,972 participants) showed that patients with T2DM, uncontrolled diabetes, and even prediabetes experience less weight loss 30 days after surgery
- Uncontrolled T2DM (HbA1C >7.5) is associated with of greater likelihood of all-cause hospital readmissions

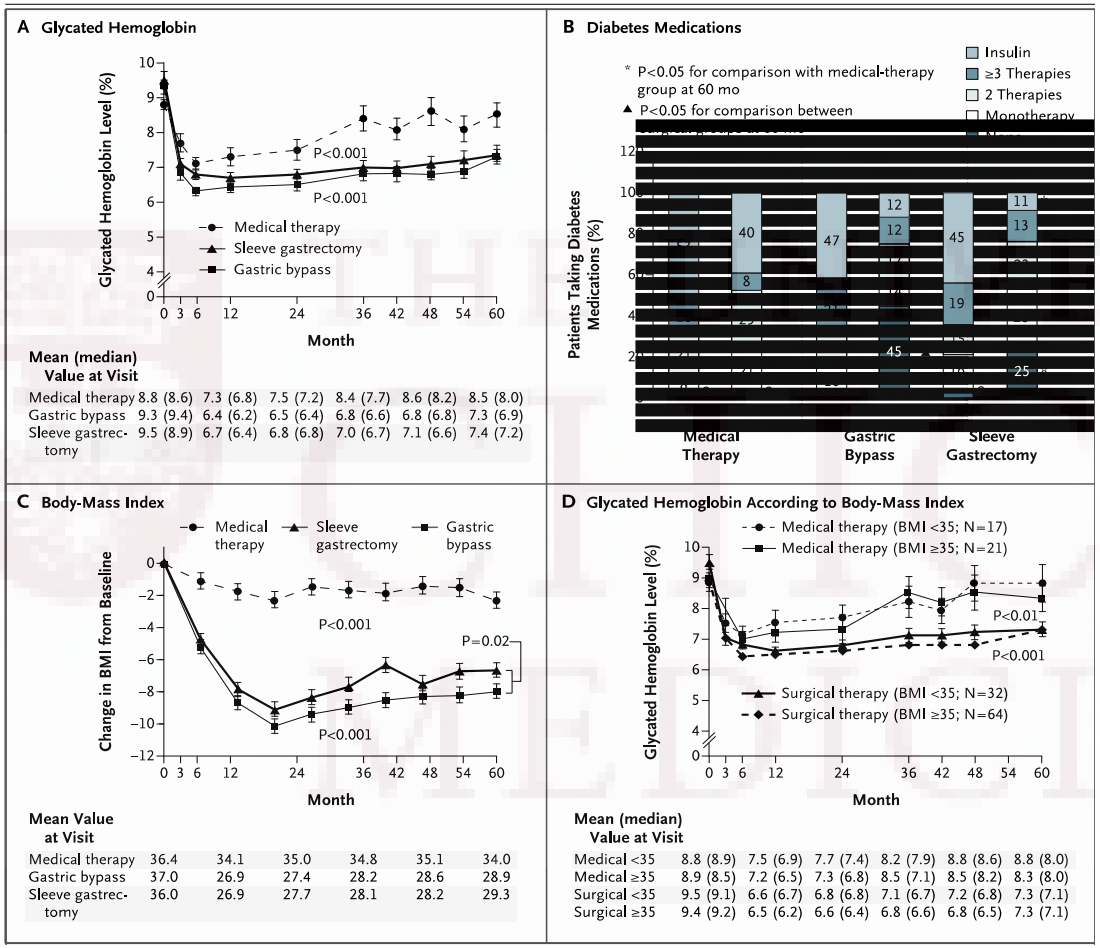
Follow up events

- Started on Lantus 40 U/d and Victoza, stop glimeperide
- Advised on 1800 cal/d and regular physical activity; referred for a sleep study and diagnosed with OSA
- One month later, HbA1C 8.5, Lantus decreased to 20 U and then discontinued, continued on Victoza 1.8 mg, Metformin started, 4 more months later HbA1C 6.7
- Underwent lap sleeve gastrectomy on 8/9/2016
- Lost 37 lbs in one month and 107 lbs in 8 months
- Discharged on no medications for diabetes, sleep study improved, CPAP stopped, but HTN persisted in the range of 160-170/100 despite being on amlodipine/valsartan 10/320

What are the expected results with sleeve gastrectomy vs other MBS and why did not BP improve?



