Relationship Between Obesity and Survival in Patients Hospitalized for Hypertensive Emergency.

Manyoo A Agarwal
University of Tennessee

Mahek Shah MD
Lehigh Valley Health Network, Mahek.Shah@lvhn.org

Lohit Garg MD
Lehigh Valley Health Network, lohit.garg@lvhn.org

Carl J Lavie
John Ochsner Heart and Vascular Institute, Ochsner Medical Center

Published In/Presented At

Agarwal, M. A., Shah, M., Garg, L., & Lavie, C. J. (2018). Relationship Between Obesity and Survival in Patients Hospitalized for Hypertensive Emergency. *Mayo Clinic proceedings*, *93*(2), 263–265. https://doi.org/10.1016/j.mayocp.2017.07.015

Diaphragmatic Pacemaker for Perry Syndrome

To the Editor: We read with a great interest the excellent article by Edwards et al[1] in the September 2017 issue of *Mayo Clinic Proceedings*. The authors elegantly reviewed the current knowledge of neurostimulation devices clinically used for neurologic disorders. These devices included deep brain stimulation, motor cortex stimulation, responsive neurostimulation, spinal cord stimulation, and vagus nerve stimulation. The authors described clinical indications for each device in detail as well as historical aspects of device development. This review is very helpful for clinicians who wish to understand and use these devices for their patients.

We would like to mention another neurostimulation device, the diaphragmatic pacemaker, which is clinically indicated for patients with neurologic disorders that require chronic respiratory support, such as brain stem/upper spinal cord injuries and congenital central hypoventilation.[2] This device produces the diaphragm muscle contracture via direct stimulation of phrenic nerves. There are 2 types of devices.[2] One requires that electrodes are placed on the diaphragm surface to stimulate the phrenic nerve at or near the neuromuscular junction. The electrodes come out through the skin and connect to the external pulse generator. The NeuRx Diaphragm Pacing System (Synapse Biomedical Inc) has been approved for clinical use. Another device consists of electrodes, radio receivers (both of which are implanted in the intrathoracic segment near the phrenic nerve), and external radio transmitters (generators/antennae). The generated radio waves are translated into stimulating pulses at the receivers. There are 2 commercially available devices: the Mark IV (Avery Biomedical Devices, Inc) and the Atrostim Phrenic Nerve Stimulator (Atrotech).

We previously reported a case of Perry syndrome treated with the Mark IV device.[3] Perry syndrome is a very rare inheritable neurodegenerative disorder caused by *DCTN1* sequence variant.[4] Central hypoventilation is one of the cardinal features of Perry syndrome and is life-threatening.[5] This patient had experienced respiratory failure and been bedridden while undergoing mechanical ventilation for several months. After the diaphragmatic pacemaker was implanted, she was successfully weaned from the ventilator. Subsequently, the patient regained her gait and became independent in daily life.[3] To our knowledge, this case is the only patient who has been treated with the diaphragmatic pacemaker so far; thus, it remains to be determined whether this neurostimulation is definitely helpful for hypoventilation due to Perry syndrome. However, it could be a promising option for such untreatable neurodegenerative disorders.

Neurostimulation technologies have the potential to be more commonly and widely utilized for neurologic disorders.

Takuya Konno, MD, PhD
Zbigniew K. Wszolek, MD
Mayo Clinic
Jacksonville, FL

Grant Support: Dr Konno is supported by Japan Society for the Promotion of Science Overseas Research Fellowships. Dr Wszolek is supported by grant P50 NS072187 from the National Institutes of Health (NIH)/National Institute of Neurological Disorders and Stroke, grant 1U01AG045390-01A1 from the NIH/National Institute on Aging (primary) and the NIH/National Institute of Neurological Disorders and Stroke (secondary), Mayo Clinic Center for Regenerative Medicine, Mayo Clinic Center for Individualized Medicine, Mayo Clinic Neuroscience Focused Research Team (Cecilia and Dan Carmichael Family Foundation and the James C. and Sarah K. Kennedy Fund for Neurodegenerative Disease Research at Mayo Clinic in Jacksonville, Florida), a gift from Carl Edward Bolch, Jr, and Susan Bass Bolch, the Sol Goldman Charitable Trust, and Donald G. and Jodi P. Heeringa.

