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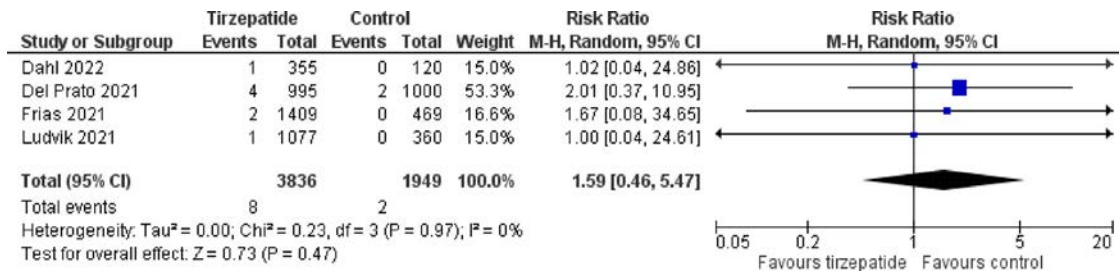


Figure 1. Effect of tirzepatide compared with control on the risk for atrial fibrillation in patients with type 2 diabetes mellitus.

on the risk for AF (risk ratio = 1.59; 95% confidence interval 0.46 to 5.47; $I^2 = 0\%$; $p = 0.47$), as shown in Figure 1. No statistical heterogeneity was shown for this comparison. All trials were graded as low risk of bias.

Therefore, tirzepatide, besides being cardiovascular safe, also does not increase the risk for AF in patients with T2DM. Previous studies seem to be insufficient in reaching definitive conclusions or speculating on potential mechanisms by which tirzepatide might have a true effect on AF.¹¹ The forthcoming SURPASS-CVOT (NCT04255433) trial should shed further light on the cardiovascular efficacy and safety of this novel agent in T2DM.

Disclosures

The authors have no conflicts of interest to declare.

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- Bell DSH, Goncalves E. Atrial fibrillation and type 2 diabetes: prevalence, etiology, pathophysiology and effect of anti-diabetic therapies. *Diabetes Obes Metab* 2019;21:210–217.
- Huxley RR, Fillion KB, Konety S, Alonso A. Meta-analysis of cohort and case-control studies of type 2 diabetes mellitus and risk of atrial fibrillation. *Am J Cardiol* 2011;108:56–62.
- Lavie CJ, Pandey A, Lau DH, Alpert MA, Sanders P. Obesity and atrial fibrillation prevalence, pathogenesis, and prognosis: effects of weight loss and exercise. *J Am Coll Cardiol* 2017;70:2022–2035.

- Patoulias D, Toumpourleka M, Papadopoulos C, Doumas M. Meta-analysis evaluating the risk of atrial fibrillation with newer antidiabetics across the cardiovascular and renal outcome trials. *Am J Cardiol* 2021;139:139–141.
- Patoulias D, Michailidis T, Papadopoulos C, Karagiannis A, Doumas M. Meta-analysis of randomized controlled trials evaluating the effect of dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonists on blood pressure levels in patients with type 2 diabetes mellitus. *Am J Cardiol* 2022;166:144–145.
- Sattar N, McGuire DK, Pavo I, Weerakkody GJ, Nishiyama H, Wiese RJ, Zoungas S. Tirzepatide cardiovascular event risk assessment: a pre-specified meta-analysis. *Nat Med* 2022;28:591–598.
- Dahl D, Onishi Y, Norwood P, Huh R, Bray R, Patel H, Rodríguez Á. Effect of subcutaneous tirzepatide vs placebo added to titrated insulin glargine on glycemic control in patients with type 2 diabetes: the SURPASS-5 randomized clinical trial. *JAMA* 2022;327:534–545.
- Frias JP, Davies MJ, Rosenstock J, Pérez Manghi FC, Fernández Landó L, Bergman BK, Liu B, Cui X, Brown K. SURPASS-2 Investigators. Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. *N Engl J Med* 2021;385:503–515.
- Ludvik B, Giorgino F, Jódar E, Frias JP, L Fernández Landó, Brown K, Bray R, Á Rodríguez. Once-weekly tirzepatide versus once-daily insulin degludec as add-on to metformin with or without SGLT2 inhibitors in patients with type 2 diabetes (SURPASS-3): a randomised, open-label, parallel-group, phase 3 trial. *Lancet* 2021;398:583–598.
- Del Prato S, Kahn SE, Pavo I, Weerakkody GJ, Yang Z, Doupis J, Aizenberg D, Wynne AG, Riesmeyer JS, Heine RJ, Wiese RJ. SURPASS-4 Investigators. Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4): a randomised, open-label, parallel-group, multicentre, phase 3 trial. *Lancet* 2021;398:1811–1824.
- Jujić A, Nilsson PM, Persson M, Holst JJ, Torekov SS, Lyssenko V, Groop L, Melander O, Magnusson M. Atrial natriuretic peptide in the high normal range is associated with lower prevalence of insulin resistance. *J Clin Endocrinol Metab* 2016;101:1372–1380.

