Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Gender and ST-elevation myocardial infarction. Response

Sexo e infarto agudo de miocardio con elevación del ST. Respuesta

To the Editor,

We read with interest the letter "Gender and ST-elevation myocardial infarction", which discussed the results of the study by Sambola et al.[1] and those of our study.[2]

The apparent contradictions between them may be for the following reasons: *a)* our study was based on data from an official audited registry, the *Registro Codi IAM* for Catalonia, on a reperfusion program in acute ST-segment elevation myocardial infarction (STEMI), which prioritized primary angioplasty (PA); *b)* the cohort was a homogeneous population with ischemic heart disease: patients with first acute STEMI and final diagnosis of infarction (20% of those with initial suspicion were excluded); the comparison of heterogeneous cohorts can involve differences in age and the prevalence of risk factors; *c)* the in-hospital mortality was not published due to the high rate of transfer from the hospital where PA was performed. If we exclude the transferred patients (12% for the study by Sambola et al.[1]), the patient profile would be skewed upward; *d)* the raw mortality data were influenced by the large age difference between men and women, so we decided not to publish them and instead focused on the total mortality reported by the National Institute of Statistics; *e)* given the impossibility of including other risk factors (collected from 2015 onward) in the models and the importance of age, we decided to match for age: the odds ratio/hazard ratio (OR/HR) of the adjustment variables were not shown, as they should not be interpreted in models that evaluate the specific effect of the variable of interest, in this case sex; nor were the discrimination capacities and goodness-of-fit described, because the objective was not to obtain predictive models, but rather to estimate the possible effect of patient sex on mortality; regardless of this consideration, the area under the curve (AUC) at 30 days was 82.6% [84.2%-85.8%] and at 1 year was 80.0% [77.8%-82.2%], and Hosmer-Lemeshow goodness-of-fit, chi-square = 39.1; $P < .001$ at 30 days and chi-square = 17.1; $p = .047$ at 1 year; and *f)* treatment delays must also be considered as confounders of the effect of sex: Sambola et al. reported lower mortality in women treated within a structured reperfusion network than outside of such a network, and, in 2015, the last year common to both studies, the rate of PA in the study by Sambola et al. was 51.7% for women vs 68% for men, and in our study the rate of PA within 120 minutes was 65% vs 71%.

Due to all these factors, we are of the opinion that: *a)* it is difficult to compare these studies; *b)* the in-hospital mortality varied greatly depending on the hospital, province, and autonomous community where the patients were treated; *c)* the strategy of reperfusion within a network has benefits for both sexes, perhaps more so in women; and *d)* the inequalities in mortality between the sexes detected more than 20 years ago[3] have been overcome, largely due to the structured reperfusion strategy, the *Codi IAM* in Catalonia, in line with what our group observed in a different patient cohort.[4]

Helena Tizón-Marcos,[a,b,c,*] Isaac Subirana,[b,d] and Jaume Marrugat[b,e]

[a]*Servicio de Cardiología, Hospital del Mar, Grupo de Investigación Biomédica en Enfermedades del Corazón, IMIM, Barcelona, Spain*
[b]*Instituto Hospital del Mar de Investigaciones Médicas (IMIM), Barcelona, Spain*
[c]*Facultat de Medicina, Universitat Autònoma de Barcelona, Bellaterra, Barcelona, Spain*
[d]*Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP), Spain*
[e]*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*

[*] Corresponding author:
E-mail address: htizon@parcdesalutmar.cat (H. Tizón-Marcos).

Available online 15 January 2021

REFERENCES

1. Sambola A, Elola FJ, Ferreiro JL, et al. Impact of sex differences and network systems on the in-hospital mortality of patients with ST-segment elevation acute myocardial infarction. *Rev Esp Cardiol.* 2020. http://doi.org/10.1016/j.rec.2020.08.001.
2. Tizón-Marcos H, Vaquerizo B, Marrugat J, et al. Differences in 30-day complications and 1-year mortality by sex in patients with a first STEMI managed by the Codi IAM network between 2010 and 2016. *Rev Esp Cardiol.* 2021;74:674–681.
3. Marrugat J, Sala J, Masia R, et al. Mortality differences between men and women following first myocardial infarction, RESCATE Investigators. Recursos Empleados en el Sindrome Coronario Agudo y Tiempo de Espera. *JAMA.* 1998;280:1405–1409.
4. Marrugat J, Garcia M, Elosua R, et al. Short-term (28 days) prognosis between genders according to the type of coronary event (Q-wave versus non-Q-wave acute myocardial infarction versus unstable angina pectoris). *Am J Cardiol.* 2004;94:1161–1165.

https://doi.org/10.1016/j.rec.2020.11.011

SEE RELATED CONTENT:
10.1016/j.rec.2020.09.030

Relationship between patent foramen ovale and COVID-19 in patients admitted to an intensive care unit

Foramen oval permeable en pacientes ingresados por COVID-19 en cuidados intensivos

To the Editor,

In December 2019, an outbreak of coronavirus disease 2019 (COVID-19), which was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), broke out in Wuhan, China.[1,2] COVID-19 was of clustering onset and mainly affected the respiratory system with some patients rapidly progressing to acute respiratory distress syndrome (ARDS).[3,4] Evidence shows that, while patients with COVID–19-associated respiratory distress syndrome meet the Berlin criteria for ARDS, they generally present with an atypical form of this syndrome.[5]