1. Edwards CA, Kouzani A, Lee KH, Ross EK. Neurostimulation devices for the treatment of neurologic disorders. *Mayo Clin Proc*. 2017;92(9):1427-1444.
2. Le Pimpec-Barthes F, Legras A, Arame A, et al. Diaphragm pacing: the state of the art. *J Thorac Dis*. 2016;8(suppl 4):S376-S386.
3. Pretelt F, Castañeda Cardona C, Tacik P, Ross OA, Wszolek ZK. Latin America's first case of Perry syndrome and a new treatment option for respiratory insufficiency [letter]. *J Neurol*. 2014;261(3):620-621.
4. Farrer MJ, Hulihan MM, Kachergus JM, et al. *DCTN1* mutations in Perry syndrome. *Nat Genet*. 2009;41(2):163-165.
5. Konno T, Ross OA, Teive HAG, Sławek J, Dickson DW, Wszolek ZK. *DCTN1*-related neurodegeneration: Perry syndrome and beyond. *Parkinsonism Relat Disord*. 2017;41:14-24.

https://doi.org/10.1016/j.mayocp.2017.11.014

In Reply—Diaphragmatic Pacemaker for Perry Syndrome

We thank Drs Konno and Wszolek for their comments and insights on our review of current implantable neurostimulation devices to treat neurologic disorders. Their presented work using a phrenic neurostimulation device to treat Perry syndrome is extremely exciting and highlights the potential for neuromodulation treatment in a broad range of disorders across many symptoms. Their work also highlights a very important aspect of emerging neurostimulation therapies, in the summative and long-term response that they observed in this study. We enthusiastically agree with the authors when they state that neurostimulation devices have great potential to treat many disorders at the circuit level with peripherally accessible targets and also at the end-organ level with direct organ stimulation.

Erika K. Ross, MS, PhD
Mayo Clinic
Rochester, MN

https://doi.org/10.1016/j.mayocp.2017.11.015

Relationship Between Obesity and Survival in Patients Hospitalized for Hypertensive Emergency

To the Editor: Recently in *Mayo Clinic Proceedings*, Carbone et al[1] discussed

the obesity paradox in patients with heart failure, and we have also discussed this paradox in patients hospitalized with pulmonary hypertension.[2] In fact, despite the clear association of obesity and increased cardiovascular disease (CVD), obese patients have also been reported to have paradoxical lower mortality, referred to as the "obesity paradox," in CVD conditions such as coronary heart disease, heart failure, peripheral arterial disease, atrial fibrillation, and hypertension (HTN).[2-4] Because data pertaining to obesity and survival in HTN emergency (HTNe) hospitalizations is lacking, we studied the association of obesity with in-hospital mortality in a propensity-matched cohort of 281,560 HTNe hospitalizations (obese vs nonobese patients).

Using the Nationwide Inpatient Sample (NIS) databases of the Healthcare Cost and Utilization Project, we identified all hospitalizations in adults with a primary diagnosis of HTNe using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes and then extracted patient demographic information, admission characteristics, and clinical comorbidities including obesity and outcomes, as done previously.[5,6] IBM SPSS statistical software, version 23.0 was used to perform propensity score matching (1:1 matching protocol without replacement and caliper width 0.1 of SD) to identify a cohort of HTNe hospitalizations with and without obesity, similar in terms of baseline characteristics as shown in the Table.

Among the 281,560 HTNe hospitalizations, 46,602 patients (16.6%) were classified as obese in the diagnostic coding. The Table describes the patient demographic features, hospital characteristics, and clinical comorbidities in the patient population. Overall mortality was 2.75% (7748 of 281,560) with significantly lower in-hospital mortality in both pre– and post–propensity-matched cohorts in those coded with obesity (both $P<.001$) (Table).

