

Comorbid Diabetes Alters Inflammatory and Cardiometabolic Biomarkers in Persons with Heart Failure

Julia Kamara, Erica Davis, PhD, RN, Melinda K Higgins, PhD, Sandra B Dunbar, PhD, RN, FAAN, FAHA, FPCNA, and Brittany Butts, PhD, RN

PCNA 30th Annual Symposium, April 18th, Orlando, Florida

Background A staggering 47.1% of persons diagnosed with HF have comorbid diabetes, intensifying the risk of mortality. Despite higher rates of both HF and diabetes among African Americans, the prevalence of comorbid HF and diabetes among **this population** is not known. Pathologic pathways linking these two conditions **are not well understood**. The **purpose** of this investigation is to **compare** biomarkers associated with cellular pathways in individuals **living with** HF with and without diabetes.

Methods Black adults living with HF (N=41) were enrolled in this pilot study. Cardiometabolic and inflammatory biomarkers were measured via multiplex immunoassay. T tests were used to identify group differences between persons with HF with comorbid diabetes (n=15) and those without (n=26). Effect sizes were calculated using Cohen's d and identified as small (d = 0.2), medium (d = 0.5), and large (d = 0.8).

Results The mean age was 57±11 years, 66% were female, and mean LVEF was 33±14%. Persons with diabetes had higher levels of biomarkers involved in regulation of cell proliferation and differentiation (p=.03, d=.716), inflammation and immune regulation (p=.011, d=.868), anticoagulation (p=.048, d=.574), neural growth and protection (p=.029, d=.734), and vascular wall proliferation and protection (p=.019, d=.791) as compared to those without diabetes.

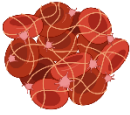
Conclusions In a population of African American persons living with HF, comorbid diabetes was associated with significant differences, with medium to large effect sizes, in biomarkers implicated in multiple physiologic processes, including immune, cellular, and vascular functions. More work understanding the pathophysiologic implications of multimorbidity in HF is needed.

Implications for practice Treatment approaches should consider the **physiologic** pathways influenced by comorbid diabetes in individuals with HF for more targeted and effective interventions. Nurses can play a further role in better understanding symptoms that may be influenced by these pathways in assessing and treating persons with HF and comorbid diabetes.

Contact: Julia Kamara, Undergraduate Research Assistant, Emory University, julia.kamara@emory.edu

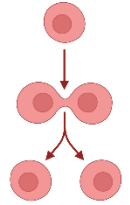
Central Figure

Cardiometabolic biomarkers and dyspnea symptoms are higher in Black adults with heart failure + type II diabetes as compared to those with heart failure alone.



Anticoagulation

Plasma serine protease inhibitor
Protein C



Cell Proliferation and Differentiation

Cadherin-1
Oncostatin M
Insulin-like growth factor-binding protein 6
Hepatocyte growth factor
Peptidyl-glycine alpha-amidating monooxygenase



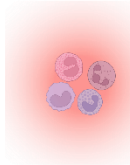
Vascular Wall Proliferation and Protection

Collagen alpha-1(XVIII) chain
Vasorin



Neural Growth and Protection

Carnosine dipeptidase 1
Lithostathine-1-alpha



Inflammation and Immune Regulation

Complement C1q tumor necrosis factor-related protein 1
Leukocyte immunoglobulin-like receptor subfamily B member 1
Complement factor H-related protein 5
Neutrophil defensin 1
Chemokine ligand 9



Dyspnea Severity

PROMIS Dyspnea Severity

References:

