Prevalence of Endogenous Hypercortisolism in Individuals With Resistant Hypertension Stratified by Kidney Function: Results From the MOMENTUM Study

Ralph A. DeFronzo,[1] Vanita R. Aroda,[2] Jan N. Basile,[3] Deepak L. Bhatt,[4] Michael J. Bloch,[5] Matthew Budoff,[6] Robert S. Busch,[7] John B. Buse,[8] Dianne S. Cheung,[9] Bradley Eilerman,[10] Yehuda Handelsman,[11] Mark Kipnes,[12] Luke Laffin,[13] John C. Parker,[14] Jorge Plutzky,[15] Julio Rosenstock,[16] Lance A. Sloan,[17] Pam R. Taub,[18] Guillermo E. Umpierrez,[19] Tina K. Schlafly,[20] Yuan Tian,[20] Daniel Einhorn[20]

[1]UT Health Science Center, San Antonio, TX; [2]Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [3]Medical University of South Carolina, Charleston, SC; [4]Mount Sinai Fuster Heart Hospital, Icahn School of Medicine at Mount Sinai, New York, NY; [5]Renown Institute for Heart and Vascular Health, Reno, NV; [6]Lundquist Institute for Biomedical Innovation at Harbor UCLA Medical Center, West Carson, CA; [7]Albany Medical College, Albany, NY; [8]University of North Carolina at Chapel Hill, Chapel Hill, NC; [9]University of California Los Angeles, Los Angeles, CA; [10]St. Elizabeth Physicians, Covington, KY; [11]The Metabolic Institute of America, Tarzana, CA; [12]Diabetes & Glandular Disease Clinic, San Antonio, TX; [13]Cleveland Clinic, Cleveland, OH; [14]Accellacare Research, Wilmington, NC; [15]Brigham and Women's Hospital, Division of Cardiovascular Medicine, Boston, MA; [16]University of Texas Southwestern Medical Center, Dallas, TX; [17]Texas Institute for Kidney and Endocrine Disorders, Lufkin, TX; [18]University of California-San Diego School of Medicine, La Jolla, CA; [19]Emory School of Medicine, Emory University, Atlanta, GA; [20]Corcept Therapeutics Incorporated, Redwood City, CA

Abstract 0055

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SUMMARY AND CONCLUSIONS

- The MOMENTUM study, involving >1,000 participants, found a hypercortisolism (HC) prevalence of 27.3% in resistant hypertension (rHTN). HC was defined as post-dexamethasone suppression test (DST) cortisol >1.8 µg/dL
- In participants with estimated glomerular filtration rate (eGFR) 60–89 mL/min/1.73 m^2 and eGFR ≥90 mL/min/1.73 m^2, the prevalence was 24.0% and 22.2%, respectively
- Participants with eGFR <60 mL/min/1.73 m^2 had a higher frequency of post-DST cortisol >1.8 µg/dL. This study could not determine the extent to which this association is due to methodologic issues with the cortisol measurement or whether it reflects a true disruption in the hypothalamic-pituitary-adrenal axis
  - Many adverse effects associated with the uremic state (eg, insulin resistance, cardiometabolic complications, or bone disease) are also characteristic of HC, suggesting a potential pathophysiologic connection
  - The assay used to measure cortisol was not tested for the potential effect of low eGFR
  - Adrenocorticotropic hormone levels were similar across eGFR groups
- Urine albumin-to-creatinine ratio trended higher in participants with HC
- A trend toward higher chronic kidney disease progression risk was also observed in participants with HC
- These results support the need for targeted HC screening in people with rHTN

ABSTRACT

MOMENTUM (NCT06829537), the first US-based trial assessing endogenous hypercortisolism (HC) in individuals with resistant hypertension (rHTN), found an HC prevalence of 27.3%. Chronic kidney disease (CKD) is a cause and consequence of rHTN; however, the relationship between CKD and HC is not well characterized in rHTN. We performed an analysis of participants in MOMENTUM by renal function to evaluate this relationship. MOMENTUM was an observational study that screened adults with rHTN (per American Heart Association criteria) using the 1-mg overnight dexamethasone suppression test (DST; HC=post-DST cortisol >1.8 µg/dL). Individuals with conditions that could confound DST interpretation were excluded. Historical estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 was exclusionary, but eGFR assessed at baseline was used for this analysis. The eGFR subgroups analyzed were <45, 45–59, and ≥60 mL/min/1.73 m^2. Of the 1,086 MOMENTUM participants, 140 (12.9%), 203 (18.7%), and 743 (68.4%) had an eGFR <45, 45–59, ≥60 mL/min/1.73 m^2, respectively, and the HC prevalence in these subgroups was 43.6%, 30.0%, and 23.6%, respectively. In participants with HC, mean eGFR was lower (P<0.0001) and mean urine albumin-to-creatinine ratio trended higher (P=0.097) compared to those without HC. Similarly, the frequency of HC was higher in the lower eGFR subgroups and higher CKD progression risk categories (P<0.0001 for any difference across groups). MOMENTUM showed that individuals with rHTN and reduced kidney function have an elevated risk of HC, supporting the need for targeted screening in this high-risk population.

