

# The impact of group II pulmonary hypertension on congestive heart failure patients admitted with ST elevation myocardial infarction, a nationwide study

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**Background:** Pulmonary hypertension (PH) is a condition where the blood pressure increases in the pulmonary arteries, leading to reduced oxygen delivery to the body's tissues due to increased blood flow resistance. This condition can result in right ventricular hypertrophy, low cardiac output, and ischemia. In this study, the authors aim to investigate the impact of group II PH (GIIPH) on patients with congestive heart failure who were admitted with ST elevation myocardial infarction (STEMI) through a retrospective cohort study.

**Methods:** Using the National Inpatient Sample (NIS) database from 2017 to 2020, a retrospective crosssectional study of adult patients with a principal diagnosis of STEMI with a secondary diagnosis with or without GIIPH according to ICD-10 (International Classification of Disease, 10th edition) codes. Several demographics, including age, race, and gender, were analyzed. The primary endpoint was mortality, while the secondary endpoints included cardiogenic shock, mechanical intubation, length of stay in days, and patient charge in dollars. Multivariate logistic regression model analysis was used to adjust for confounders, with a P value less than 0.05 considered statistically significant.

**Results:** The study included 26,925 patients admitted with a STEMI, 95 of whom had GIIPH. The mean age for patients with and without PH was 66.6 and 67.5 years, respectively. In the PH group, 37% were females compared to 34% in the non-PH group. The in-hospital mortality rate was higher in the PH group (31.6% *vs.* 9.6%, P<0.001, adjusted odds ratio (aOR) =3.33, P=0.02). The rates and adjusted odds of cardiogenic shock and mechanical ventilation were higher in the PH groups (aOR =1.15 and 2.14, respectively) but not statistically significant. Patients with PH had a longer length of stay and a higher total charge.

**Conclusions:** GIIPH was associated with worse clinical and economic outcomes in heart failure patients admitted with STEMI.

**Keywords:** ST elevation myocardial infarction (STEMI); group II pulmonary hypertension (GIIPH); National Inpatient Sample (NIS); cardiogenic shock; hospital charges

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#### Introduction

Coronary artery disease (CAD) remains the leading cause of death and disability worldwide in adults (1,2). Myocardial infarction (MI) occurs due to CAD and is classified as transmural MI and non-transmural MI. In contrast to a non-transmural MI, a transmural MI affects the epicardium, myocardium, and endocardium (3). ST segment elevations or depressions are key findings that allow an MI to be detectable on electrocardiograms (ECGs). Patients with presenting symptoms are streamlined into different treatment regimens based on the ST elevation myocardial infarction (STEMI) versus non-ST elevation myocardial infarction (NSTEMI) paradigm. This paradigm can delay life-saving treatments, i.e., emergent reperfusion, in patients without suspecting ECG findings yet with complete acute coronary occlusion (4).

Pulmonary hypertension (PH) is characterized by elevated blood pressure in the pulmonary arteries, resulting in increased blood flow resistance and reduced oxygen delivered to the body's tissues. PH is defined as a mean

#### Highlight box

#### Key findings

• Congestive heart failure patients with group II pulmonary hypertension (GIIPH) have worse outcomes in acute ST-elevation myocardial infarction (STEMI) compared to those without pulmonary hypertension (PH).

#### What is known and what is new?

- Elevated pulmonary arterial pressure is associated with increased right ventricle (RV) afterload, myocardial dysfunction, and impaired hemodynamics.
- The authors present data on all-cause mortality and cardiogenic shock in patients with and without GIIPH. The results reflect worse outcomes even after adjusting for underlying confounders such as age and comorbidities.
- We also report the trends of STEMI admissions in this patient population before [2017-2018-2019] and after [2020] the coronavirus disease 2019 (COVID-19) pandemic.

