

# Continuation of Newly Initiated Midodrine Therapy After Intensive Care and Hospital Discharge: A Single-Center Retrospective Study

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**Objectives:** Midodrine is an  $\alpha_1$ -agonist approved for orthostatic hypotension. Recently, it has received attention as an oral vasopressor to facilitate ICU discharge. The purpose of this study was to identify the incidence of continuation of newly initiated midodrine upon ICU and hospital discharge and identify risk factors associated with its occurrence.

**Design:** Single-center retrospective study.

**Setting:** ICU patients from January 2011 to October 2016 at Mayo Clinic, Rochester.

**Patients:** Adult patients admitted to any ICU who received new midodrine for hypotension and survived to discharge.

**Interventions:** None.

**Measurements and Main Results:** During the study period, 1,010 patients were newly started on midodrine and survived to ICU discharge. Midodrine was continued in 67% (672/1,010) of patients at ICU discharge. Admission to cardiovascular surgery ICU and mixed medical/surgical ICU was a risk factor for midodrine continuation at ICU discharge (odds ratio, 3.94 [2.50–6.21] and 2.03 [1.29–3.20], respectively). At hospital discharge, 34% (311/909) of patients were continued on midodrine therapy. History of congestive heart failure predicted midodrine continuation at hospital discharge (odds ratio, 1.49 [1.05–2.12]). Hypertension and use

of mechanical ventilation were associated with a decreased odds of midodrine prescription at both ICU and hospital discharge. Of those discharged from the ICU or hospital on midodrine, 50% were concomitantly prescribed antihypertensives. Discharge from the ICU on midodrine was associated with a significantly shorter ICU length of stay ( $7.5 \pm 8.9$  vs  $10.6 \pm 13.4$  d) and reduced risk of in-hospital mortality (hazard ratio, 0.47 [95% CI, 0.32–0.70];  $p < 0.001$ ), despite no difference in baseline severity of illness scores. In contrast, patients discharged from the hospital on midodrine had a higher risk of 1-year mortality (hazard ratio, 1.60 [95% CI, 1.26–2.04];  $p < 0.001$ ).

**Conclusions:** This study established a high prevalence of midodrine continuation in transitions of care. The risks and benefits of this practice remain unclear. Future studies should explore the impact of this practice on patient outcomes and resource utilization. These insights could be used to model interventions for proper tapering, discontinuation, or follow-up of new start midodrine. (*Crit Care Med* 2019; XX:00–00)

**Key Words:** medication reconciliation; midodrine; polypharmacy; shock

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Circulatory shock affects about one third of ICU patients (1). Initial shock management includes fluid resuscitation and hemodynamic support with IV vasoactive medications (2). Midodrine, an  $\alpha_1$ -agonist, has received attention as an oral therapy to augment blood pressure and facilitate liberation from continuous IV vasopressors (3–5). This off-label use of oral midodrine in shock was first reported in 1979 (6). In the past decade, a resurgence in utilization has occurred, with observational evidence indicating that midodrine improves hemodynamics in critical illness (3, 5, 7–9).

Like other ICU medications, new start midodrine is usually for an acute reversible indication. Midodrine continuation upon ICU discharge could be inadvertent, or it may be intentionally prescribed to allow liberation from IV vasopressors and the ICU. In either case, it may be a surrogate for patients who have yet to achieve hemodynamic stability and are at risk

for deterioration in a nonmonitored setting. Thus, at ICU discharge, plans for midodrine discontinuation, tapering, or reevaluation should be clearly outlined and the risks and benefits of this practice should be evaluated.

The purpose of this study was to identify the incidence of midodrine continuation in patients leaving the ICU and the hospital and identify risk factors associated with its occurrence. Secondarily, we explored the clinical outcomes associated with midodrine continuation after ICU discharge.

## METHODS

### Setting and Participants

Eligible participants were adults ( $\geq 18$  yr old) started on midodrine in any ICU at Mayo Clinic, in Rochester, MN, from January 1, 2011, to October 31, 2016. We excluded patients on midodrine prior to hospital admission, who died prior to ICU discharge, or who denied review of medical records for research. If a patient received multiple courses of midodrine during the study timeframe, only the earliest course was included. The Mayo Clinic Institutional Review Board approved the protocol with a waiver of informed consent.