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Right Ventricular Abnormality in Patients Hospitalized With COVID-19 Infection During Omicron Variant Surge

Echocardiographic changes in the acute phase of COVID-19 infection have been extensively reported during the COVID-19 pandemic. Measures of right ventricular (RV) performance during acute infection have been associated with mortality.^{1–3} We aimed at studying the association of in-hospital mortality with echocardiographic measures of RV performance during the COVID-19 infection surge in New York City attributed to the spread of the Omicron variant.²

In this retrospective study, we enrolled consecutive patients hospitalized with COVID-19 infection who underwent clinically indicated echocardiograms from December 15, 2021, to January 26, 2022. Omicron became the predominant strain in the United States in December 2021 and accounted for >99% of COVID-19 cases. Echocardiograms were performed adhering to a focused, time-efficient protocol with appropriate use of personal protective equipment and limited viral exposure time. Portable ultrasound machines were used: CX50 (Philips Medical Systems, Bothell, Washington) and Vivid S70 (GE Healthcare Systems, Milwaukee, Wisconsin). Echocardiographic studies were interpreted by experienced echocardiography attending physicians. RV abnormality was defined as basal RV diastolic diameter >4.1 cm in the RV-focused apical view and/or tricuspid annular plane systolic excursion <1.7 cm from the apical 4-chamber view. The primary end point was in-



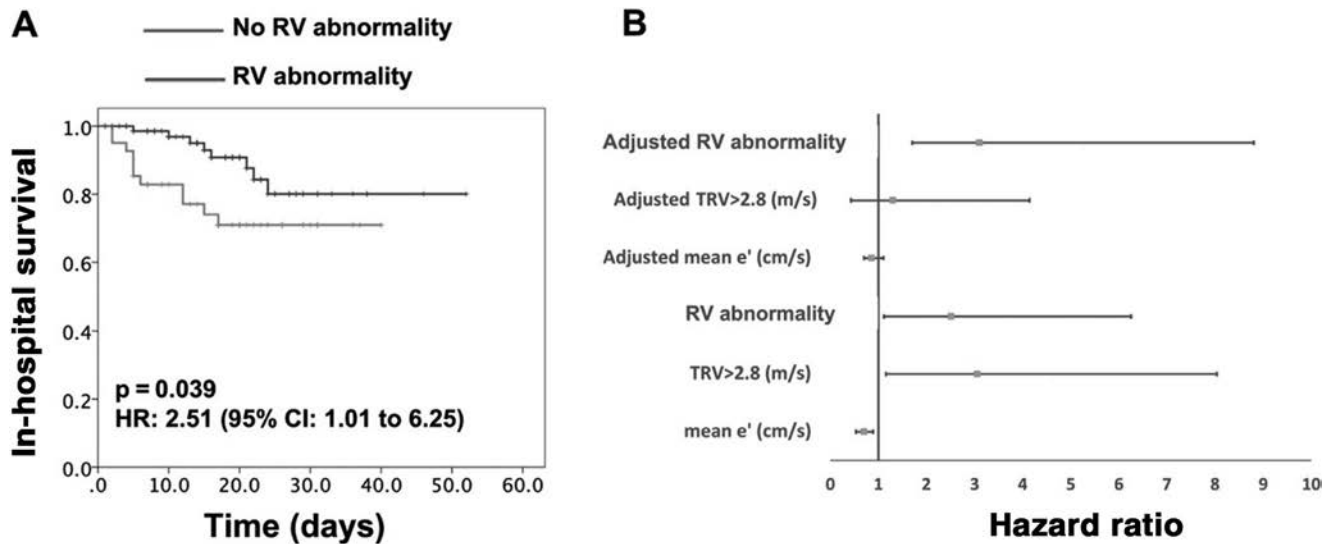


Figure 1. Echocardiographic predictors of in-hospital mortality. (A) Kaplan-Meier curve showing worse in-hospital mortality in patients with RV abnormality compared with patients without RV dysfunction. (B) Hazard ratios for echocardiographic predictors of mortality adjusted for age, mechanical ventilation, and admission troponin I levels. TRV = tricuspid regurgitation velocity.

hospital mortality. Kaplan-Meier curves and Cox regression analysis were used to explore the associations of clinical and echocardiographic predictors with in-hospital mortality. The study protocol was approved by the Institutional Review Board.