#### What is the implication, and what should change now?

- Clinical providers should be aware that patients with PH are at high risk for increased mortality and morbidity during their hospitalization. This necessitates proper triage to higher levels of care on admission.
- The authors believe that patients with congestive heart failure should be screened for associated PH in the outpatient setting. This will facilitate the identification of such high-risk patients on admission for an acute event such as a STEMI.

pulmonary arterial pressure (PAP)  $\geq 20$  mmHg at rest, measured via right heart catheterization (5). However, a clinical diagnosis can be made with significant left heart disease or chronic lung disease. The pathogenesis of PH is multifactorial and can involve multiple systems; therefore, PH is subdivided into five groups based on pathophysiology. Group I PH also referred to as pulmonary arterial hypertension; group II PH (GIIPH), which arises from left heart disease; group III PH, which results from chronic lung disease and/or hypoxemia; group IV PH, due to chronic thromboembolic disease; and group V PH, caused by multifactorial mechanisms (6). The link between PH and MI has been established, with PH being a known risk factor for MI through right ventricular hypertrophy, decreased cardiac output (CO), and subsequent ischemia of the myocardium, in addition to other mechanisms. In this study, we further explore the clinical and economic impact of GIIPH on patients admitted with STEMI. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/ view/10.21037/jtd-24-221/rc).

#### **Methods**

#### Design and description of the database

We conducted a retrospective study using the National Inpatient Sample (NIS) from 2017 to 2020. We compared the clinical outcomes of patients with and without PH admitted with STEMI. The NIS is part of the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality (AHRQ) (7). The NIS is the largest inpatient hospital discharge database in the United States. It approximates a 20% stratified sample of discharges from US community hospitals, excluding rehabilitation and long-term acute care hospitals. The AHRQ has developed linkable files called the cost-to-charge ratio (CCR) that can convert total charges into the actual cost of hospital services. The cost information was obtained from the hospital accounting reports in the Healthcare Cost Report Information System (HCRIS) files collected by the Centers for Medicare & Medicaid Services (CMS). CCR files have hospitalspecific CCRs based on all-payer inpatient or emergency department costs for most hospitals in the corresponding NIS. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

# Data user agreement

Dr. M.E.L. (first author) completed the data user agreement with HCUP-AHRQ. The HCUP datasets are publicly available and hence are considered exempt from full or expedited institutional review boards (IRB) review [Federal Regulations 45 CFR 46.101 (b)].

# Selection of cases and outcome variables examined

In the NIS dataset, the principal diagnosis is the main ICD-10 [International Classification of Disease, 10th edition, clinical modification (ICD-10-CM)] code of admission to the hospital and is linked to inpatient status. Final ICD-10 codes are based on final diagnoses after the hospitalization is complete. The secondary diagnosis is a medical condition the patient has on the problem list that could have happened before or during that admission. All procedure codes detected via NIS are linked to the hospitalization. In our study, STEMI was selected as the principal diagnosis. Our inclusion criteria included adult patients (age 18 years or older) with a history of congestive heart failure presenting with a non-elective/ urgent admission under a principal diagnosis of STEMI from 2017 to 2020. As this was a retrospective crosssectional study using a large dataset, the authors included all patients who met the criteria. Therefore, the study size wasn't calculated and authors do not report missing data. We divided the sample into two groups-one with GIIPH and the other without. Due to the nature of this study, the diagnosis of PH is based on the ICD-10 code rather than diagnostic tools such as echocardiogram and right heart catheterization. As the patient dataset is de-identified, the authors do not have access to the patients' records to further evaluate whether such diagnostic procedures were performed. ICD-10 codes were also used to identify secondary diagnoses that included diabetes mellitus (DM), essential hypertension, supraventricular tachycardia (SVT), chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), dementia, obesity, and sepsis. The Charlson Comorbidity Index (CCI) also describes patients' comorbidities. Outcomes, including mortality, cardiogenic shock, mechanical ventilation, length of stay, and total charges, were generated from the NIS dataset. Our exclusion criteria included patients with acute decompensated congestive heart failure and patients with PH other than group two. Our outcomes included all-cause inpatient mortality, total length of stay, and total hospital

charge, all of which are readily available variables extracted from the NIS dataset. We also looked at the incidence and odds of the development of cardiogenic shock, which we were able to identify as a secondary diagnosis using the ICD-10 code R57.0, and the need for invasive ventilation, which was identified using a set of procedure codes linked to the admission. Appendix 1 includes the ICD-10 codes that were used for the study.