During the study timeframe, midodrine was used per provider preference. No protocolized utilization schema existed, but doses typically ranged from 5 to 40 mg every 8–12 hours. Midodrine use followed two general patterns: either in the early phase of hemodynamic instability as a vasopressor-sparing agent or in the stabilization and dereuscitation phases to wean IV drugs (3). The study center has 24-hour in-house intensivist coverage in all ICUs and clinical pharmacist coverage as part of the multidisciplinary care team in ICU and non-ICU areas from 7:00 AM to 10:30 PM.

### Endpoints

The primary endpoint was incidence of midodrine continuation at ICU discharge, defined as any midodrine exposure in the 24 hours after transfer from ICU to hospital ward. Informed by previous work on transitions of care, we explored whether the admitting diagnosis, comorbid conditions, type of admission (medical or surgical), and time of discharge (weekend vs weekday) were associated with midodrine continuation (10, 11). Secondary endpoints included incidence of discharge from the hospital on midodrine and concurrent use of antihypertensive drugs among patients continued on midodrine therapy at ICU transfer and hospital discharge. ICU length of stay (LOS) and in-hospital mortality were compared between patients according to whether midodrine was continued at ICU discharge. One-year mortality was compared between patients who were continued on midodrine at hospital discharge and those who were not.

### Statistical Analysis

Continuous data were summarized with the mean  $\pm$  SD or median with interquartile range (IQR) depending on distribution. Categorical data were represented as numbers and percentages. Univariate endpoints between arms were compared

using the Pearson chi-square test or Fisher exact test for categorical variables and the Student *t* test or Wilcoxon rank sum test for continuous data. A multivariable logistic regression was fit to evaluate predictors of midodrine continuation at ICU and hospital discharge. Results were reported as odds ratios (ORs) with 95% CIs. The Kaplan-Meier method and Cox proportional hazard models were fit to compare in-hospital and 1-year mortality according to midodrine continuation. Results for these analyses were reported as hazard ratios (HRs) and 95% CI. Multivariable analyses for mortality were adjusted for age, sex, severity of illness, and type of ICU. Analyses used SAS version 9.4 statistical software (SAS Institute, Cary, NC). The *p* values less than 0.05 were considered statistically significant.

## RESULTS

### Patients

During the study period, 1,119 patients were newly initiated on midodrine in an ICU (3), 1,010 (90%) of which survived to ICU discharge and were included in this study sample. The majority of these patients were admitted for a surgical indication ( $n = 583$ ; 58%). IV vasopressors were ongoing in 587 patients (58%) at the time of midodrine initiation (Table 1).

### Endpoints

Midodrine continued for a median of 5 days (IQR, 2–11 d) beyond ICU discharge in 67% (672/1,010) of the patients. Severity of illness and prevalence of comorbidities were similar between patients who continued therapy and those who did not (Table 1). In a multivariable model, history of hypertension and use of invasive mechanical ventilation were associated with a decreased odds of midodrine continuation at ICU discharge (hypertension: OR, 0.70 [95% CI, 0.50–0.96];  $p = 0.029$ ; and mechanical ventilation: OR, 0.46 [95% CI, 0.32–0.66];  $p < 0.001$ ) (Table S1, Supplemental Digital Content 1, <http://links.lww.com/CCM/E589>). Admission to a cardiovascular (CV) surgery ICU (CV-ICU) or a mixed medical/surgical ICU when compared with the medical ICU was associated with greater odds of midodrine continuation at ICU discharge ( $p < 0.001$  and 0.002, respectively; Table S1, Supplemental Digital Content 1, <http://links.lww.com/CCM/E589>).

The mean ICU LOS was shorter for patients discharged from the ICU on midodrine therapy ( $7.5 \pm 8.9$  vs  $10.6 \pm 13.4$  d). After adjustment for Acute Physiology and Chronic Health Evaluation III score, Sequential Organ Failure Assessment score, age, sex, and type of ICU, use of midodrine at ICU discharge was independently associated with a decrease in ICU LOS ( $p < 0.001$ ). Risk of in-hospital mortality was also significantly lower for patients continued on midodrine therapy at ICU discharge (unadjusted HR, 0.47 [95% CI, 0.32–0.70];  $p < 0.001$ ; adjusted HR, 0.45 [95% CI, 0.30–0.68];  $p < 0.001$ ) (Table 2).