Bariatric Surgery versus Intensive Medical Therapy for Diabetes — 5-Year Outcomes



Mean (median) Value at Visit

Medical therapy	8.8 (8.6)	7.3 (6.8)	7.5 (7.2)	8.4 (7.7)	8.6 (8.2)	8.5 (8.0)
Gastric bypass	9.3 (9.4)	6.4 (6.2)	6.5 (6.4)	6.8 (6.6)	6.8 (6.8)	7.3 (6.9)
Sleeve gastrectomy	9.5 (8.9)	6.7 (6.4)	6.8 (6.8)	7.0 (6.7)	7.1 (6.6)	7.4 (7.2)

Mean Value at Visit

Medical therapy	36.4	34.1	35.0	34.8	35.1	34.0
Gastric bypass	37.0	26.9	27.4	28.2	28.6	28.9
Sleeve gastrectomy	36.0	26.9	27.7	28.1	28.2	29.3

Mean (median) Value at Visit

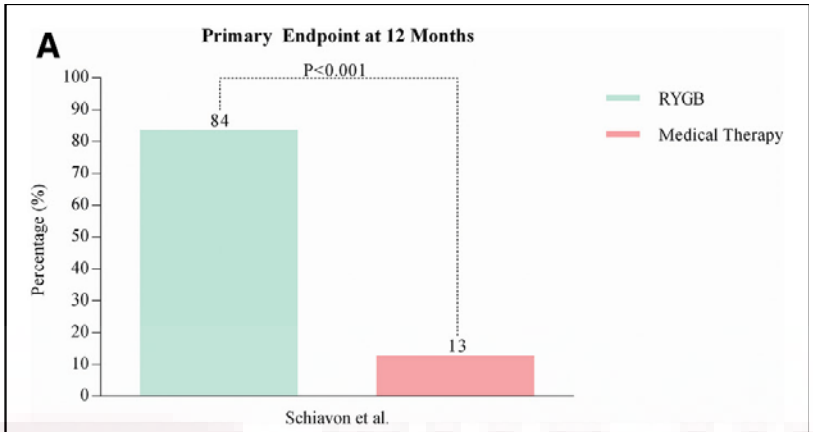
Medical <35	8.8 (8.9)	7.5 (6.9)	7.7 (7.4)	8.2 (7.9)	8.8 (8.6)	8.8 (8.0)
Medical ≥35	8.9 (8.5)	7.2 (6.5)	7.3 (6.8)	8.5 (7.1)	8.5 (8.2)	8.3 (8.0)
Surgical <35	9.5 (9.1)	6.6 (6.7)	6.8 (6.8)	7.1 (6.7)	7.2 (6.8)	7.3 (7.1)
Surgical ≥35	9.4 (9.2)	6.5 (6.2)	6.6 (6.4)	6.8 (6.6)	6.8 (6.5)	7.3 (7.1)

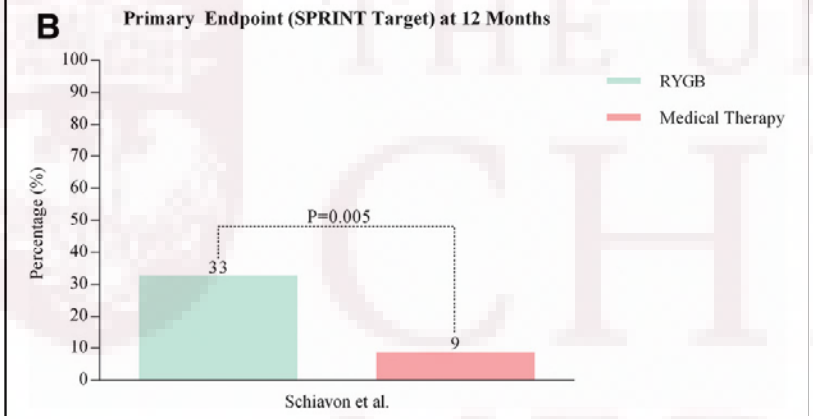
At 5-year follow up bariatric surgery was superior to intensive medical therapy in terms of glycemic control, weight reduction, medication reductions, improvement in lipids, and quality of life

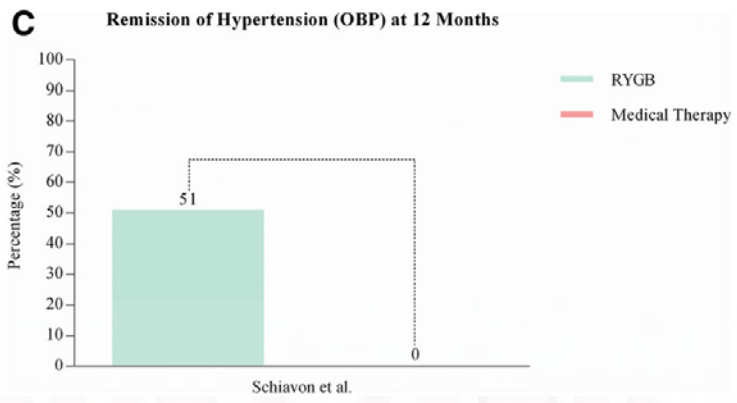
LDL cholesterol — mg/dl						
At baseline	100.9±36.8	91.4±28.9	105.7±40.2			
At 5 yr	95.8±41.9	93.3±35.5	115.1±42.4			
% Change from baseline to 5 yr	3.7±55.3	12.4±53.8	16.6±48.6	0.99	0.4	0.99
HDL cholesterol — mg/dl						
At baseline	48.7±12.8	45.8±13.2	44.3±12.1			
At 5 yr	50.4±12.4	60.0±20.2	57.0±16.6			
% Change from baseline to 5 yr	7.0±44.5	31.9±29.1	29.6±29.5	0.012	0.016	0.75
Median triglycerides (IQR) — mg/dl						
At baseline	166 (97 to 235)	171 (125 to 257)	160 (119 to 214)			
At 5 yr	118 (85 to 169)	114 (81 to 165)	108 (81 to 123)			
% Change from baseline to 5 yr	-8.3 (-37.9 to 22.2)	-39.8 (-58.4 to 7.1)	-29.4 (-51.4 to -2.9)	0.03	0.04	0.47
Systolic blood pressure — mm Hg						
At baseline	135.6±17.7	134.7±18.9	136.7±17.9			
At 5 yr	131.5±14.55	131.4±18.77	128.3±11.60			
Change from baseline to 5 yr	-4.0±20.1	-3.3±22.8	-8.3±20.4	0.88	0.78	0.78
Diastolic blood pressure — mm Hg						
At baseline	82.0±11.4	81.8±10.2	82.2±11.7			
At 5 yr	77.62±9.83	75.98±11.57	74.11±11.49			
Change from baseline to 5 yr	-4.2±11.4	-5.8±12.6	-8.1±14.7	0.86	0.57	0.86