Echocardiograms of 122 consecutive patients were reviewed. The mean age was 69 ± 14.5 years, and 62 patients (51%) were women. Thirty-seven patients (30%) were admitted to the intensive care unit, and 25 (21%) were intubated and mechanically ventilated at the time of the echocardiographic examination. The mean RV diastolic diameter was 3.5 ± 0.78 cm, with >4.1 cm in 27 patients (22%). The mean tricuspid annular plane systolic excursion was 2.1 ± 0.5 cm with <1.7 cm in 22 patients (18%). Despite consideration of the Omicron strain as a milder variant, 41 patients (34%) had RV dysfunction, comparable with previous reports of COVID-19 infections with earlier strains. Patients with and without RV abnormality did not differ significantly in age, gender, body mass index, major cardiovascular co-morbidities, and COVID-19 vaccination status. There were also no significant differences in the admission values of white blood cell count, C-reactive protein, serum creatinine, D-dimer levels, or serum lactate levels. However, patients with RV abnormality had higher serum troponin I levels (1.5 ± 5.5 vs 0.25 ± 0.8 ng/mL, $p=0.048$). There were no

differences between groups in the use of therapeutic anticoagulation (68% vs 71%, $p = 0.8$) or corticosteroid therapy (61% vs 53%, $p = 0.38$). Patients with RV abnormality had lower left ventricular ejection fraction (52 ± 14 vs $58 \pm 10\%$, $p = 0.012$; 29% vs 14% with EF $<50\%$, $p = 0.046$), and greater left atrial volume index (40 ± 22 vs 32 ± 15 ml/m², $p = 0.03$) and tricuspid regurgitation velocity (2.5 ± 0.7 vs 2.2 ± 0.7 m/s, $p = 0.019$). By the end of study, 19 patients (16%) had died; 11 (27%) with RV abnormality and 8 (10%) without RV dysfunction, $p = 0.019$ (Figure 1). Univariate Cox regression analysis showed that age (hazards ratio [HR] 1.04, $p = 0.037$, 95% confidence interval [CI] 1.003 to 1.1), admission troponin I level (HR 1.2, $p < 0.001$, 95% CI 1.08 to 1.28), and mechanical ventilation (HR 16.1, $p < 0.001$, 95% CI 5.34 to 48.7) were clinical variables associated with in-hospital mortality. The mean e' velocity (HR 0.76, $p = 0.008$, 95% CI 0.62 to 0.931), tricuspid regurgitation velocity >2.8 m/s (HR 3.1, $p = 0.024$, 95% CI 1.16 to 8.04), and RV abnormality (HR 2.51, $p = 0.047$, 95% CI 1.01 to 6.25) were echocardiographic variables associated with in-hospital mortality, although left ventricular ejection fraction was not associated with the outcome. After adjusting for the clinical variables (age, troponin I level, and mechanical ventilation), only RV abnormality remained associated with in-hospital

mortality (HR 3.1, $p = 0.032$, 95% CI 1.1 to 8.8).

This study confirms that RV abnormality remained prevalent in hospitalized patients with COVID-19 infection during the Omicron surge in New York City. RV abnormality was strongly and independently associated with in-hospital mortality. Prospective studies should elucidate the role of therapeutic interventions on the measures of RV performance in these patients.

Disclosures

The Adolfo García-Sastre laboratory has received research support from Pfizer, Senhwa Biosciences, Kenall Manufacturing, Avimex, Johnson & Johnson, Dynavax, 7 Hills Pharma, Pharmamar, ImmunityBio, Accurius, nanoComposix, Hexamer, N-fold LLC, Model Medicines, Atea Pharmaceuticals and Merck, outside of the reported work. Dr. García-Sastre has consulting agreements for the following companies involving cash and/or stock: Vivaldi Biosciences, Contrafact Corporation, 7 Hills Pharma, Avimex, Vaxalto, Pagoda, Accurius, Esperovax, Farmak, Applied Biological Laboratories, Pharmamar, Paratus, CureLab Oncology, CureLab Veterinary, Synairgen, and Pfizer, outside of the reported work. Dr. García-Sastre is the inventor of patents and patent applications on the use of antivirals and vaccines for the treatment and prevention of virus infections and cancer, owned by the

Icahn School of Medicine at Mount Sinai, New York, outside of the reported work. The other authors have no conflicts of interest to declare.