- Allen, L. A., Stevenson, L. W., Grady, K. L., Goldstein, N. E., Matlock, D. D., Arnold, R. M., Cook, N. R., Felker, G. M., Francis, G. S., Hauptman, P. J., Havranek, E. P., Krumholz, H. M., Mancini, D., Riegel, B., & Spertus, J. A. (2012). Decision making in advanced heart failure: a scientific statement from the American Heart Association. *Circulation*, *125*(15), 1928-1952. <https://doi.org/10.1161/CIR.0b013e31824f2173>
- Anand, I. S., Latini, R., Florea, V. G., Kuskowski, M. A., Rector, T., Masson, S., Signorini, S., Mocarelli, P., Hester, A., Glazer, R., & Cohn, J. N. (2005). C-Reactive Protein in Heart Failure. *Circulation*, *112*(10), 1428-1434. <https://doi.org/10.1161/CIRCULATIONAHA.104.508465>
- Baxter, R. C. (2023). Signaling Pathways of the Insulin-like Growth Factor Binding Proteins. *Endocrine Reviews*, *44*(5), 753-778. <https://doi.org/10.1210/edrv/bnad008>
- Butts, B., Alford, T., Brewster, G., Carlson, N., Coleman, E., Davis, E., Ferranti, E., Kimble, L. P., Narapareddy, L., Wells, J., & Yang, I. (2022). Adaptation of Metabolomics and Microbiomic Research Protocols During the COVID-19 Pandemic. *Nursing Research*, *71*(2), 128-137. <https://doi.org/10.1097/nnr.0000000000000574>
- Castillo, E. C., Vázquez-Garza, E., Yee-Trejo, D., García-Rivas, G., & Torre-Amione, G. (2020). What Is the Role of the Inflammation in the Pathogenesis of Heart Failure? *Current Cardiology Reports*, *22*(11), 139. <https://doi.org/10.1007/s11886-020-01382-2>
- Charlson, M., Pompei, P., Ales, K., & MacKenzie, C. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Diseases*, *40*(5), 373-383.
- Deng, W., Ednie, A. R., Qi, J., & Bennett, E. S. (2016). Aberrant sialylation causes dilated cardiomyopathy and stress-induced heart failure. *Basic Research in Cardiology*, *111*(5), 57. <https://doi.org/10.1007/s00395-016-0574-1>
- Dunlay, S. M., Givertz, M. M., Aguilar, D., Allen, L. A., Chan, M., Desai, A. S., Deswal, A., Dickson, V. V., Kosiborod, M. N., Lekavich, C. L., McCoy, R. G., Mentz, R. J., & Piña, I. L. (2019). Type 2 Diabetes Mellitus and Heart Failure: A Scientific Statement From the American Heart Association and the Heart Failure Society of America: This statement does not represent an update of the 2017 ACC/AHA/HFSA heart failure guideline update. *Circulation*, *140*(7), e294-e324. <https://doi.org/10.1161/cir.0000000000000691>
- Elendu, C., Amaechi, D. C., Elendu, T. C., Ashna, M., Ross-Comptis, J., Ansong, S. O., Egbunu, E. O., Okafor, G. C., Jingwa, K. A., Akintunde, A. A., Ogah, C. M., Edeko, M. O., Ibitoye, A. V., Ogunseye, M. O., Alakwe-Ojimba, C. E., Omeludike, E. K., Oguine, C. A., Afuh, R. N., Olawuni, C. A., . . . Aborisade, O. (2023). Heart failure and diabetes: Understanding the bidirectional relationship. *Medicine (Baltimore)*, *102*(37), e34906. <https://doi.org/10.1097/md.00000000000034906>
- Gene [Internet]*. (2004, 2024). National Library of Medicine (US), National Center for Biotechnology Information. <https://www.ncbi.nlm.nih.gov/gene/>

Haw, J. S., Shah, M., Turbow, S., Egeolu, M., & Umpierrez, G. (2021). Diabetes Complications in Racial and Ethnic Minority Populations in the USA. *Current Diabetes Reports*, 21(1), 2. <https://doi.org/10.1007/s11892-020-01369-x>

Health Measures. (2023, 11/3/2023). *PROMIS score cut point*. <https://www.healthmeasures.net/score-and-interpret/interpret-scores/promis/promis-score-cut-points>

Huang, Y., & Kyriakides, T. R. (2020). The role of extracellular matrix in the pathophysiology of diabetic wounds. *Matrix Biol Plus*, 6-7, 100037. <https://doi.org/10.1016/j.mbplus.2020.100037>

Jeon, Y. K., Kim, M. R., Huh, J. E., Mok, J. Y., Song, S. H., Kim, S. S., Kim, B. H., Lee, S. H., Kim, Y. K., & Kim, I. J. (2011). Cystatin C as an early biomarker of nephropathy in patients with type 2 diabetes. *Journal of Korean Medical Science*, 26(2), 258-263. <https://doi.org/10.3346/jkms.2011.26.2.258>

Kaburagi, T., Kizuka, Y., Kitazume, S., & Taniguchi, N. (2017). The Inhibitory Role of α 2,6-Sialylation in Adipogenesis. *Journal of Biological Chemistry*, 292(6), 2278-2286. <https://doi.org/10.1074/jbc.M116.747667>

Kosmas, C. E., Bousvarou, M. D., Kostara, C. E., Papakonstantinou, E. J., Salamou, E., & Guzman, E. (2023). Insulin resistance and cardiovascular disease. *Journal of International Medical Research*, 51(3), 3000605231164548. <https://doi.org/10.1177/03000605231164548>

Laiteerapong, N., Huang, E. S., & Chin, M. H. (2011). Prioritization of care in adults with diabetes and comorbidity. *Annals of the New York Academy of Sciences*, 1243, 69-87. <https://doi.org/10.1111/j.1749-6632.2011.06316.x>

