

SCREENING OF DIABETIC PATIENTS USING U500 INSULIN UNCOVERS A HIGH PERCENTAGE OF UNDIAGNOSED HYPERCORTISOLISM CONSISTENT WITH CUSHING SYNDROME



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ABSTRACT

Background: Studies screening patients with diabetes for hypercortisolism indicate that 2% to 10% of patients have undiagnosed Cushing syndrome (CS), and those authors conclude that screening of all diabetics for CS is prohibitively expensive. However, patients with type 2 diabetes (T2DM) requiring concentrated insulin (Humulin R U500, Lilly) have severe insulin resistance and hyperglycemia that may be a result of undiagnosed and uncontrolled hypercortisolism. To our knowledge, this is the first report on screening patients using U500 insulin for CS.

Methods: In a community endocrine practice, 34 patients with T2DM using U500 insulin were randomly screened for excess cortisol secretion using an overnight dexamethasone suppression test (DST), late-night salivary cortisol (LNSC), and 24-hour urinary free cortisol (UFC) test.

Results: Out of the 34 patients screened, 21 (62%) had a clinical presentation and/or biochemical indicators suggesting hypercortisolism, prompting radiologic imaging. 9 patients had either adrenal hyperplasia or adrenal adenoma(s).

Conclusion: In this community practice, 62% of screened patients using concentrated U500 insulin were found to have underlying hypercortisolism. The U500 insulin population appears enriched with patients who have undiagnosed hypercortisolism, and this group would benefit from testing and treatment.

INTRODUCTION

- 2% to 10% of patients with diabetes have been shown to have underlying hypercortisolism¹⁻³
- Thus, the benefit of routine screening of patients with diabetes for hypercortisolism has been questioned¹

- Patients requiring concentrated U500 insulin are highly insulin resistant⁴
- The prevalence of hypercortisolism in this population is unknown

HYPOTHESIS

- Underlying, undiagnosed hypercortisolism is prevalent in diabetic patients with severe insulin resistance, requiring treatment with concentrated U500 insulin

METHODS

- Patients with type 2 diabetes (T2DM) using concentrated U500 insulin from this community practice were identified using electronic medical records and were randomly selected for hypercortisolism screening during a 1-year period
- Patients were initially evaluated using the 1-mg dexamethasone suppression test (DST); if they were found to be unsuppressed (>1.8 µg/dL), additional late-night salivary cortisol (LNSC) and urinary free cortisol (UFC) were measured
- If patients had two positive biochemical tests or if their presentation triggered a high index of suspicion, they were referred for imaging

RESULTS

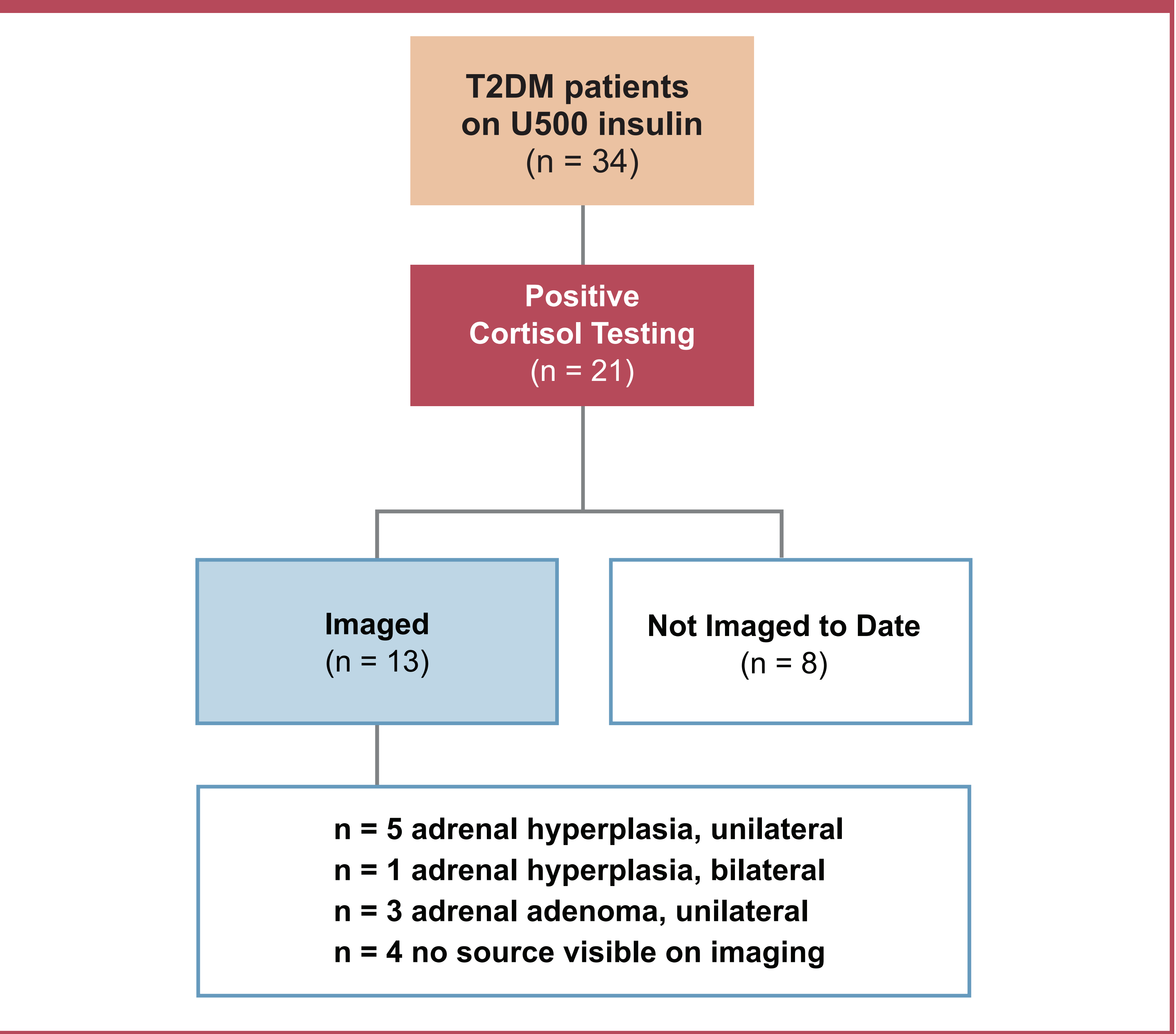
- 34 patients with T2DM who were using concentrated U500 insulin were screened for hypercortisolism (Table 1)
 - Screening was performed using DST, LNSC, and UFC
 - 21 patients had a biochemical indicator suggesting hypercortisolism, prompting radiologic imaging (Table 2)
 - Of those 21 patients, 13 underwent imaging (Figure 1)
 - 9/13 patients had radiologically confirmed hyperplasia or adenoma
 - 13 patients did not have a biochemical indicator suggesting hypercortisolism