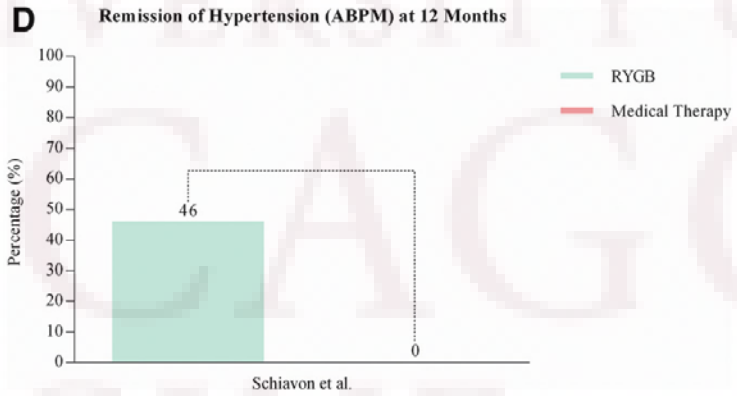
CVD outcomes after MBS

				N of subjects contributing
Excess weight loss (EWL)	54%			19 021
	Baseline	**%Resolution/ Improvement**	**Corrected effect estimates (95% confidence interval)**	
Hypertension	44.4%	62.5%	0.36 (0.31 to 0.42)	14 402 baseline, 15 443 follow-up
Diabetes mellitus	24.0%	73.2%	0.26 (0.21 to 0.31)	15 989 baseline, 15 306 follow-up
Hyperlipidaemia	43.6%	65.2%	0.34 (0.28 to 0.40)	9764 baseline, 11 302 follow-up
	Baseline	**Follow-up**		
Blood Pressure (mm Hg)				
Systolic	140.2	129.6		6488 baseline, 5649 follow-up
Diastolic	87.6	80.2		6413 baseline, 5649 follow-up









Randomized, single-center, nonblinded GATEWAY (Gastric bypass to treat obese patients with steady hypertension) trial assessed bariatric surgery in obese patients with hypertension

Referred for evaluation to the Hypertension center

PE: Wt 239 lbs, BMI 30.7, HR 86, BP 180/97

Amlodipine/Valsartan discontinued, started on Edarbi (azilsartan) 40 mg and diltiazem 240 bid, KCl 20 mEq

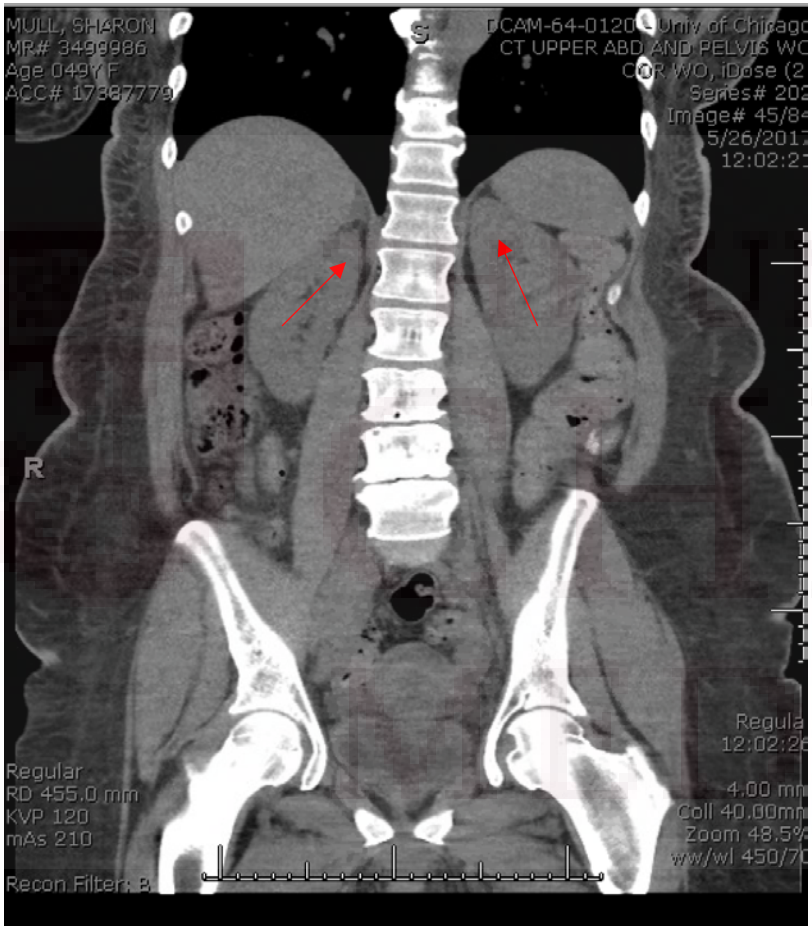
	5/2/2017
Sodium	142
Potassium	3.2
Chloride	102
CO2	25
BUN	25
Cr	2.0
GFR	26
Calcium	9.0
Albumin	4.1
HbA1C	4.8