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- Omar A, De La Cruz Tejada A, Ronderos D, Hernandez N, Miranda J, Rehmani A, Nicu M, Chilimuri S, Bella JN. Echocardiography derived predictors of worse outcomes in the acute phase of COVID-19 patients compared to matched controls. *J Am Coll Cardiol* 2021;77:3168.
- Argulian E, Sud K, Vogel B, Bohra C, Garg VP, Talebi S, Lerakis S, Narula J. Right ventricular dilation in hospitalized patients with COVID-19 infection. *JACC Cardiovasc Imaging* 2020;13:2459–2461.
- Diaz-Arocutipia C, Saucedo-Chinchay J, Argulian E. Association between right ventricular dysfunction and mortality in COVID-19 patients: a systematic review and meta-analysis. *Clin Cardiol* 2021;44:1360–1370.

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Trends in Timing of Coronary Angiography in Patients With Out-of-Hospital Cardiac Arrest and Non-ST Elevation Myocardial Infarction: A Real-World Analysis

Although immediate coronary angiography (CA) is recommended for

patients with out-of-hospital cardiac arrest (OHCA) and ST-elevation myocardial infarction,¹ recent trials do not support routine early CA for patients presenting with OHCA and non-ST elevation myocardial infarction (NSTEMI).^{2,3} To understand the potential impact of recent trials on clinical practice, we examined trends in the timing of CA and in-hospital mortality associated with early versus delayed CA for patients with OHCA and NSTEMI using data from the Nationwide Inpatient Sample (NIS) during a period before recent trials were published.

Using the International Classification of Diseases (ICD), Ninth Revision (ICD-9) and ICD-Tenth Revision, we identified patients in the NIS with OHCA (ICD-9: 427.5, ICD-Tenth Revision: I46, I46.2, I46.8, I46.9, positive predictive value 78% to 94%)⁴ and NSTEMI, who underwent CA during 2005 to 2019. We excluded patients with procedure codes for cardiopulmonary resuscitation (to avoid capturing in-hospital cardiac arrest),^{4,5} and those with missing data for age, gender, survival to discharge, or timing of CA. Timing of CA was categorized as early (day of admission) versus delayed.⁶ For our primary outcome, we evaluated trends in early versus delayed CA. As a secondary outcome, we evaluated trends in in-hospital mortality. We constructed a multivariable logistic regression model that included treatment, calendar year, and an interaction between treatment and year to explore whether change in mortality over time differed by treatment strategy. We also examined predictors of early CA by constructing a separate multivariable logistic regression model. To allow for national estimation because the NIS is a stratified sample, all analyses were weighted. Analyses were evaluated at a 2-sided significance level of 0.05. This study was deemed exempt by the institutional review board as data were deidentified.

A total of 49,861 patients with OHCA and NSTEMI underwent CA, of whom 18,427 had early CA (37.0%). Patients who underwent early versus delayed CA were less frequently women (30.7% vs 36.2%), younger (median [interquartile range] of 67 [48 to 86] vs 68 [49 to 87] years), and had a

higher prevalence of shockable cardiac arrest (56.6% vs 49.8%), history of CAD (82.5% vs 76.1%), cardiogenic shock (27.7% vs 18.9%), use of mechanical circulatory support (25.2% vs 13.7%), and higher in-hospital mortality (31.2% vs 22.1%); *p* for all <0.001. Rates of early CA modestly decreased between 2005 and 2019 (35.7% to 34.2%, *p*-trend <0.001; **Figure 1**). In-hospital mortality decreased from 34.2% in 2005 to 23.2% in 2019 overall (*p*-trend <0.001) and decreased both for patients who underwent early CA (32.8% to 28.8%; *p*-trend <0.001) and delayed CA (34.9% to 20.3%; *p*-trend <0.001), with no difference between the strategies in the magnitude of the mortality trend (*p* for interaction = 0.76). Younger age, male gender, weekday admission, having mechanical complications, using mechanical circulatory support, cardiogenic shock, and shockable cardiac arrest were independent predictors of early CA (**Figure 1**).

There are relevant limitations to this analysis. Although our approach to identify patients with OHCA has been validated,⁵ the risk of mis- or undercoding remains. We did not examine patients with OHCA and NSTEMI who did not receive CA because we were unable to determine type 1 versus type 2 NSTEMI using ICD-9 codes. Moreover, the NIS lacks data on neurologic recovery, coronary anatomy, time-to-return of spontaneous circulation, and severity of shock; some of these factors may have contributed to survival bias in the delayed CA group; the difference in in-hospital mortality between both groups should be considered exploratory.

In a contemporary, nationwide analysis of patients with OHCA and NSTEMI who underwent CA during the index admission, there was a slight decrease in use of early CA between 2005 and 2019. In-hospital mortality decreased over time in those who underwent early CA and delayed CA, with no difference in the reduction between both groups. These results provide real-world data on trends in early CA and outcomes in patients with OHCA before recent trials. Further analysis will be needed during years that follow publication of trials demonstrating no benefit with early CA in this population.