Table 1. Demographic Information^a

	Patients on U500 Insulin (n=34)
Female (%)	62
Age, yrs	57 (17-73)
Weight, pounds	272 (165.5-442)
A1C, %	8.6 (6.3-13.6)
Fasting blood glucose, mg/dL	197.5 (101-468)
TDD insulin, U	179 (40-420)

^aExcept for the percentage of female patients, each value is a mean (range). A1C, glycated hemoglobin; TDD, total daily dose.

Figure 1. T2DM Patients Screened for Hypercortisolism



T2DM, type 2 diabetes.

Table 2. Demographics and Screening of U500 Insulin Patients With Elevated Cortisol

Sex M/F	Age, Yrs	Wt, lbs	FBG, mg/dL	A1C, %	U500, IU/d	Imaging Source
Patients Imaged						
F	70	177.8	184	6.3	260	UAH
F	63	311	234	8.8	170	UAH
M	60	294.4	239	10.1	140	UAH
F	68	195	153	6.3	80	UAH
F	68	188	155	7.3	75	UAH
F	67	188	262	10.3	420	UAA
F	70	303.8	164	10.8	140	UAA
F	68	199	165	7.7	115	UAA
F	66	224.2	468	13.6	130	BAH
M	46	442.2	182	7.2	298	NSV
M	58	371.4	200	8.6	240	NSV
F	55	209.8	108	7.0	235	NSV
F	37	270	268	7.6	90	NSV
Not Imaged to Date						
M	55	324.2	149	9.2	249	-
F	45	353	300	8.7	115	-
M	66	320.8	101	6.5	260	-
M	61	313.2	157	6.7	240	-
M	59	320	150	7.4	190	-
M	70	339.6	189	12.5	160	-
M	68	254	233	9.8	120	-
F	56	385.6	229	8.9	270	-

A1C, glycated hemoglobin; BAH, bilateral adrenal hyperplasia; FBG, fasting blood glucose; NSV, no source visible on imaging; UAA, unilateral adrenal adenoma; UAH, unilateral adrenal hyperplasia.

CONCLUSION

Hypercortisolism appears to be prevalent in the population of patients requiring concentrated U500; the majority of these patients appear to have an adrenal etiology of hypercortisolism.

REFERENCES

- Catargi B, et al. *J Clin Endocrinol Metab.* 2003;88:5808-13.
- Leibowitz O, et al. *Clin Endocrinol.* 1996;44:717-22.
- Chiodini I, et al. *Eur J Endocrinol.* 2005;153:837-44.
- Lamos EM, et al. *Ther Clin Risk Manag.* 2016;12:389-400.

DISCLOSURES

JWM: Speaker, Corcept Therapeutics.
JJS: Employee, Corcept Therapeutics.

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