Among the 909 patients (81%) who survived to hospital discharge, 53% (484/909) received midodrine in the 24 hours before hospital discharge and midodrine was listed on 34% (311/909) of the hospital discharge summaries (Table S2,

**TABLE 1. Patient and Provider Characteristics Associated With Midodrine Continuation at ICU Discharge**

Characteristic	All Patients <sup>a</sup> ( <i>n</i> = 1,010)	Midodrine Discontinued at ICU Discharge <sup>a</sup> ( <i>n</i> = 338)	Midodrine <b>Continued</b> After ICU Discharge <sup>a</sup> ( <i>n</i> = 672)	<i>p</i>
Age (yr)	63.6 ± 14.8	62.7 ± 15.4	64.1 ± 14.4	0.28
Male, <i>n</i> (%)	580 (57.4)	195 (57.7)	385 (57.3)	0.90
Weight (kg)	85.8 ± 24.2	85.7 ± 25.7	85.9 ± 23.4	0.47
Body mass index (kg/m <sup>2</sup> )	29.9 ± 9.2	29.9 ± 8.8	29.9 ± 9.4	0.79
Acute Physiology and Chronic Health Evaluation III score	78.0 ± 25.6	78.7 ± 26.2	77.6 ± 25.3	0.71
Sequential Organ Failure Assessment score	6.5 ± 6.3	7.0 ± 7.7	6.2 ± 5.5	0.89
Comorbid conditions, <i>n</i> (%)				
Diabetes mellitus	316 (31.3)	104 (30.8)	212 (31.5)	0.80
Liver disease	170 (16.8)	60 (17.8)	110 (16.4)	0.58
Chronic kidney disease	308 (30.5)	92 (27.2)	216 (32.1)	0.11
Congestive heart failure	295 (29.2)	96 (28.4)	199 (29.6)	0.69
Cerebrovascular accident	108 (10.7)	39 (11.5)	69 (10.3)	0.54
End-stage renal disease	60 (5.9)	20 (5.9)	40 (6.0)	0.98
Hypertension	605 (59.9)	212 (62.7)	393 (58.5)	0.19
Malignancy	301 (29.8)	103 (30.5)	198 (29.5)	0.74
Admitting ICU, <i>n</i> (%)				< 0.001
Medical ICU	264 (26.1)	115 (34.0)	149 (22.2)	
Surgical ICU (non–cardiovascular surgery)	192 (19.0)	85 (25.1)	107 (15.9)	
Cardiovascular surgery ICU	391 (38.7)	92 (27.2)	299 (44.5)	
Mixed medical/surgical ICU	163 (16.1)	46 (13.6)	117 (17.4)	
Sepsis, <i>n</i> (%)	660 (65.3)	238 (70.4)	422 (62.8)	0.016
Mechanical ventilation, <i>n</i> (%)	618 (61.2)	226 (66.9)	392 (58.3)	0.009
Duration of mechanical ventilation (d)	3.9 ± 8.6	5.9 ± 11.7	2.9 ± 6.2	< 0.001
IV vasopressor use at midodrine initiation, <i>n</i> (%)	587 (58.1)	182 (53.8)	405 (60.3)	0.051
Total dose of IV vasopressor in norepinephrine equivalent (μg/min) at midodrine initiation	16.1 ± 41.2	12.2 ± 32.6	18.1 ± 44.8	0.013
Weekend discharge, <i>n</i> (%)	259 (25.6)	84 (24.9)	175 (26.0)	0.68
Midodrine utilization				
Time to start from ICU admit (d)	4.2 ± 6.1	4.7 ± 7.2	4.1 ± 5.5	0.98
Duration of therapy (d)	11.8 ± 20.9	7.4 ± 19	14.1 ± 21.5	< 0.001
ICU length of stay (d)	8.5 ± 10.7	10.6 ± 13.4	7.5 ± 8.9	< 0.001
Hospitalization is a readmission <sup>b</sup>	111 (11.0)	37 (10.9)	74 (11.0)	0.98