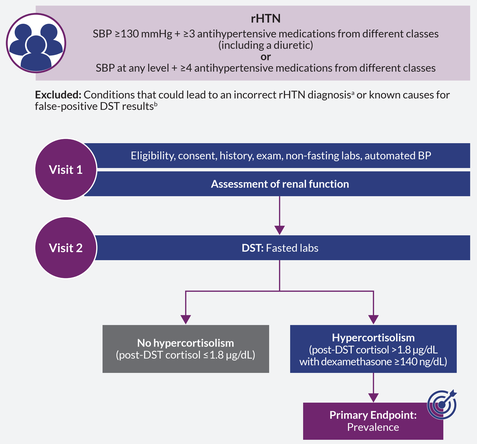
BACKGROUND AND OBJECTIVE

- MOMENTUM (NCT06829537), the first US-based trial to assess hypercortisolism (HC) prevalence in individuals with resistant hypertension (rHTN), found an HC prevalence of 27.3% based on the 1-mg overnight dexamethasone suppression test (DST)[1]
- Chronic kidney disease (CKD) is a cause and consequence of rHTN[2]
  - CKD is more common in individuals with rHTN than in those with hypertension that is not treatment resistant, and rHTN is associated with worse renal outcomes, including increased risk of CKD progression and end-stage renal disease[3,4]
- Uremia is well characterized as an insulin-resistant state, and HC also causes insulin resistance[5,6]
- Whether there is a relationship between decreased estimated glomerular filtration rate (eGFR) and insulin resistance in individuals with HC is not fully understood and requires further study
- In the presence of reduced eGFR, there is a potential for cross-reactivity of cortisol metabolites in the DST immunoassay and a prolongation of cortisol half-life. The quantitative extent of that impact has been explored but not conclusively established[7]
- We analyzed the frequency of post-DST cortisol >1.8 µg/dL and characteristics of participants in MOMENTUM by eGFR

METHODS

- MOMENTUM was a US, multicenter, prospective, observational study that screened adults aged ≥18 years with rHTN per American Heart Association criteria using the 1-mg overnight DST after causes of "false-positive" testing were excluded (**Figure 1**)

Figure 1. MOMENTUM Study Schema



[a]Including white-coat hypertension and nonadherence to antihypertensives.
[b]Including use of oral contraceptive pills; excessive alcohol consumption; severe untreated sleep apnea; severe psychiatric, medical, or surgical illness; night-shift work; hemodialysis/end-stage renal disease.
BP, blood pressure; DST, dexamethasone suppression test; rHTN, resistant hypertension; SBP, systolic blood pressure.

- Cortisol was measured by electrochemiluminescence immunoassay (cobas, MedPace Reference Laboratories, Cincinnati, OH)
- Historical eGFR <30 mL/min/1.73 m^2 was exclusionary, but eGFR assessed at baseline was used for the analysis

RESULTS

- Of the 1,086 MOMENTUM participants, 12.9%, 18.7%, and 68.4% had an eGFR <45[a], 45–59, ≥60 mL/min/1.73 m^2, respectively (**Table 1**)