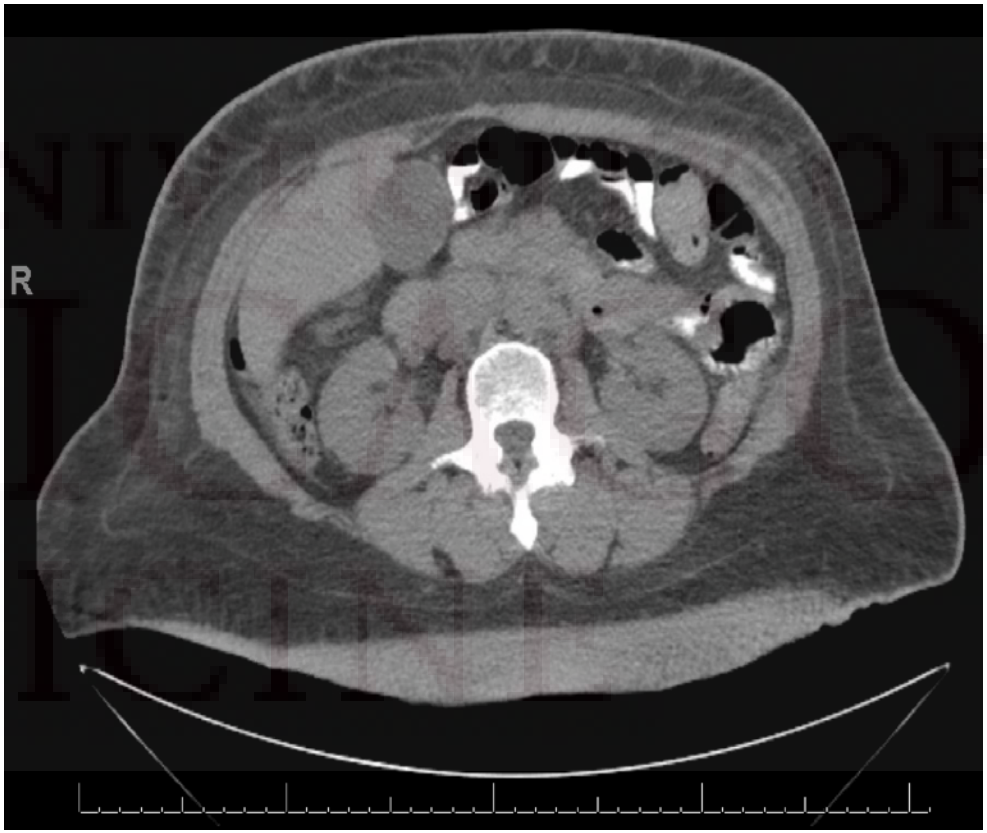
	5/2/2017
Normetanephrine	0.79
Metanephrine	<0.2
Aldosterone	13 ng/dl
Renin	< 0.6

What is next?

Advised on high-sodium diet and had 24h urine aldosterone = 22 (Ref 2.0-20.0 mcg/d)

CT abdomen without contrast





MRI w/wo contrast

Bilateral adrenal glands are within normal limits without measurable nodularity

What is the next step?

Adrenal venous sampling

	Aldosterone ng/dL	Cortisol ug/100 ml	Cortisol-corrected Aldosterone ratio	Average	Lateralization Right/Left
Right adrenal vein	14,000	483.1	29.0	25.9	9.6
Right adrenal vein	12,000	525.5	22.8		
Left adrenal vein	773	282.2	2.7	2.7	
Left adrenal vein	900	331.1	2.7		
Femoral vein	41	21.9	1.9	1.9	
Femoral vein	39	21.2	1.8		

Who should we screen for primary aldosteronism?

What is the algorithm for diagnosis?