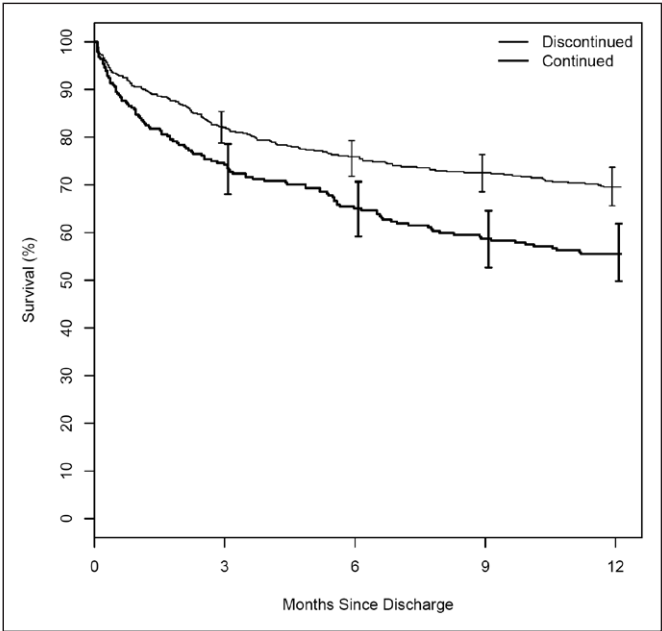
<sup>a</sup>Values are expressed as means ± SD unless noted.<sup>b</sup>The current hospitalization reflects a patient who was admitted within the past 30 d.

Supplemental Digital Content 1, <http://links.lww.com/CCM/E589>). In a multivariable model of factors associated with midodrine continuation at hospital discharge, **history of congestive heart failure predicted a greater odds of discharge on midodrine** ( $p = 0.027$ ) (Table S3, Supplemental Digital Content

1, <http://links.lww.com/CCM/E589>). In contrast, history of hypertension ( $p < 0.001$ ), use of invasive mechanical ventilation ( $p < 0.001$ ), and surgical ICU admission (non-CV surgery;  $p = 0.036$ ) were associated with decreased odds of midodrine continuation at hospital discharge (Table S3, Supplemental

**TABLE 2. Multivariable Cox Proportional Hazard Model for In-Hospital Mortality After ICU Discharge**

Variable	Hazard Ratio (95% CI)	p
Age (per decade)	1.44 (1.22–1.71)	< 0.001
Male	0.75 (0.50–1.12)	0.16
Acute Physiology and Chronic Health Evaluation III score (per 10 points)	1.04 (0.96–1.13)	0.35
Sequential Organ Failure Assessment score (per point)	0.99 (0.96–1.02)	0.55
Admitting ICU		
Medical ICU	Reference	Reference
Surgical ICU (non–cardiovascular surgery)	0.61 (0.35–1.07)	0.083
Cardiovascular surgery ICU	0.35 (0.20–0.61)	< 0.001
Mixed medical/surgical ICU	0.98 (0.55–1.75)	0.94
Continued on midodrine at ICU discharge (yes vs no)	0.45 (0.30–0.68)	< 0.001



**Figure 1.** One-year survival after hospital discharge in those continued on newly initiated oral midodrine at hospital discharge when compared with those in whom midodrine was stopped prior to hospital discharge.

Digital Content 1, <http://links.lww.com/CCM/E589>). In a sensitivity analysis of the CV-ICU patients, where oral midodrine use was frequent, findings were consistent (Table S4, Supplemental Digital Content 1, <http://links.lww.com/CCM/E589>).

The cumulative incidence of death at 1 year was 45% (95% CI, 38%–50%) in patients continued on midodrine therapy at hospital discharge. In patients where midodrine was discontinued at hospital discharge, the cumulative incidence of death at 1 year was 31% (95% CI, 26%–34%). Discharge from the hospital on midodrine was associated with a 1.6-fold higher risk of death in next year (unadjusted HR for 1-year mortality, 1.60 [95% CI, 1.26–2.04];  $p < 0.001$ ; adjusted HR, 1.56 [95% CI, 1.23–1.99];  $p < 0.001$ ) (Fig. 1 and Table 3).

Among the survivors who discharged from the ICU and hospital on midodrine, 50% were also on medications that can lower blood pressure. These included diuretics and  $\beta$ -blockers primarily, with a small minority receiving calcium channel blockers, angiotensin-converting enzyme inhibitors, or other such medications (Fig. 2).

In a manual review of 10% (69/672) of the sample discharged from the ICU on midodrine, we found that a clinical pharmacist addressed and documented an intervention on the midodrine prescription in 20% of the patients (14/69). In 71% of the cases (10/14) where a pharmacist intervened, midodrine prescription was reevaluated by providers, deeming the pharmacy intervention helpful.