Lewsey, S. C., & Breathett, K. (2021). Racial and ethnic disparities in heart failure: current state and future directions. *Current Opinion in Cardiology*, 36(3), 320-328. <https://doi.org/10.1097/hco.0000000000000855>

Li, W., Zhao, J., Zhu, L. L., & Peng, Y. F. (2022). Serum vitamin B12 levels and glycemic fluctuation in patients with type 2 diabetes mellitus. *Therapeutic Advances in Endocrinology and Metabolism*, 13, 20420188221102800. <https://doi.org/10.1177/20420188221102800>

Liu, C., He, L., Li, Y., Yang, A., Zhang, K., & Luo, B. (2023). Diabetes risk among US adults with different socioeconomic status and behavioral lifestyles: evidence from the National Health and Nutrition Examination Survey. *Front Public Health*, 11, 1197947. <https://doi.org/10.3389/fpubh.2023.1197947>

Merkler, D. J., Hawley, A. J., Eipper, B. A., & Mains, R. E. (2022). Peptidylglycine α -amidating monooxygenase as a therapeutic target or biomarker for human diseases. *British Journal of Pharmacology*, 179(13), 3306-3324. <https://doi.org/10.1111/bph.15815>

Mir, F. A., Abdesselem, H. B., Cyprian, F., Iskandarani, A., Doudin, A., Samra, T. A., Alkasem, M., Abdalhakam, I., Taheri, S., & Abou-Samra, A. B. (2023). Inflammatory protein signatures in individuals with obesity and metabolic syndrome. *Scientific Reports*, 13(1), 22185. <https://doi.org/10.1038/s41598-023-49643-8>

- Morris, A., Shah, K. S., Enciso, J. S., Hsich, E., Ibrahim, N. E., Page, R., & Yancy, C. (2022). The Impact of Health Care Disparities on Patients With Heart Failure. *Journal of Cardiac Failure*, 28(7), 1169-1184. <https://doi.org/10.1016/j.cardfail.2022.04.008>
- Nayak, A., Hicks, A. J., & Morris, A. A. (2020). Understanding the Complexity of Heart Failure Risk and Treatment in Black Patients. *Circulation: Heart Failure*, 13(8), e007264. <https://doi.org/10.1161/circheartfailure.120.007264>
- Peek, M. E., Cargill, A., & Huang, E. S. (2007). Diabetes health disparities: a systematic review of health care interventions. *Medical Care Research and Review*, 64(5 Suppl), 101s-156s. <https://doi.org/10.1177/1077558707305409>
- Sauerhöfer, S., Yuan, G., Braun, G. S., Deinzer, M., Neumaier, M., Gretz, N., Floege, J., Kriz, W., van der Woude, F., & Moeller, M. J. (2007). L-carnosine, a substrate of carnosinase-1, influences glucose metabolism. *Diabetes*, 56(10), 2425-2432. <https://doi.org/10.2337/db07-0177>
- Tangvarasittichai, S. (2015). Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. *World Journal of Diabetes*, 6(3), 456-480. <https://doi.org/10.4239/wjd.v6.i3.456>
- Tello-Montoliu, A., Patel, J. V., & Lip, G. Y. (2006). Angiogenin: a review of the pathophysiology and potential clinical applications. *Journal of Thrombosis and Haemostasis*, 4(9), 1864-1874. <https://doi.org/10.1111/j.1538-7836.2006.01995.x>
- Tousoulis, D., Oikonomou, E., Siasos, G., & Stefanadis, C. (2014). Diabetes Mellitus and Heart Failure. *Eur Cardiol*, 9(1), 37-42. <https://doi.org/10.15420/ecr.2014.9.1.37>
- Tsalamandris, S., Antonopoulos, A. S., Oikonomou, E., Papamikroulis, G. A., Vogiatzi, G., Papaioannou, S., Deftereos, S., & Tousoulis, D. (2019). The Role of Inflammation in Diabetes: Current Concepts and Future Perspectives. *Eur Cardiol*, 14(1), 50-59. <https://doi.org/10.15420/ecr.2018.33.1>
- Yount, S. E., Choi, S. W., Victorson, D., Ruo, B., Cella, D., Anton, S., & Hamilton, A. (2011). Brief, valid measures of dyspnea and related functional limitations in chronic obstructive pulmonary disease (COPD). *Value in Health*, 14(2), 307-315. <https://doi.org/10.1016/j.jval.2010.11.009>
- Yuan, T., Yang, T., Chen, H., Fu, D., Hu, Y., Wang, J., Yuan, Q., Yu, H., Xu, W., & Xie, X. (2019). New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. *Redox Biol*, 20, 247-260. <https://doi.org/https://doi.org/10.1016/j.redox.2018.09.025>