Kantonsspital St.Gallen

Effect of a Strategy of Comprehensive Vasodilation vs Usual Care on Mortality and Heart Failure Rehospitalization Among Patients With Acute Heart Failure: The GALACTIC Randomized Clinical Trial

Nikola Kozhuharov,Assen Goudev,Dayana Flores,Micha T. Maeder,Joan Walter, Samyut Shrestha,Danielle Menosi Gualandro,Mucio Tavares De Oliveira Junior,Zaid Sabti,Beat Müller,Markus Noveanu,Thenral Socrates,Ronny Ziller,Antoni Bayés-Genís,Alessandro Sionis,Patrick Simon,Eleni Michou,Samuel Gujer,Tommaso Gori, Philip Wenzel,Otmar Pfister,David Conen,Ioannis Kapos,Richard Kobza,Hans Rickli, Tobias Breidthardt,Thomas Münzel,Paul Erne,Christian Mueller & GALACTIC Investigators

Importance
Short-term infusions of single vasodilators, usually given in a fixed dose, have not improved outcomes in patients with acute heart failure (AHF).

Objective
To evaluate the effect of a strategy that emphasized early intensive and sustained vasodilation using individualized up-titrated doses of established vasodilators in patients with AHF.

Design, Setting, and Participants
Randomized, open-label blinded-end-point trial enrolling 788 patients hospitalized for AHF with dyspnea, increased plasma concentrations of natriuretic peptides, systolic blood pressure of at least 100 mm Hg, and plan for treatment in a general ward in 10 tertiary and secondary hospitals in Switzerland, Bulgaria, Germany, Brazil, and Spain. Enrollment began in December 2007 and follow-up was completed in February 2019.

Interventions
Patients were randomized 1:1 to a strategy of early intensive and sustained vasodilation throughout the hospitalization (n = 386) or usual care (n = 402). Early intensive and sustained vasodilation was a comprehensive pragmatic approach of maximal and sustained vasodilation combining individualized doses of sublingual and transdermal nitrates, low-dose oral hydralazine for 48 hours, and rapid up-titration of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or sacubitril-valsartan.

Main Outcomes and Measures
The primary end point was a composite of all-cause mortality or rehospitalization for AHF at 180 days.

Results
Among 788 patients randomized, 781 (99.1%; median age, 78 years; 36.9% women) completed the trial and were eligible for primary end point analysis. Follow-up at 180 days was completed for 779 patients (99.7%). The primary end point, a composite of all-cause mortality or rehospitalization for AHF at 180 days, occurred in 117 patients (30.6%) in the intervention group (including 55 deaths [14.4%]) and in 111 patients (27.8%) in the usual care group (including 61 deaths [15.3%]) (absolute difference for the primary end point, 2.8% [95% CI, -3.7% to 9.3%]; adjusted hazard ratio, 1.07 [95% CI, 0.83-1.39]; P = .59). The most common clinically significant adverse events with early intensive and sustained vasodilation vs usual care were hypokalemia (23% vs 25%), worsening renal function (21% vs 20%), headache (26% vs 10%), dizziness (15% vs 10%), and hypotension (8% vs 2%).

Conclusions and Relevance
Among patients with AHF, a strategy of early intensive and sustained vasodilation, compared with usual care, did not significantly improve a composite outcome of all-cause mortality and AHF rehospitalization at 180 days.

Trial Registration
ClinicalTrials.gov Identifier: NCT00512759.

type	journal paper/review (English)
date of publishing	2019
journal title	JAMA (322/23)
ISSN electronic	1538-3598
pages	2292-2302