Table 1. Baseline Demographics and Characteristics Across eGFR Subgroups

	eGFR <45 mL/min/1.73 m^2 (n=140)[a]	eGFR 45–59 mL/min/1.73 m^2 (n=203)	eGFR ≥60 mL/min/1.73 m^2 (n=743)
Age, years, mean (SD)	69.5 (10.2)	69.9 (9.4)	63.3 (10.6)
Female, n (%)	62 (44.3)	113 (55.7)	380 (51.1)
Race, n (%)			
Asian	2 (1.4)	11 (5.4)	22 (3.0)
Black or African American	42 (30.0)	63 (31.0)	291 (39.2)
White	93 (66.4)	126 (62.1)	401 (54.0)
Other[b]	3 (2.1)	3 (1.5)	29 (3.9)
Ethnicity not Hispanic/Latino, n (%)	105 (75.0)	166 (81.8)	524 (70.5)
Weight, kg, mean (SD)	92.2 (21.5)	93.2 (23.6)	95.1 (24.2)
BMI, kg/m^2, mean (SD)	31.8 (6.1)	33.3 (7.3)	33.3 (7.1)
Waist circumference, cm, mean (SD) [n]	109.9 (17.9) [138]	108.3 (16.9) [200]	108.5 (17.3) [739]
SBP, mmHg, mean (SD)	137.4 (18.8)	137.8 (19.7)	141.9 (16.7)
DBP, mmHg, mean (SD)	79.1 (12.2)	79.9 (12.9)	86.1 (11.9)

[a]35/1,086 (3.2%) had eGFR <30 mL/min/1.73 m^2 at visit 1, despite having historical eGFR ≥30 mL/min/1.73 m^2, which was the basis for eligibility. Unless presented separately, these participants are included in the eGFR <45 mL/min/1.73 m^2 category. [b]Race "Other" includes Aboriginal Australian, American Indian/Alaskan Native, Native Hawaiian or Pacific Islander, multiple, other, and not disclosed.
BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; SD, standard deviation.

- Post-DST adrenocorticotropic hormone (ACTH) levels were generally similar across eGFR subgroups in the overall population and among participants with HC; among participants with HC, morning ACTH values were also broadly comparable across eGFR subgroups (**Table 2**)
- Similar to Garg et al, higher post-DST cortisol was observed in participants with reduced renal function, although the mean values in each group were higher compared with Garg et al[5]

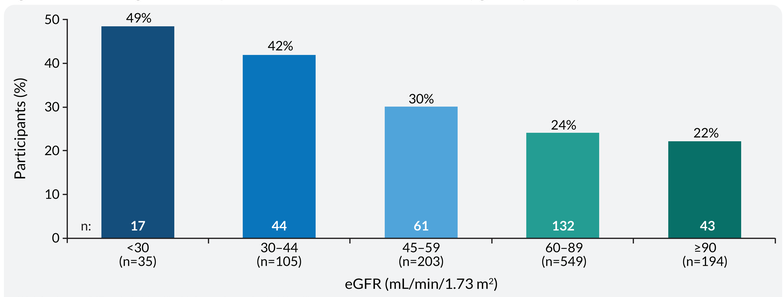
Table 2. Post-DST Cortisol and ACTH Levels Across eGFR Subgroups

	eGFR <45 mL/min/1.73 m^2 (n=140)	eGFR 45–59 mL/min/1.73 m^2 (n=203)	eGFR ≥60 mL/min/1.73 m^2 (n=743)
Post-DST cortisol, µg/dL, mean (SD) [n]			
Overall	2.4 (2.5) [140]	2.1 (2.3) [203]	1.9 (2.2) [743]
HC	3.9 (3.3) [61]	4.1 (3.4) [61]	4.4 (3.5) [175]
Post-DST ACTH, ng/L, mean (SD) [n]			
Overall	5.3 (5.8) [140]	4.9 (5.0) [203]	4.9 (5.8) [739]
HC	7.3 (8.3) [61]	7.5 (8.3) [61]	8.5 (9.1) [175]
8AM ACTH in participants with HC, ng/L, mean (SD) [n]	23.3 (15.4) [55]	18.8 (11.4) [51]	21.9 (11.7) [169]

ACTH, adrenocorticotropic hormone; DST, dexamethasone suppression test; eGFR, estimated glomerular filtration rate; HC, hypercortisolism; SD, standard deviation.

- HC prevalence was higher in the subgroups with lower eGFR (**Figure 2**)

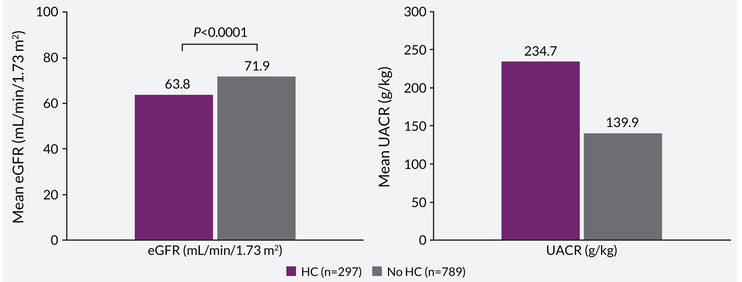
Figure 2. Percentage of Participants With Post-DST Cortisol >1.8 µg/dL by Kidney Function



HC defined as post-DST cortisol >1.8 µg/dL with dexamethasone level ≥140 ng/dL.
DST, dexamethasone suppression test; eGFR, estimated glomerular filtration rate; HC, hypercortisolism.