Hypertensive patients who should be screened for primary aldosteronism

Drug-resistant hypertension by current definitions (49,52)

Systo-diastolic hypertension (BP >150/100 mm Hg confirmed in repeated measures)

Spontaneous or diuretic-induced hypokalemia

Incidentally discovered adrenal mass (incidentaloma)

Obstructive sleep apnea

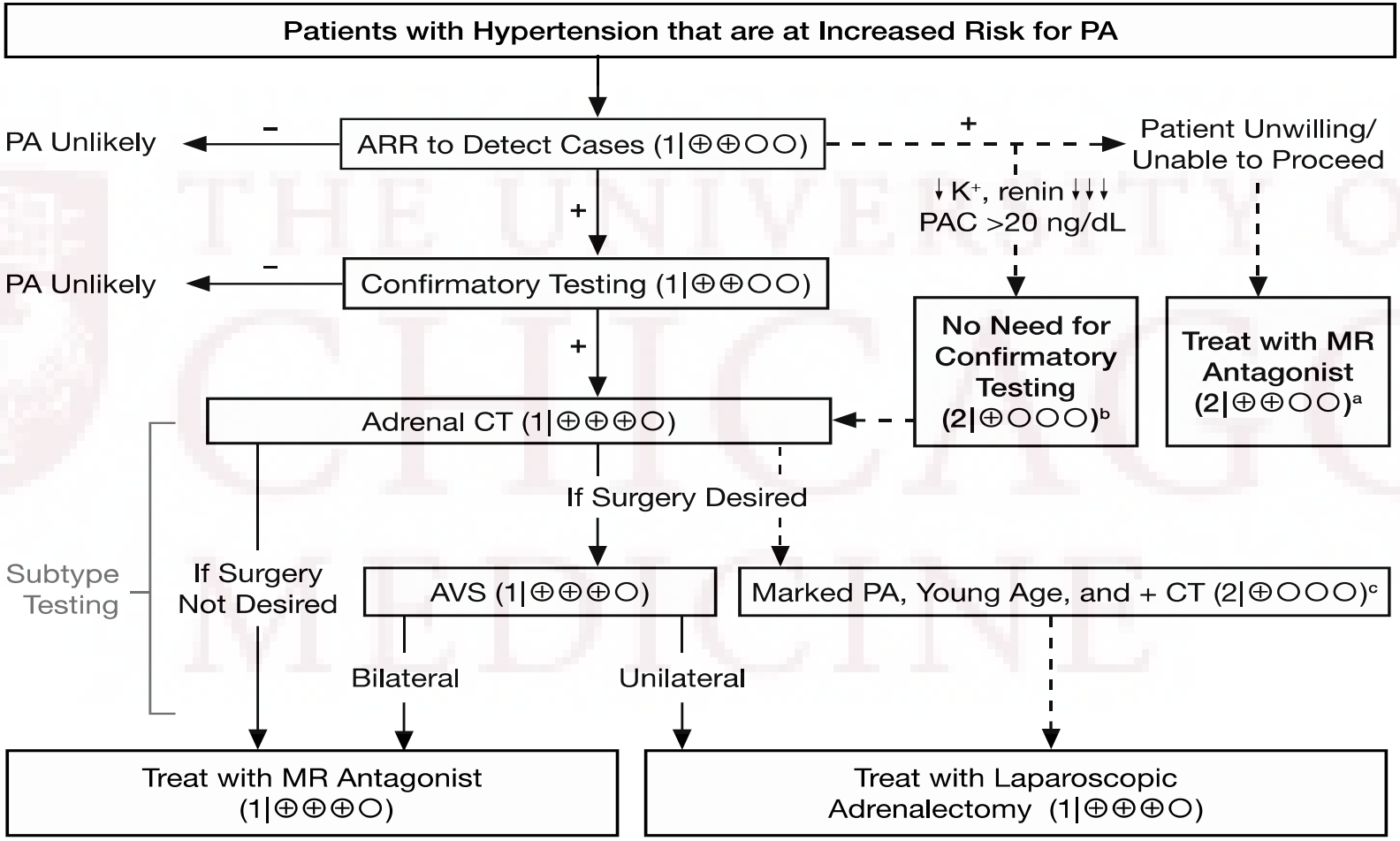
Family history of PA and/or early onset hypertension or cerebrovascular accident at a young age

Unexplained atrial fibrillation

Evidence of hypertension-mediated organ damage (LVH, diastolic dysfunction, microalbuminuria, chronic kidney disease) in excess of what expected based on blood pressure values