**DISCUSSION**

In the ICU, numerous acute care medications are initiated that require reevaluation at transitions of care. In this study, we demonstrated that an alarming 67% (672/1,010) of patients newly treated with midodrine during their ICU stay, continued on it at ICU discharge. Similarly, 34% (311/909) of individuals who survived were continued on midodrine therapy after hospital discharge. Fifty percent of those discharged from either the ICU or the hospital on midodrine were concomitantly prescribed agents that could decrease blood pressure (Fig. 2). We found that despite similar baseline severity of illness scores and comorbidities, discharge from the ICU on midodrine was associated with a shorter ICU LOS and a decreased risk of in-hospital mortality (HR, 0.47 [95% CI, 0.32–0.70];  $p < 0.001$ ). Yet in long-term follow-up, midodrine continuation at hospital discharge was associated with an increased risk of mortality in the 1 year after discharge (HR, 1.60 [95% CI, 1.26–2.04];  $p < 0.001$ ).

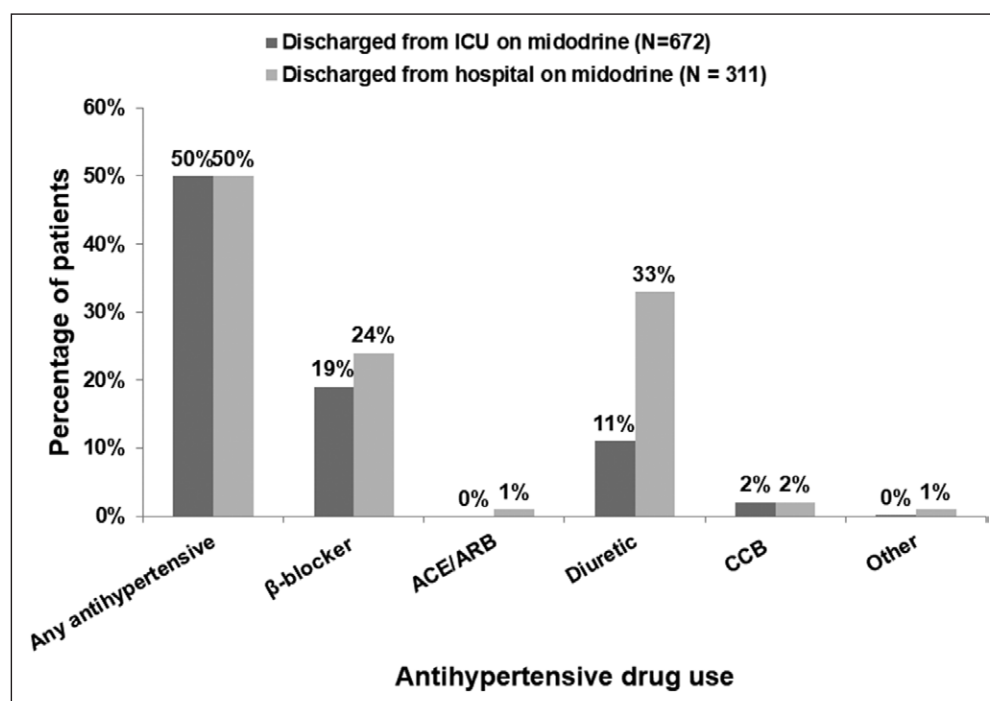
Patient admission type (surgical vs medical) was a strong predictor of midodrine continuation. Postoperative vasoplegia is a common surgical sequela (12) that is generally managed with low-dose IV vasopressors. As an oral  $\alpha_1$ -agonist,

**TABLE 3. Multivariable Cox Proportional Hazard Model for 1-Year Mortality After Hospital Discharge**

Variable	Hazard Ratio (95% CI)	p
Age (per decade)	1.23 (1.12–1.35)	< 0.001
Male	1.17 (0.91–1.49)	0.23
Acute Physiology and Chronic Health Evaluation III score (per 10 points)	1.04 (0.99–1.09)	0.12
Sequential Organ Failure Assessment score (per point)	1.03 (1.01–1.05)	0.002
Admitting ICU		
Medical ICU	Reference	Reference
Surgical ICU (non–cardiovascular surgery)	0.61 (0.44–0.85)	0.003
Cardiovascular surgery ICU	0.29 (0.21–0.40)	< 0.001
Mixed medical/surgical ICU	0.66 (0.46–0.94)	0.021
Continued on midodrine at hospital discharge (yes vs no)	1.56 (1.23–1.99)	< 0.001