Patent foramen ovale (PFO) is an integral part of the normal fetal circulation. The anatomical closure of the foramen ovale occurs around the second year of life in the majority of the population.[6] Autopsy and detailed contrast echocardiography studies demonstrate that anatomic closure is incomplete in approximately 1 in every 4 adults, with the frequency being similar in both sexes.[7]

PFO may have significant clinical implications. It may lead to several pathological conditions, notably right-to-left shunt, paradoxical embolism, hypoxemia, and cerebral fat embolism.[8–11] Older patients with cryptogenic embolism and PFO exhibited a higher burden of cardiovascular risk factors.[12]

Mechanical ventilation, especially in patients with ARDS, may stretch the pulmonary vasculature and right ventricle, thus reversing the interatrial pressure gradient, leading to the foramen ovale opening and a right-to-left shunt.[13,14] The prevalence of PFO is reported to be between 16% and 19% even in ARDS patients mechanically ventilated with protective ventilation strategies.[15–17] A PFO shunt is associated with decreased effectiveness of positive end-expiratory pressure titration in improving oxygenation, greater use of adjunctive interventions, and longer times on mechanical ventilation and in the intensive care unit.[17]

For this reason, we decided to evaluate patients with COVID-19 under mechanical ventilation to identify PFO and the pathophysiological effects of this structural heart disorder on the treatment process of patients with COVID-19 and also to obtain an appropriate strategy for managing mechanical ventilation in these patients and evaluating its effectiveness in their recovery.

FUNDING

The authors received no financial support for the research, authorship, and/or publication of this article.

AUTHORS' CONTRIBUTIONS

S. Eskandari conceived of the presented idea and P. Jalali developed the theory. P. Jalali wrote the article in consultation with S. Eskandari.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

Saber Eskandari[a] and Pooya Jalali[b,*]

[a]*Department of Nursing, School of Nursing & Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[b]*Department of Medicine, Islamic Azad University Tabriz Branch, Tabriz, Iran*

* Corresponding author:
E-mail address: Pooya.jalali1995@gmail.com (P. Jalali).

Available online 04 May 2021

REFERENCES

1. Huang C, Wang Y, Li X, et al. Clinical features of patients with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395:497–506.
2. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.* 2020;382:727–733.
3. Chan JF., Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020;395:514–523.
4. Phan LT, Nguyen TV, Luong QC, et al. Importation and human-to-human transmission of a novel coronavirus in Vietnam. *N Engl J Med.* 2020;382:872–874.
5. Nader DN, Ata M. COVID-Associated Respiratory Distress Syndrome [CARDS] in Pregnancy; What Makes it so Different? *IJWHR.* 2020;8:336–337.
6. Kutty S, Sengupta PP, Khandheria BK. Patent foramen ovale: the known and the to be known. *J Am Coll Cardiol.* 2012;59:1665–1671.
7. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc.* 1984;59:17–20.
8. Seward JB, Hayes DL, Smith HC, et al. Platypnea-orthodeoxia: clinical profile, diagnostic workup, management, and report of seven cases. *Mayo Clin Proc.* 1984;59:221–231.
9. Ranoux D, Cohen A, Cabanes L, Amarenco P, Bousser MG, Mas JL. Patent foramen ovale: is stroke due to paradoxical embolism? *Stroke.* 1993;24:31–34.
10. Rimoldi SF, Ott S, Rexhaj E, et al. Patent Foramen Ovale Closure in Obstructive Sleep Apnea Improves Blood Pressure and Cardiovascular Function. *Hypertension.* 2015;66:1050–1057.
11. Pell AC, Hughes D, Keating J, Christie J, Busuttil A, Sutherland GR. Brief report: fulminating fat embolism syndrome caused by paradoxical embolism through a patent foramen ovale. *N Engl J Med.* 1993;329:926–929.
12. Wintzer-Wehekind. Alperi A, Houde C, et al. Transcatheter closure of patent foramen ovale in patients older than 60 years of age with cryptogenic embolism. *Rev Esp Cardiol.* 2020;73:219–224.
13. Asrress KN, Marciniak M, Marciniak A, Rajani R, Clapp B. Patent foramen ovale: the current state of play. *Heart.* 2015;101:1916–1925.
14. Cujec B, Polasek P, Mayers I, Johnson D. Positive end-expiratory pressure increases the right-to-left shunt in mechanically ventilated patients with patent foramen ovale. *Ann Intern Med.* 1993;119:887–894.
15. Lhéritier G, Legras A, Caille A, et al. Prevalence and prognostic value of acute cor pulmonale and patent foramen ovale in ventilated patients with early acute respiratory distress syndrome: a multicenter study. *Intensive Care Med.* 2013;39:1734–1742.
16. Boissier F, Katsahian S, Razazi K, et al. Prevalence and prognosis of cor pulmonale during protective ventilation for acute respiratory distress syndrome. *Intensive Care Med.* 2013;39:1725–1733.
17. Dessap AM, Boissier F, Leon R, et al. Prevalence and prognosis of shunting across patent foramen ovale during acute respiratory distress syndrome. *Crit Care Med.* 2010;38:1786–1792.

https://doi.org/10.1016/j.rec.2021.04.012