2. Flannery AH, Bastin ML, Magee CA, Bensadoun ES. Vitamin C in sepsis: When it seems too sweet, it might (literally) be. *Chest*. 2017;152(2):450-451.
3. Fowler AA III, Syed AA, Knowlson S, et al. Phase I safety trial of intravenous ascorbic acid in patients with severe sepsis. *J Transl Med*. 2014;12:32.
4. Cho J, Ahn S, Yim J, et al. Influence of vitamin C and maltose on the accuracy of three models of glucose meters. *Ann Lab Med*. 2016;36(3):271-274.
5. Ceriotti F, Kaczmarek E, Guerra E, et al. Comparative performance assessment of point-of-care testing devices for measuring glucose and ketones at the patient bedside. *J Diabetes Sci Technol*. 2015;9(5):268-277.

Response

To the Editor:

In a retrospective before and after study, we demonstrated that the combination of vitamin C, hydrocortisone, and thiamine limited the progression of organ failure and reduced the mortality of patients with severe sepsis and septic shock.[1] In their letter, Hager et al correctly note that with point of care (POC) glucose monitors that use the glucose-dehydrogenase method of testing (eg, Accu-Chek), spuriously elevated POC glucose levels have been reported in patients with burns who received large doses of vitamin C (> 50 g/d).[2] Furthermore, Ma et al[3] demonstrated a linear correlation between the POC true glucose difference and the serum vitamin C concentration. Based on available pharmacokinetic data,[4] we predicted that the serum concentration of vitamin C obtained with our dosing regimen (1.5 g intravenously every 6 hours)[1] would result in a clinically insignificant error using the Accu-Chek POC device. However, because the kidney excretes > 50% of the administered dose, elevated levels of vitamin C and spuriously elevated POC glucose measurements may be obtained in patients with renal compromise. We have confirmed these postulates in a retrospective observational study conducted in our ICU (Paul E. Marik, MD, FCCP, unpublished data, 2018). These data suggest that in patients with severe kidney failure and those with end-stage renal disease, POC blood glucose measurements using the Accu-Chek device be confirmed using the central laboratory. Furthermore, these observations may only be clinically relevant in those ICUs aiming for tight glycemic control.

Paul E. Marik, MD, FCCP
Norfolk, VA

AFFILIATIONS: From the Division of Pulmonary and Critical Care Medicine, East Virginia Medical School.

FINANCIAL/NONFINANCIAL DISCLOSURES: See earlier cited article for author conflicts of interest.

CORRESPONDENCE TO: Paul E. Marik, MD, FCCP, Division of Pulmonary and Critical Care Medicine, East Virginia Medical School, 825 Fairfax Ave, Ste 410, Norfolk, VA 23507; e-mail: marikpe@evms.edu

DOI: https://doi.org/10.1016/j.chest.2018.03.020

References

1. Marik PE, Khangoora V, Rivera R, et al. Hydrocortisone, vitamin C and thiamine for the treatment of severe sepsis and septic shock: a retrospective before-after study. *Chest*. 2017;151(6):1229-1238.
2. Kahn SA. Fictitious hyperglycemia: point-of-care glucose measurement is inaccurate during high-dose vitamin C infusion for burn shock resuscitation. *J Burn Care Res*. 2015;36(2):e67-e71.
3. Ma Y, Sullivan GG, Schrick E, et al. A convenient method for measuring blood ascorbate concentration in patients receiving high-dose intravenous ascorbate. *J Am Coll Nutr*. 2013;32(3):187-193.
4. de Grooth HJ, Manubulu-Choo WP, Zandvliet AS, et al. Vitamin C pharmacokinetics in critically ill patients: a randomized trial of four IV regimens. *Chest*. 2018;153(6):1368-1377.

Survival After an ICU Hospitalization for Pulmonary Hypertension

To the Editor:

The critical care management of patients with pulmonary hypertension (PH) is challenging[1] and is associated with high mortality.[2-5] Long-term outcomes of patients with PH who survive an episode of critical illness have not been characterized. Our study aimed to elucidate the clinical features, mortality, and predictors of long-term mortality after an admission to the medical ICU (MICU) in patients with PH.

We conducted a retrospective cohort study of adult groups of 1, 4, or 5 patients with PH enrolled in the Cleveland Clinic PH registry (institutional review board number 8097) admitted to the MICU between January 2009 and June 2011. We collected clinical, functional, hemodynamic, and laboratory data before MICU admission (considered baseline) and during MICU admission. Primary outcome was post-MICU discharge mortality. Study patients were compared with matched patients that did not have a MICU admission during the study period. Patients were matched to be within the same age categories defined by decade, gender, and year of diagnostic right heart catheterization.