midodrine may be a **unique alternative to facilitate ICU liberation**. We **hypothesize** that **midodrine continuation** was either a **function** of the distinctive **nature** of the **hypotensive** episodes in **surgical** ICU patients (e.g., **vasoplegia**, **hemorrhage**) versus **medical** ICU (e.g., **sepsis**) or attributable to differences in the care **teams**. The CV-ICU and surgical ICUs are anesthesia-directed care teams, whereas the medical ICU is overseen by pulmonary-critical care physicians. At ICU discharge, handoff occurs to the primary surgical or medical services. The background, experience, and practice of these distinct provider types may have affected the midodrine use patterns independent of the patient presentation.

Use of mechanical ventilation and history of hypertension were associated with a decreased odds of discharge from the ICU and hospital on midodrine. Hypotension in ventilated patients is often a function of sedation and positive pressure which resolves with ventilator liberation (13). History of hypertension may lead to improved hemodynamics or a medication reevaluation when home antihypertensives are reconciled at care transitions. One key factor that predicted midodrine continuation at hospital discharge was a history of congestive heart failure. In **patients with heart failure, blood pressure augmentation with midodrine may facilitate hemodynamic stability to allow prescription of home cardiac medications**.



**Figure 2.** Concomitant antihypertensive drug use in patients discharged from the ICU and hospital on oral midodrine. ACE = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, CCB = calcium channel blocker.

We found that parallel use of diuretics and  $\beta$ -blockers was common with midodrine (Fig. 2). Yet, the clinical **implications** of discharging a heart failure patient on an agent that directly increases afterload are **unknown**. Future studies are required to evaluate risks and benefits of this practice. Other patient and provider factors studied were not associated with midodrine continuation at ICU or hospital discharge.

Ultimately, we demonstrated that **ICU clinicians are routinely using midodrine and that it is being continued well after discharge** in the majority of patients. The clinical impact of midodrine continuation in care transitions remains unknown. We found a **decreased ICU LOS** and **decreased in-hospital mortality** in patients



transitioned out of the ICU on midodrine which could be clinically important and needs further scrutiny in prospective studies. In contrast, discharge from the hospital on midodrine was associated with a 1.6-fold increased risk of mortality out to 1 year, a finding that is worrisome. In our previous study of 1,119 patients treated with midodrine in the ICU, the most common adverse event within 72 hours of midodrine initiation was asymptomatic bradycardia, which occurred in 15% (172/1,119) of the cohort (3). Ischemic events were rare (0.002%; 2/1,119) and deemed multifactorial. Given midodrine has been associated with side effects with sustained exposure in an unmonitored setting (14–17), these associations need to be further explored.

No established guidance exists on the optimal approach to withdraw midodrine in the setting of clinical improvement, but it is clear that an iterative reevaluation of its use throughout a patient's course is warranted. Given a proportion of midodrine continuations in transitions of care may be inadvertent, clinical pharmacists now participate in the hospital dismissal reconciliation for each patient. Dismissal summaries and discharge prescriptions are reviewed in detail by clinical pharmacists. This practice may promote a reevaluation of the ongoing need for midodrine or introduce an opportunity to consider a taper or more comprehensive monitoring after discharge.

Although this is the largest study to date to explore the patterns of midodrine use in transitions of care, several limitations remain. This was a retrospective single-center study. Other than mortality, we were unable to evaluate the rate of adverse drug events in the outpatient setting because these would be difficult to retrospectively capture after dismissal. We did not capture hemodynamic data including discharge blood pressures in the two groups (on midodrine and off midodrine) which could have allowed better perspective on appropriateness of midodrine continuation. Also avoidable costs or cost-benefits incurred from midodrine continuation could not be calculated with these data.

## CONCLUSIONS

In a study of new start midodrine therapy in the ICU, we found a high prevalence of midodrine continuation at ICU and hospital discharge and identified several risk factors for its occurrence. These findings raise awareness for the importance of medication reconciliation in transitions of care, especially for midodrine therapy. We demonstrated, in a subset, that intervention by a clinical pharmacist may aide in reevaluating the continued need for oral midodrine to limit polypharmacy and

therapeutic antagonism. The finding of a shorter ICU stay and decreased in-hospital mortality in patients discharged from the ICU on midodrine is clinically relevant and an avenue for future research.

