Midodrine Use and Mortality in Heart Failure with Reduced Ejection Fraction

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Background

- Hypotension is a common limitation in the titration of guideline-directed medical therapy(GDMT) in patients with heart failure with reduced ejection fraction (HFrEF). Midodrine, an alpha-1 agonist, is frequently used to mitigate concurrent hypotension in HFrEF and allow for the implementation of guideline-directed medical therapy (GDMT). Despite its utilization in clinical practice, there is limited evidence regarding the impact of Midodrine use in patients with HFrEF.

Objective

- This study aims to determine the effects of Midodrine on mortality outcomes in patients with HFrEF.

Methods

- This multicenter retrospective study included patients admitted with a diagnosis of acute on chronic systolic (congestive) heart failure (I50. 23) between January 2018 and December 2022. We utilized Hospital Corporation of America West Florida Division's database, which is a comprehensive network of 15 hospitals. We excluded patients with a diagnosis of hepatorenal syndrome (HRS) (K76. 7), postural orthostatic tachycardia syndrome (POTS) (G90. A), or end-stage renal disease (ESRD) (N18. 6). Logistic regression with Firth adjustment was used to analyze the relationship between mortality and Midodrine use before admission and the data was summarized as odds ratios (OR) with 95% confidence intervals (CI). The model was adjusted for age, sex, previous GDMT use, and the Elixhauser Comorbidity Index.

Results

- Number of observations: 17,882 patients met inclusion criteria
  - 610 patients excluded due to diagnosis of HRS (K76.7), POTS (G90.A), or ESRD (N18.6)
  - 87 patients excluded due to lack of demographic data
  - 3,338 patients excluded due to lack of documented BMI data
    - 13,847 patients with complete data were utilized in analysis

Results Continued

Table 1. Outcome and Confounders Summary

Variables	Midodrine (taken at home)					
	No Midodrine		Midodrine		Overall	
	n	%	n	%	n	%
n, %	13,504	97.52	343	2.48	13,847	100
Mortality	373	2.8	31	9	404	2.9
Readmit (30 days)	3706	27.4	130	37.9	3,836	27.7
Readmit (90 days)	5182	38.4	161	46.9	5,343	38.6
GDMT						
Beta Blockers	7,775	57.6	229	66.8	8,004	57.8
ACE/ARB/ARNi	7,294	54	153	44.6	7,447	53.8
Mineralocorticoid	2,715	20.1	95	27.7	2,810	20.3
SGLT2	549	4.1	27	7.9	576	4.2
Other Meds						
Furosemide	2,983	22.1	84	24.5	3,067	22.1
Bumetanide	221	1.6	15	4.4	236	1.7
Torsemide	69	0.5	6	1.7	75	0.5
Variables	**M**	**SD**	**M**	**SD**	**M**	**SD**
Age	64.4	11.59	67.6	10.15	64.48	11.57
LOS	5.1	6.39	5.33	5.63	5.11	6.38
Elixhauser	4.58	2.27	5.49	2.23	4.60	2.28

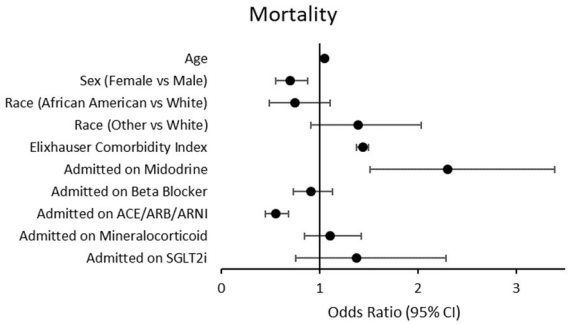

Table 2. Medications - Admitted vs. Discharged

GDMT	Admitted		Discharged		p-value
	n	%	n	%	
Beta Blockers	8,004	57.8	8,602	62.1	0.0001*
ACE/ARB/ARNi	7,447	53.8	7,719	55.7	0.0153*
MRA	2,810	20.3	3,126	22.6	0.0328*
SGLT2	541	3.9	463	3.3	0.6312
Other Meds					
Midodrine	343	2.5	380	2.7	0.8662
Furosemide	3,067	22.2	3,347	24.2	0.0582
Torsemide	64	0.5	55	0.4	0.9358
Bumetanide	236	1.7	255	1.8	0.9328

Discussion

- Of the 13,847 patients included in our final analysis, 343 were taking Midodrine on admission (2.48 %). Midodrine use prior to hospital admission was significantly associated with the likelihood of mortality when controlling for other variables (OR 2.29, 95% CI 1.512-3.389). Patients taking Midodrine prior to hospital admission were more likely to be taking Beta Blockers (OR 1.48, 95% CI 1.179-1.858), Mineralocorticoid Receptor Antagonists (OR 1.52, 95% CI 1.197-1.936), and Sodium-Glucose Transport Protein 2 (SGLT2) Inhibitors (OR 2.13, 95% CI 1.383-3.293) when compared to those not taking Midodrine. Patients taking Midodrine prior to hospital admission were less likely to be taking Angiotensin-Converting Enzyme (ACE) Inhibitors, Angiotensin Receptor Blockers (ARBs), or Angiotensin Receptor Neprilysin Inhibitors (ARNI) (OR 0.59, 95% CI 0.474-0.729).
- Due to the complex pathophysiology of heart failure, it can be difficult to initiate GDMT. Midodrine is used to treat concurrent hypotension and allow for maximum utilization of GDMT, but there is limited research investigating the implications of this practice. Our findings demonstrate a significant association with mortality and Midodrine use when adjusting for comorbidities, but large randomized controlled trials are needed to demonstrate the potential risks and benefits of this medication in patients with heart failure.

Conclusion

- Midodrine use was significantly associated with mortality even when adjusting for comorbidities and GDMT use. Large randomized controlled trials are needed to assess the risks and benefits of Midodrine use in conjunction with GDMT in patients with HFrEF.

References

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This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

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