In this largest nationalized study to date, patients with HTNe who had a coexisting discharge diagnosis of obesity (present in 46,362 of 281,560 [16.5%]) in a propensity score–matched cohort had lower in-hospital mortality. This finding is in line with the previous observations of an obesity paradox in various CVDs and related risk factors such as HTN,[4] which we now report but for the first time in patients with HTNe.[3] Obviously, the limitation with such a large database is that some potential confounding factors may not be available, many obese patients may not be coded as such, measures of body composition are not available in this database, including body mass indices, and some overweight patients could be coded as being obese. Despite these limitations, a

TABLE. Pre– and Post–Propensity-Matched Baseline Demographic Information, Characteristics, and Outcomes Comparing Obese and Nonobese Hypertensive Emergency Hospitalizations[a]

Variable	Pre–propensity match			Post–propensity match		
	Obese (n=46,602)	Nonobese (n=234,958)	*P* value	Obese (n=46,362)	Nonobese (n=46,362)	*P* value
Age (y)	58.9±14.8	66.9±16.5	<.001	59.0±14.8	58.7±16.4	.001
Female	25,212 (54.1)	121,943 (51.9)	<.001	25,035 (54.0)	24,943 (53.8)	.56
Race			<.001			.64
White	17,709 (38.0)	94,923 (40.4)		17,664 (38.1)	17,618 (38.0)	
Black	18,128 (38.9)	70,017 (29.8)		17,942 (38.7)	17,942 (38.7)	
Hispanic	3775 (8.1)	20,911 (8.9)		3755 (8.1)	3801 (8.2)	
Other	6990 (15.0)	49,107 (20.9)		7001 (15.1)	7001 (15.1)	
Payer Status			<.001			.60
Medicare	22,788 (48.9)	152,723 (65.0)		22,764 (49.1)	22,625 (48.8)	
Medicaid	6850 (14.7)	25,845 (11.0)		6815 (14.7)	6908 (14.9)	
Private	10,951 (23.5)	34,539 (14.7)		10,849 (23.4)	10,895 (23.5)	
Self-pay	4334 (9.3)	15,272 (6.5)		4312 (9.3)	4358 (9.4)	
No Charge	421 (0.9)	1410 (0.6)		417 (0.9)	417 (0.9)	
Other	1258 (2.7)	5169 (2.2)		1205 (2.6)	1159 (2.5)	
Median household income (percentile)			<.001			.64
0 to 25th	18,641 (40.0)	89,049 (37.9)		18,545 (40.0)	18,684 (40.3)	
26th to 50th	12,023 (25.8)	59,679 (25.4)		11,961 (25.8)	11,822 (25.5)	
51st to 75th	9647 (20.7)	48,871 (20.8)		9597 (20.7)	9597 (20.7)	
76th to 100th	6291 (13.5)	37,359 (15.9)		6259 (13.5)	6259 (13.5)	