- In participants with HC, mean eGFR was lower (P<0.0001) and mean urine albumin-to-creatinine ratio trended higher (P=0.097) compared with those without HC (**Figure 3**)

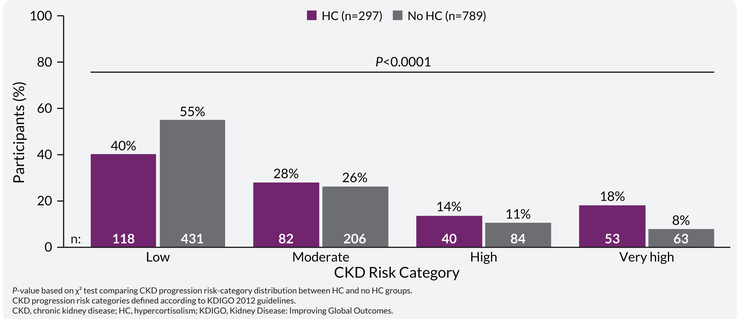
Figure 3. Markers of Kidney Function by Hypercortisolism Status



P-values based on t-test.
eGFR, estimated glomerular filtration rate; HC, hypercortisolism; UACR, urine albumin-to-creatinine ratio.

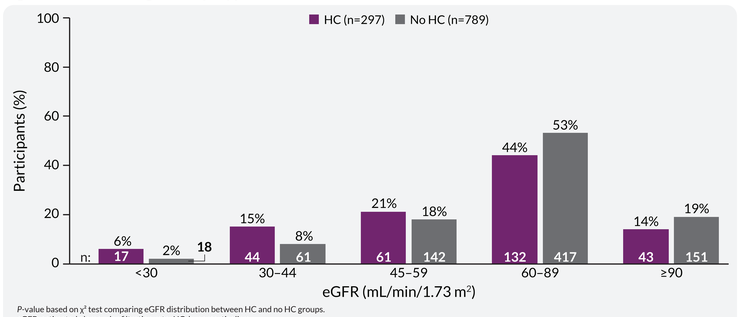
- Similarly, HC frequency was higher among individuals with higher CKD progression risk and in those with lower eGFR (**Figures 4 and 5**)

Figure 4. CKD Progression Risk Categories by Hypercortisolism Status



P-value based on χ^2 test comparing CKD progression risk-category distribution between HC and no HC groups.
CKD progression risk categories defined according to KDIGO 2012 guidelines.
CKD, chronic kidney disease; HC, hypercortisolism; KDIGO, Kidney Disease: Improving Global Outcomes.

Figure 5. eGFR Categories by Hypercortisolism Status



P-value based on χ^2 test comparing eGFR distribution between HC and no HC groups.
eGFR, estimated glomerular filtration rate; HC, hypercortisolism.

References

1. Bhatt DL, et al. Presented at: American College of Cardiology Annual Meeting; March 28–30, 2026; New Orleans, LA. **2.** Carey RM, et al. *Hypertension*. 2018;72(5):e53–e90. **3.** Daugherty SL, et al. *Circulation*. 2012;125(13):1635–1642. **4.** Sim JJ, et al. *Kidney Int*. 2015;88(3):622–632. **5.** DeFronzo RA, et al. *J Clin Invest*. 1978;62(2):425–435. **6.** DeFronzo RA, Auchus RJ. *Diabetes*. 2025;74(12):2168–2178. **7.** Garg R, et al. *J Endocr Soc*. 2024;8(3):bvae002.

Acknowledgments

The authors want to thank all those who participated in this study: the study participants and their families, the investigators, and the sponsor team. This study is sponsored by Corcept Therapeutics Incorporated. Medical writing assistance was provided by R&R Healthcare Communications.

Presenter Disclosure

Ralph A. DeFronzo reports: advisory board with AstraZeneca, Novo Nordisk, Boehringer Ingelheim, Intarcia, Renalytix, and Corcept Therapeutics; research support from Boehringer Ingelheim and AstraZeneca; speaker's bureau with AstraZeneca.

Presented at: 10th Annual Heart in Diabetes; June 19–21, 2026