# Statistical analysis

Statistical analyses were conducted using STATA BE version 17.0. All statistical tests were two-sided, and a P value of <0.05 was considered statistically significant. Chi-square analysis was used to describe the difference in patients' characteristics and secondary diagnoses according to the presence and absence of PH. The impact of PH on outcomes was defined using two methods: Chi-square analysis to compare outcomes' rates and multivariable regression models to describe the isolated impact of PH on the odds of the outcome. All the regression models in our study had a significant F value (Prob > F < 0.01), which in turn confirms that the independent variables reliably predict the studied variable. The following variables were included in the regression model: age, female gender, race [white (as the reference), black, Hispanic, Asian/Pacific, native American, other), CCI as categories [group 0 (score of 0, this was the reference), group 1 (score of 1), group 2 (score of 2), group 3 (score of  $\geq$ 3)], insurance status [Medicare (reference), Medicaid, private insurance, self-pay], type II DM, obesity, hypertension, CKD, SVT, sepsis, COPD, and dementia.

### Results

The study analyzed 26,925 patients who were hospitalized with STEMI from 2017 to 2020, out of which 95 had associated GIIPH. *Table 1* represents the patient demographics from the study and is separated based on the presence or absence of GIIPH. The average age of patients without PH was 67.5 years, and that of patients with PH was 66.6 years. The differences in the proportion of patients with and without PH across ethnicities were not statistically significant. CCI scores of three or more were relatively increased in the patients with GIIPH compared to non-GIIPH patients. All comorbidities were increased in patients with GIIPH than in patients without GIIPH; SVT

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Table 1 Clinical an	d demographic	characteristics
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STEMI         26,830         95         -           Female, n [%]         9,140 [34]         35 [37]         0.78           Age (years)         67.5         66.6         -           Year, n [%]         0.06         -           2017         5,780 [21.5]         0           2018         6,010 [22.4]         40 [42]           2019         7,350 [27.4]         35 [37]           2020         7,690 [28.7]         20 [21]           Race, n [%]         0.67           White         19,020 [71]         55 [58]           Black         3,640 [14]         25 [26]           Hispanic         2,365 [9]         10 [11]           Asian or Pacific Islander         820 [3]         0 [0]           Native American         165 [0.6]         0           O         0         0         *           0         0         0         *           1         0         0         *           1         0         0         *           0         0         0         *           1         0         0         *           1         0         0         *      <	Characteristics	Without GIIPH		P value
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SVT         6,707 [25]         54 [57]         <0.001           COPD         4,561 [17]         14 [15]         0.85           Dementia         1,341 [5]         5 [5]         0.95	DMII	11,805 [44]	44 [47]	0.77
COPD4,561 [17]14 [15]0.85Dementia1,341 [5]5 [5]0.95	HTN	23,342 [87]	90 [95]	0.34
Dementia 1,341 [5] 5 [5] 0.95	SVT	6,707 [25]	54 [57]	<0.001
	COPD	4,561 [17]	14 [15]	0.85
CKD 5,098 [19] 44 [47] <0.001	Dementia	1,341 [5]	5 [5]	0.95
	CKD	5,098 [19]	44 [47]	<0.001

\*, as there is a zero in the marginals, it is not possible to compute the statistics. GIIPH, group II pulmonary hypertension; STEMI, ST elevation myocardial infarction; DMII, type II diabetes mellitus; HTN, hypertension; SVT, supraventricular tachycardia; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease. and CKD were substantially more prevalent in patients with PH. There were more than twice as many patients with SVT and CKD in the GIIPH group.

#### Primary and secondary outcomes

Rates and odds of all-cause in-hospital mortality were significantly higher in patients with GIIPH and STEMI (P<0.001) (*Table 2*). Patients with GIIPH had worse secondary outcomes as well. Rates and odds of in-hospital cardiogenic shock and mechanical ventilation were relatively increased in patients with STEMI (*Table 2*). Though not statistically significant, the mean length of stay and total hospital charges (*Figure 1*) were more prolonged and higher in patients with GIIPH and STEMI.

### Discussion

### Demographics

Compared to the same race in the GIIPH cohort, white patients had a higher proportion of patients without GIIPH. (8) The discrepancy in the proportion of patients with and without GIIPH in one race may be due to extrinsic factors-for instance, lack of recruitment of minority races and socioeconomic status. Most research published on PH reflects white participants. A study out of Columbia University Medical Center has shown that white patients had a significantly lesser degree of socioeconomic distress than their black counterparts (9). This is consistent with black patients having a higher proportion of PH. Physician and medical research distrust among minority populations could account for discrepancies in race representation in research (10). Additionally, there could be a lack of understanding of medical trials amongst minority races due to language barriers or the overuse of medical jargon.