Continued on next page

TABLE. Continued

Variable	Pre–propensity match			Post–propensity match		
	Obese (n=46,602)	Nonobese (n=234,958)	*P* value	Obese (n=46,362)	Nonobese (n=46,362)	*P* value
US Region			<.001			.98
Northeast	5546 (11.9)	39,004 (16.6)		5563 (12.0)	5517 (11.9)	
Midwest	10,485 (22.5)	49,576 (21.1)		10,385 (22.4)	10,385 (22.4)	
South	23,254 (49.9)	109,490 (46.6)		23,135 (49.9)	23,274 (50.2)	
West	7317 (15.7)	36,888 (15.7)		7279 (15.7)	7186 (15.5)	
Hospital size			<.001			.30
Small	5778 (12.4)	28,430 (12.1)		5749 (12.4)	5703 (12.3)	
Medium	12,350 (26.5)	61,089 (26.0)		12,332 (26.6)	12,193 (26.3)	
Large	28,474 (61.1)	145,439 (61.9)		28,281 (61.0)	28,466 (61.4)	
Urban, teaching hospital	21,111 (45.3)	105,261 (44.8)	<.001	21,002 (45.3)	21,002 (45.3)	.99
Elective admission	3262 (7.0)	17,857 (7.6)	<.001	3245 (7.0)	3245 (7.0)	.81
Weekend admission	10,252 (22.0)	52,396 (22.3)	.12	10,200 (22.0)	10,200 (22.0)	.40
Comorbidities						
Smoking	11,837 (25.4)	49,811 (21.2)	<.001	11,776 (25.4)	11,822 (25.5)	.91
Alcohol abuse	1212 (2.6)	7754 (3.3)	<.001	1205 (2.6)	1252 (2.7)	.27
Diabetes mellitus	27,449 (58.9)	95,863 (40.8)	<.001	27,214 (58.7)	27,122 (58.5)	.58
Dyslipidemia	20,784 (44.6)	76,831 (32.7)	<.001	20,585 (44.4)	20,446 (44.1)	.33
Coronary artery disease	17,988 (38.6)	98,212 (41.8)	<.001	17,896 (38.6)	17,710 (38.2)	.23
Atrial fibrillation	8575 (18.4)	49,106 (20.9)	<.001	8531 (18.4)	8299 (17.9)	.07
Heart failure	4753 (10.2)	26,315 (11.2)	<.001	4729 (10.2)	4775 (10.3)	.92
Chronic lung disease	15,239 (32.7)	60,384 (25.7)	<.001	15,068 (32.5)	14,743 (31.8)	.02
Carotid artery disease	419 (0.9)	3289 (1.4)	<.001	464 (1.0)	417 (0.9)	.92
Electrolyte abnormalities	14,307 (30.7)	76,361 (32.5)	<.001	14,279 (30.8)	14,187 (30.6)	.57
Peripheral vascular disease	5918 (12.7)	21,851 (9.3)	<.001	4312 (9.3)	4497 (9.7)	.05
Renal failure	14,400 (30.9)	66,728 (28.4)	<.001	14,326 (30.9)	14,094 (30.4)	.14
Liver disease	1072 (2.3)	5874 (2.5)	<.001	1066 (2.3)	1066 (2.3)	.59
In-hospital mortality	699 (1.5)	7049 (3.0)	<.001	695 (1.5)	835 (1.8)	<.001

[a]Data are presented as No. (percentage) of patients except for age, which is reported as mean ± SD.

strong obesity paradox was noted for the first time in patients with HTNe.

Finally, obesity is a well-known risk factor for the development of CVD, as well as CVD morbidity and mortality; however, the existence of an obesity paradox, now extended to the cohort hospitalized with HTNe, demands further research to better explain the reasoning behind this noteworthy and intriguing finding.

Manyoo A. Agarwal, MD
University of Tennessee Health Science Center,
Memphis, TN

Mahek Shah, MD
Lohit Garg, MD
Lehigh Valley Health Network
Allentown, PA

Carl J. Lavie, MD
John Ochsner Heart and Vascular Institute,
Ochsner Medical Center
New Orleans, LA

1. Carbone S, Lavie CJ, Arena R. Obesity and heart failure: focus on the obesity paradox. *Mayo Clin Proc*. 2017;92(2):266-279.
2. Agarwal M, Agrawal S, Garg L, Lavie CJ. Relation between obesity and survival in patients hospitalized for pulmonary arterial hypertension (from a nationwide inpatient sample database 2003-2011). *Am J Cardiol*. 2017;120(3):489-493.
3. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *J Am Coll Cardiol*. 2009;53(21):1925-1932.
4. Uretsky S, Messerli FH, Bangalore S, et al. Obesity paradox in patients with hypertension and coronary artery disease. *Am J Med*. 2007;120(10):863-870.
5. Shah M, Patil S, Patel B, et al. Trends in hospitalization for hypertensive emergency, and relationship of end-organ damage with in-hospital mortality. *Am J Hypertens*. 2017;30(7):700-706.
6. Healthcare Cost and Utilization Project (HCUP) Overview of the National (Nationwide) Inpatient Sample (NIS). Rockville, MD: Agency for Healthcare Research and Quality website. http://www.hcup-us.ahrq.gov/nisoverview.jsp. Updated March 22, 2017. Accessed March 24, 2017.

https://doi.org/10.1016/j.mayocp.2017.07.015