Funder et al. J Clin Endocrinol Metab. 2016

Algorithm suggested by current guidelines 2016

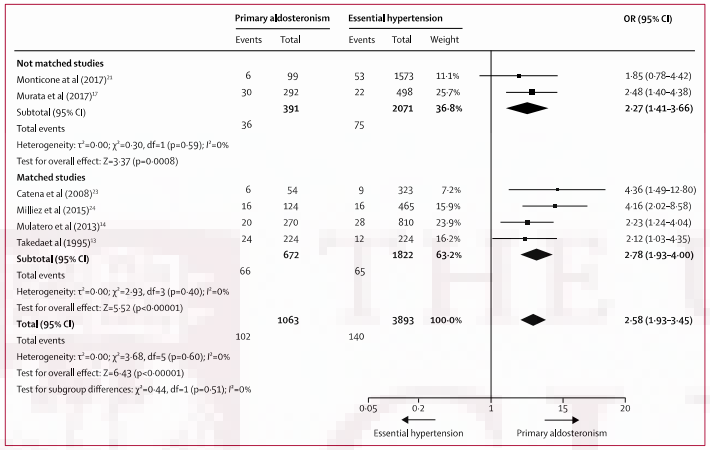


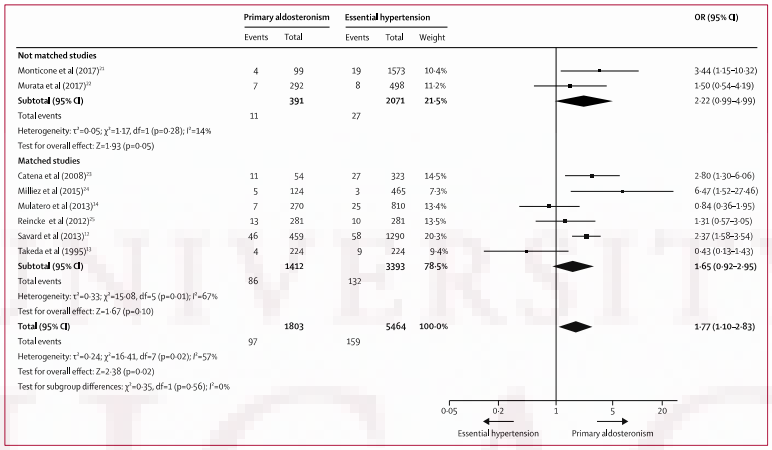
Funder et al. J Clin Endocrinol Metab. 2016

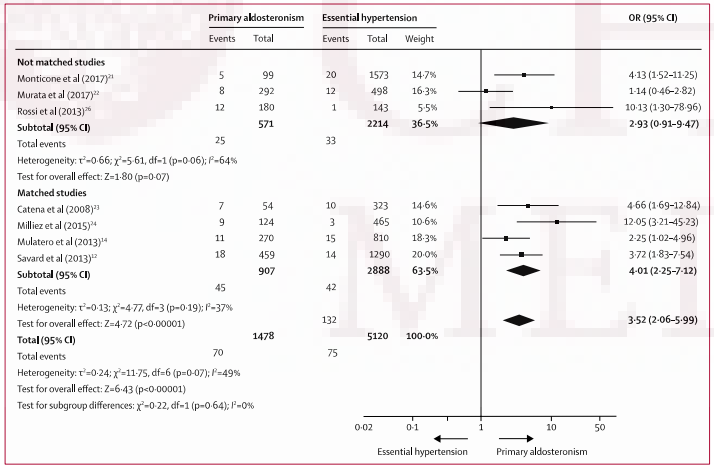
Reasons for lower detection of PA

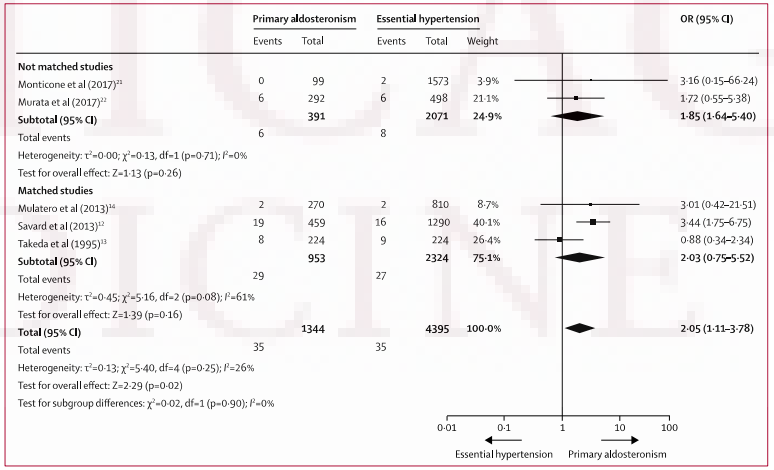
- Low screening for PA, only hypokalemic hypertensive patients are screened
- Documented existence of cases where the only clue is low plasma renin
- Pulsatile secretion of aldosterone that is influenced by salt intake
- Variable sensitivity of the kidney and vasculature to aldosterone across ethnicities, African-American are very sensitive to aldosterone

Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis







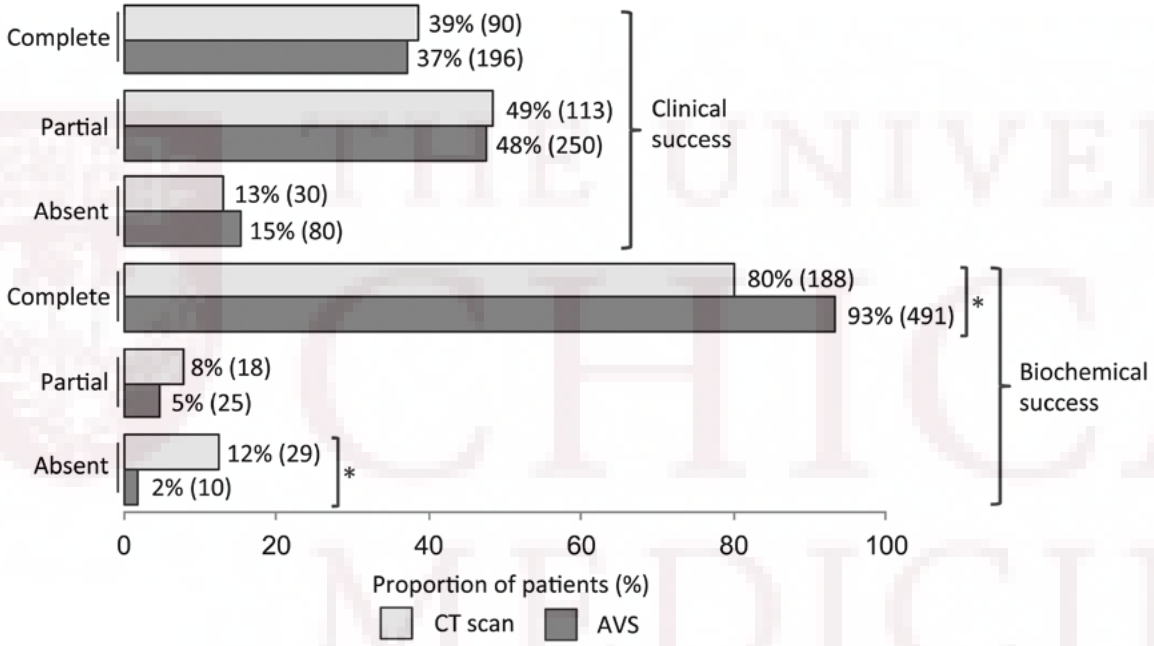


Adrenal vein sampling versus CT scan to determine treatment in primary aldosteronism: an outcome-based randomised diagnostic trial

- No significant difference in intensity of antihypertensive medications at 1 year. Target blood pressure was achieved in 42% in CT-based and 45% in AVS groups (p=0.82)
- Biochemical cure was achieved at a similar proportion between groups (80% vs 89%, p=0.25)

CT vs AVS

- Based on retrospective data from 18 internationally distributed centers



Diagnosis by CT was associated with decreased likelihood of complete biochemical remission compared to AVS (OR 0.28; 0.16-0.50; p<0.001)

Outcomes after adrenalectomy for unilateral primary aldosteronism: an international consensus on outcome measures and analysis of remission rates in an international cohort

Complete clinical success
Normal blood pressure* without the aid of antihypertensive medication

Partial clinical success
The same blood pressure as before surgery† with less antihypertensive medication‡§ or a reduction in blood pressure with either the same amount or less antihypertensive medication

Absent clinical success
Unchanged or increased blood pressure† with either the same amount or an increase in antihypertensive medication‡¶

Complete biochemical success
Correction of hypokalaemia‖ (if present pre-surgery) and normalisation of the aldosterone-to-renin ratio**; in patients with a raised aldosterone-to-renin ratio post surgery, aldosterone secretion should be suppressed in a confirmatory test†††‡‡

Partial biochemical success
Correction of hypokalaemia‖ (if present pre-surgery) and a raised aldosterone-to-renin ratio** with one or both of the following (compared with pre-surgery): ≥50% decrease in baseline plasma aldosterone concentration; or abnormal but improved post-surgery confirmatory test result‡‡

Absent biochemical success
Persistent hypokalaemia‖ (if present pre-surgery) or persistent raised aldosterone-to-renin ratio**, or both, with failure to suppress aldosterone secretion with a post-surgery confirmatory test‡‡

Outcome assessment
Outcome assessment should first be done in the 3 months post surgery, but final outcome should be assessed at 6–12 months

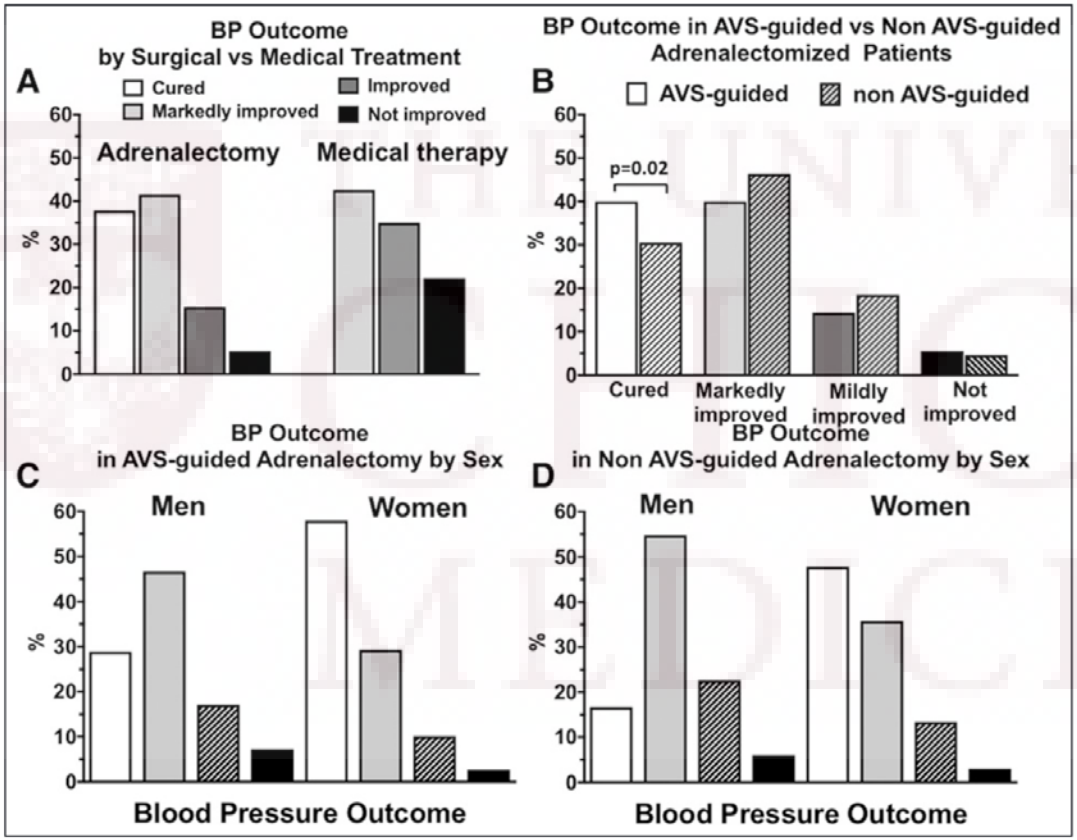
Annual reassessment
Outcome should be reassessed annually§§