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## Midodrine Helps Early Discharge of Patients From the ICU, Though Results in Higher Rate of Natural Death

### To the Editor:

We read with great interest the article published in a recent issue of *Critical Care Medicine* by Rizvi et al (1). The authors illustrated the high prevalence of midodrine continuation in patients at transitions of care and its association to shorter ICU length of stay (LOS) and reduced risk of in-hospital mortality but increases out of hospital mortality.

The authors have done a great job of objectively documenting high prevalence of midodrine prescription and its impact composition. We would like to make few points that may be of interest to authors and readers of the article by Rizvi et al (1). How common is this midodrine practice in shock patients? If authors could provide the total number of ICU admissions with shock during this time frame or total number of ICU beds in the participating hospitals, readers may understand its occurrence. We have observed increasing similar practice in our hospitals in the Middle East; our patients are being treated with phenylephrine via peripheral vein or midodrine orally before transferring out of ICU. Conversely, they are also being used on medical floor to avoid transfer to ICU secondary to lack of resources or patients' or family's desire to avoid ICU admission for social or financial reasons.

We could not understand the statement that "patients were excluded if they denied chart review for research study" although study did not require informed consent. How many charts were excluded? Midodrine dosage used in the study was mentioned as 5–40 mg every 8–12 hours, which means some patients may receive up to 120 mg/24 hr, which appears to be similar as in other studies (2). It will be interesting for others to know that midodrine is only available as 2.5 mg tablet in the Middle East and maximum dosage we could use is total 30–40 mg/d as patients refused to take larger number of pills. The authors mention a very valid and interesting point that history of hypertension was associated with decreased odds of midodrine continuation at ICU discharge, this reflects the physicians' underappreciation of baseline blood pressure (BP) of patients. Acknowledgment of higher baseline BP at ICU discharge as checklist may have an impact on clinical outcomes as patients with past medical history of hypertension may continue to suffer subclinical hypoperfusion. Emerging trend of individualized patient care by electronic alerts regarding these variables may improve clinical practice. Authors mentioned decrease in ICU LOS but did not mention hospital LOS which could also be more informative. Increase in post discharge, out of hospital mortality suggests that patients on midodrine may be discharged with subclinical hypoperfusion secondary to pseudo-normalization of vital signs, although it may be more complex. We also noted that their data showed no significant difference between the two studied groups (with and without midodrine) in terms of advanced liver disease and end stage

renal failure which suggest that their patient population is different from ours, as our patients with midodrine usage are more likely to have liver disease or renal failure; they are associated with lower diastolic pressure owing to vasodilation (3, 4). Last, authors mention that among the 909 patients (81%) who survived to hospital discharge, 53% (484/909) received midodrine in the 24 hours before hospital discharge and midodrine was listed on 34% (311/909) of the hospital discharge summaries. Review of discharge prescription can be more accurate. Nevertheless, discontinuation of midodrine 24 hours before discharge without any adverse impact on clinical parameters is a very useful finding which may help clinician optimize management before discharge. Future studies should consider inclusion of post discharge follow-up of clinical and medication profiles.

Dr. Nadeem disclosed that he does not have any potential conflicts of interest.

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### The authors reply:

We thank Dr. Nadeem for his interest (1) in our recently published article (2) in *Critical Care Medicine*. The author continues a thoughtful discussion on the prescription of midodrine, an oral alpha-1 agonist, at transitions of care after an ICU stay. The observation of a similar practice at the hospitals in the middle east is particularly informative and further highlights the pressing need for large, well-designed trials to explore the impact of this practice on important outcomes like ICU and hospital length of stay (LOS), mortality and complications.

At our 1,264 bed tertiary care institution, which includes 158 adult ICU beds, we previously demonstrated a steady increase in the prescription of midodrine for shock across the ICUs (2). Compared to the year 2011, where we identified only 56 new prescriptions of midodrine across the ICUs, 338 patients were newly initiated on midodrine between January 1, 2016, and October 31, 2016 (2). We identified two practice patterns, one where midodrine is prescribed to facilitate IV vasopressor weaning; the other as an early intervention to potentially spare the need for IV vasopressors or decrease their dose and duration (2). Dr.