Table 1 shows the baseline clinical features of the 63 study patients and the matched PH cohort without a MICU admission. The most common reason for

TABLE 1] Baseline Characteristics: Study Group (n = 63) and Matched Group (n = 58)

Characteristic	Total, Study Group, %	Total, Matched Group, %	*P* Value
Age, y	51 ± 15	52 ± 15	.89
Female	48 (76.2)	43 (74.1)	> .99
PH categories			.37
PAH	51 (81)[a]	47 (81.0.3)[b]	
CTEPH	6 (9.5)	6 (10.3)	
Miscellaneous	6 (9.5)[c]	4 (6.9)[d]	
6MWD, m	273 ± 135 (n = 48)	286 ± 160 (n = 57)	.2
NYHA class			.054
I-II	14 (33.3)	16 (53.4)	
III-IV	28 (66.7)	14 (46.7)	
BNP, pg/mL (n = 42)	451 ± 622	276 ± 433	.045
Pericardial effusion	14/50 (28.0)	13/55 (23.6)	.69
Right heart catheterization			
RAP, mm Hg	12.2 ± 6.6 (n = 58)	8.2 ± 6.5	.001
Mean PAP, mm Hg	54.2 ± 12.5 (n = 60)	42.2 ± 15.0	< .001
CI, L/min/m^2	2.59 ± 1.05 (n = 57)	2.11 ± 1.7	.75
PVR, Wood units	10.0 ± 5.4 (n = 53)	7.12 ± 5.0 (n = 53)	.003
PAWP, mm Hg	14.4 ± 9.7 (n = 57)	11.7 ± 5.4	.15
PAH therapies	52 (89.7)	52 (89.7)	> .99
Prostacyclin	30 (51.7)	11 (19.0)	< .001
PDE5-inhibitor	39 (67.2)	23 (39.7)	.003
ERA	14 (24.1)	18 (31)	.41

Data presented as mean ± SD unless otherwise indicated. 6MWD = 6-min walk distance; BNP = B-type natriuretic peptide; CI = cardiac index; CTEPH = chronic thromboembolic pulmonary hypertension; ERA = endothelin receptor antagonist; PAH = pulmonary arterial hypertension; PAWP = pulmonary artery wedge pressure; PAP = pulmonary artery pressure; PDE5 = phosphodiesterase; PVR = pulmonary vascular resistance; RAP = right atrial pressure.
[a]16 idiopathic, 3 heritable, 1 hereditary hemorrhagic telangiectasia, 1 anorexygen, 15 connective tissue disease, 6 congenital heart disease, 7 portal hypertension, 2 pulmonary veno-occlusive disease.
[b]13 idiopathic, 3 heritable, 1 COPD, 2 ILD, 1 diastolic dysfunction.
[c]3 sarcoid, 1 pulmonary histiocytosis, 1 fibrosing mediastinitis, 1 chronic renal failure.
[d]3 sarcoid, 1 pulmonary histiocytosis, 1 fibrosing mediastinitis, 1 chronic renal failure.

admission was right heart failure (RHF), followed by septic shock. The MICU mortality rate was 22.2% (14/63). Eleven of 14 patients who died in the MICU were admitted for worsening RHF; the remaining three had sepsis. RHF was the cause of death in 64% (9/14).

Mortality rates 6, 12, and 24 months after discharge were 26.5%, 40.8%, and 45.8%, respectively. In the postdischarge period, 85% (17/20) died of RHF. Independent factors that predicted post-MICU discharge mortality were age (hazard ratio [HR], 1.66; 95% CI, 1.13-2.43), baseline mean right atrial pressure (HR, 1.43. 95% CI, 0.98-2.09), and platelet count (HR, 1.37. 95% CI, 0.99-1.90) at time of MICU admission. Compared with matched patients (n = 58), those admitted to the MICU had reduced survival since the date of PH diagnosis (Fig 1).

The main finding of our study is that a MICU admission for PH is associated with poor survival after discharge. Older age, baseline RHF, and severity of organ dysfunction while in the MICU were independent predictors of long-term mortality. Close monitoring and aggressive therapy are warranted for patients with PH who survive an episode of critical illness.

Vickram Tejwani, MD
Baltimore, MD
Divya C. Patel, MD
Gainesville, FL
Joe Zein, MD, FCCP
Jorge A. Guzman, MD
Cleveland, OH
Enrique Diaz-Guzman, MD
Birmingham, AL