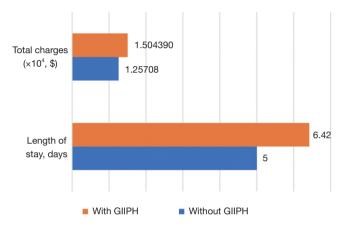
## Individual comorbidities and the CCI score

There were more patients in our analysis with CCI scores of three or more who had GIIPH. Given the relative increase in comorbidities, patients with GIIPH may generally be sicker. PH may be idiopathic but is also commonly associated with other diseases. Metabolic disorders, certain types of cancers, lung disease, and left heart disease are just a few diseases that put patients at risk for developing PH or are associated with PH (11). There was a relative increase in the number of patients with each comorbidity with respect to the GIIPH cohort compared to the non-PH cohort.

## Table 2 Primary and secondary outcomes

STEMI	Total, n [%] –	GIIPH, n [%]			Adjusted	050/ 01	P value
		Without	With	P value	odds ratio	95% CI	P value
In-hospital mortality rates and odds	2,610 [10]	2,580 [9.6]	30 [31.6]	<0.001	3.33	1.2–9.22	0.02
In-hospital cardiogenic shock rates and odds	3,894 [14]	3,874 [14]	20 [21]	0.41	1.15	0.35–3.76	0.81
In-hospital mechanical ventilation rates and odds	3,481 [13]	3,451 [13]	30 [31.6]	0.01	2.14	0.74–6.18	0.16

STEMI, ST elevation myocardial infarction; GIIPH, group II pulmonary hypertension; CI, confidence interval.



**Figure 1** Mean length of stay and total charges. GIIPH, group II pulmonary hypertension.

SVT and CKD were both significantly more prevalent in patients with GIIPH compared to patients without PH. SVT can result in heart failure (12). CHF can cause elevated hydrostatic pressures in the pulmonary vasculature, leading to the development of GIIPH (13-15). Similarly, there were significantly more patients with CKD in the PH cohort. CKD may incite pulmonary vascular dysfunction and eventual PH through the release of uremic toxins and subsequent inflammation and endothelial dysfunction; thus, GIIPH is a highly prevalent disease in patients with CKD (16).

# In-hospital mortality and cardiogenic shock

Patients with GIIPH had significantly higher in-hospital mortality and cardiogenic shock rates after a STEMI compared to those without GIIPH, even after adjustment with the CCI. Although the in-hospital mortality outcome reflects all-cause inpatient mortality, those with GIIPH have more systemic complications than those without GIIPH, which could contribute to the increased risk of in-hospital mortality. Elevated PAP is associated with right ventricle (RV) afterload, myocardial dysfunction, and impaired hemodynamics. The impaired perfusion due to low CO and the systemic congestion caused by impaired RV function affects multiple organs. For example, systemic consequences of PH include congestive hepatopathy in the liver, low perfusion renal injury in the kidneys, and increased systemic inflammation due to the release of soluble pro-inflammatory chemokines/cytokines (17). Furthermore, elevated PAP in the chronic state also causes RV dysfunction that causes eccentric remodeling and contractile dysfunction of the RV (17). The higher rates of cardiogenic shock are likely due to the RV dysfunction. RV dilation and increased RV size cause a mechanical septal leftward shift, leading to compression of the left ventricle (LV) (18). As a result, the LV displays a "D-shape", and there is an increased LV eccentricity index (17). Furthermore, low CO from the RV dysfunction can contribute to the underfilling of the LV, leading to reduced LV CO and further exacerbating the cardiogenic shock. This effect can be further exacerbated during MI, such as an inferior MI in which the RV is affected, further contributing to RV dysfunction. Cardiogenic shock is a severe complication of acute MI (AMI); those with cardiogenic shock and STEMI have higher fatality rates than those with NSTEMI (19). There was a relatively higher rate of cardiogenic shock in patients with PH/STEMI. This occurrence is likely due to ischemia that can occur as a result of chronic PH and RV dysfunction, as STEMI is due to transmural infarction and a greater burden of ischemia (19). These consequences, in addition to RV failure and hemodynamic instability, contribute to the higher risk of in-hospital mortality and cardiogenic shock in these patients.