Complete clinical success in 37% (17-62%), complete biochemical success averaged 94%. Female sex and younger age were independently associated with clinical success

Williams et al. Lancet Diabetes Endocrinol. 2017

AVIS-2 study: clinical benefits of AVS

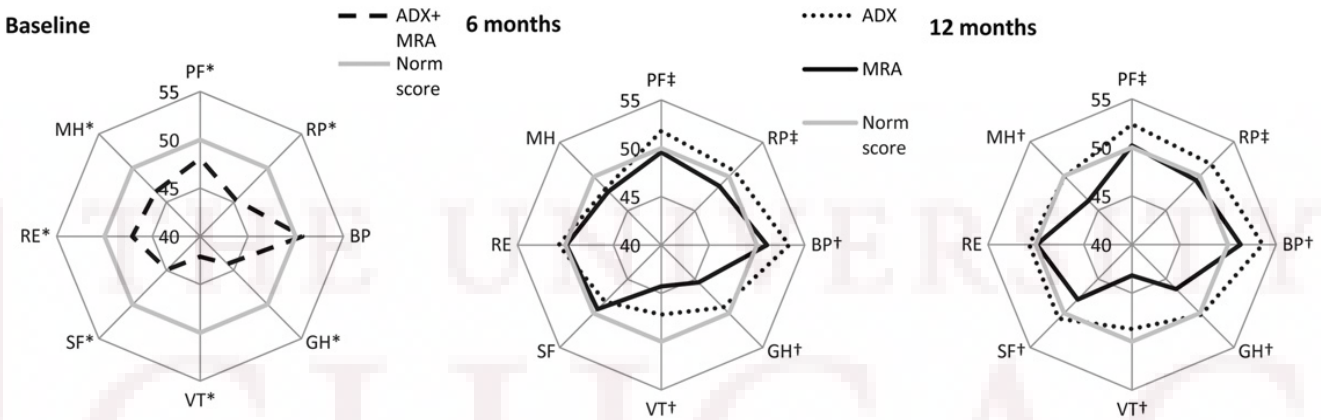
- Data of 1625 p. in 19 tertiary centers

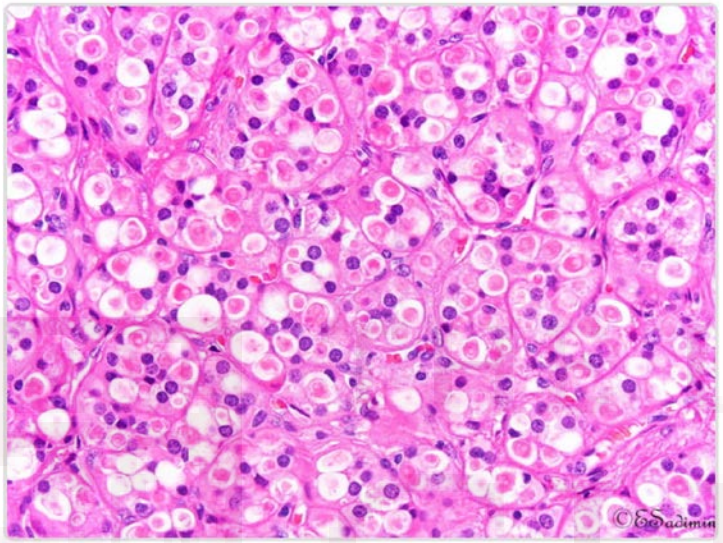


Follow up

- Underwent Right adrenalectomy on 9/21/2017
- Pathology showed nodular adrenocortical hyperplasia
- Aldosterone on 9/22/17 was < 4.0 ng/dL
- Over the following 3 months, diltiazem discontinued, started on amlodipine/Olmesartan 10/40, remained stable until last year when BP 150/90.
- Weight stable, HbA1C 4.8, Cr stable 1.4, GFR 52, normal electrolytes (K 4.3)
- Added Indapamide 2.5 mg

Treatment and QoL





Thank you!