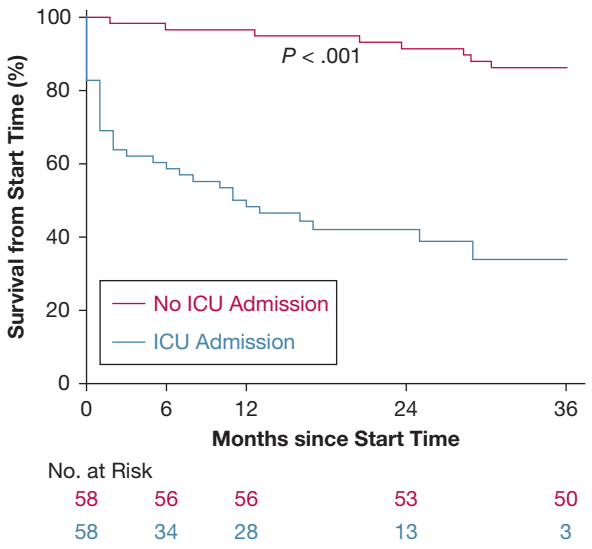

Figure 1 – *Post-MICU discharge survival in our cohort compared with matched patients without MICU admission during the study period. Patients admitted to the MICU had a 1- and 2-year survival rates of 48.3% and 42.0%, respectively, compared with 96.5% and 91.31% (hazard ratio, 7.79; 95% CI, 3.68-16.49). MICU = medical ICU.*

Eduardo Mireles-Cabodevila, MD
Raed A. Dweik, MD, FCCP
Gustavo A. Heresi, MD
Cleveland, OH

AFFILIATIONS: From Pulmonary and Critical Care (Dr Tejwani), Johns Hopkins Hospital; Pulmonary and Critical Care Faculty (Dr Patel), University of Florida; Pulmonary and Critical Care Faculty (Drs Zein, Guzman, Mireles-Cabodevila, Dweik, and Heresi), Cleveland Clinic; and Pulmonary and Critical Care Faculty (Dr Diaz-Guzman), University of Alabama-Birmingham.

FINANCIAL/NONFINANCIAL DISCLOSURES: See earlier cited article for author conflicts of interest.

CORRESPONDENCE TO: Gustavo A. Heresi, MD, Pulmonary and Critical Care Faculty, 9500 Euclid Avenue, A90, Cleveland Clinic, Cleveland, OH 44195; e-mail: heresig@ccf.org

DOI: https://doi.org/10.1016/j.chest.2018.03.028

References

1. Hoeper MM, Granton J. Intensive care unit management of patients with severe pulmonary hypertension and right heart failure. *Am J Respir Crit Care Med*. 2011;184(10):1114-1124.
2. Sztrymf B, Souza R, Bertoletti L, et al. Prognostic factors of acute heart failure in patients with pulmonary arterial hypertension. *Eur Respir J*. 2010;35(6):1286-1293.
3. Campos A, Mathai SC, Le Pavec J, et al. Outcomes of hospitalisation for right heart failure in pulmonary arterial hypertension. *Eur Respir J*. 2011;38(2):359-367.
4. Huynh TN, Weigt SS, Sugar CA, Shapiro S, Kleerup EC. Prognostic factors and outcomes of patients with pulmonary hypertension admitted to the intensive care unit. *J Crit Care*. 2012;27(6):739.
5. Tonelli AR, Arelli V, Minai OA, et al. Causes and circumstances of death in pulmonary arterial hypertension. *Am J Respir Crit Care Med*. 2013;188(3):365-369.

Children With Cystic Fibrosis May Be Performing Oscillating Positive Expiratory Pressure Therapy Incorrectly

To the Editor:

For more than 40 years, chest physiotherapy has been the primary mechanism to remove excess secretions and break the cycle of obstruction, infection, inflammation, and damage to pulmonary tissue in patients with cystic fibrosis (CF). Oscillating positive expiratory pressure (OPEP) devices have become ubiquitous internationally as aids to remove excess secretions and trapped gas for patients with hypersecretory conditions.[1] During OPEP therapy, patients are instructed to inspire slightly more deeply than normal, to hold their breath briefly, and then to exhale with the help of abdominal muscles through the device to below their functional residual capacity level but not all the way to residual volume.[2] The accepted target therapeutic pressure range is 10 to 20 cmH_2O, at a flow rate of 10 to 20 L/min,[3] repeated 10 to 20 times with 2 to 3 additional "huff" coughs to clear any loosened secretions.

Although instructions for patients are relatively clear, we have observed considerable variation in adherence to recommended OPEP techniques by pediatric patients with CF and have designed a study to evaluate whether the potential therapeutic benefit was being diminished. With appropriate ethical approval and consents, a convenience sample of 21 pediatric patients was recruited. Each had a history of adhering to use of an OPEP device twice daily and had received standardized training and instructions from the same CF physiotherapist. Performance was evaluated using a flow and pressure sensor placed in-line between the participant's mouth and device. To avoid infection risks,[4] a disposable bacteria and virus filter was placed proximal to the sensor for each participant.

Recorded peak flow and pressure measurements raise concerns because none were within the therapeutic target range detailed above. Peak pressures were several times the maximum therapeutic range, whereas peak flows of more than eight times the prescribed maximum were seen (Fig 1). Well-intentioned parents were observed actively encouraging their child to complete shorter and more forceful expirations, relying on the premise that "more is better", as would be the norm