#### Mechanical ventilation

GIIPH was an independent risk factor for needing mechanical ventilation after AMI. There are no studies in the current literature that investigate this trend. One possible explanation is related to the effects of PH on skeletal muscles and the diaphragm. PH has been shown to adversely affect striated muscles other than the RV, such as the diaphragm and peripheral skeletal muscle (20). Studies investigating the pathophysiology of this occurrence have yet to show consistent results. Still, there is evidence in the literature of both decreased maximal tension (21) and decreased slow twitch fibers in the diaphragm, which correlated with maximal inspiratory pressure (20).

#### Admission length of stay and total cost

Patients with GIIPH experienced more extended hospital stays following MI after adjusting for comorbidities and their CCI scores. Patients had spent an average of 34.08 hours more in the hospital. One explanation for this is that after undergoing percutaneous coronary intervention (PCI), patients are at an increased risk of cardiomyocyte reperfusion injury that could result in heart failure (22). These effects may be exacerbated in patients who already have GIIPH in addition to its associated right ventricular heart failure (23). The likelihood of ventricular wall rupture and mortality are significantly increased in patients with elevated PAP (24). More extended hospital stays and consecutive post-MI interventions precipitate more considerable hospital costs, as shown in Figure 1. Patients with GIIPH had more expensive hospital stays than patients without PH. In 2015, Plent et al. calculated the median cost for patients undergoing an uncomplicated PCI in their study to be about \$18,419 (25). Therefore, on top of the baseline cost of treating a patient with MI, patients with GIIPH who are already at an increased risk of complications may end up costing the hospital hundreds to thousands of additional dollars.

#### Limitations

There are some limitations to our study. We conducted a retrospective study using the NIS, an administrative database that limits the uniformity of STEMI and GIIPH diagnosis with potential misclassification secondary to the use of the ICD-10 CM codes. Second, because of the administrative nature of our database, our analysis did not include the severity of the disease (such as the degree of right ventricular dysfunction at baseline and admission) at admission or the types, dosages, and frequencies of different STEMI-specific treatments. Third, the primary cause of mortality is not specified in NIS; therefore, we presented the total all-cause mortality. Finally, since this is not a randomized controlled trial, the conclusion that GIIPH significantly impacts the outcomes of STMEI should be viewed with caution. Our study continued into 2020, during the time when the coronavirus disease 2019 (COVID-19) pandemic had already begun. Unfortunately, COVID-19 cases were underreported, limiting our ability to determine the frequency of infections accurately. To address this limitation, we conducted a subanalysis over 4 years. The results indicate no significant difference in the number of STEMI patients between the two groups across the 4 years (P=0.06, Table 1). Despite these limitations, this study is an important contribution to understanding the relationship between STEMI and GIIPH. This study is the first to investigate that relationship using the NIS and, hence, with a remarkably large sample size. Although we only identified 95 patients with GIIPH, our results are statistically significant. However, further investigations will require a larger sample size of patients with GIIPH. Moreover, we investigated how GIIPH affected the total charges during hospital stays, which is not traditionally included in most studies.

#### Conclusions

Our study, investigating the clinical and economic impact GIIPH has on patients admitted to the hospital with an AMI, reveals important insights into this highrisk population's clinical outcomes and management. Our findings indicate that the presence of GIIPH significantly impacts the prognosis of patients with AMI. The demographic analysis highlights the need for tailored approaches, as certain populations may be more vulnerable to the detrimental effects of PH. GIIPH is an independent risk factor for in-hospital mortality, cardiogenic shock, and mechanical ventilation, underscoring the importance of early identification and appropriate management of this condition. Secondary to the nature of this study the generalizability of the results could be limited due to the lack of clinical diagnostics. Nonetheless, these results emphasize the need for healthcare providers to be vigilant and proactive in recognizing and addressing PH in patients

with STEMI to optimize patient outcomes and reduce morbidity and mortality.

Further research should focus on elucidating the underlying mechanisms behind why PH is an independent risk factor for post-MI complications and investigating targeted interventions to improve the prognosis of this complex patient population.

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# Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://jtd. amegroups.com/article/view/10.21037/jtd-24-221/rc

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-221/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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