

Metformin Discontinuation in Acute Heart Failure

Curtis Wong¹, Erica Junqueira², Nayda Parisio-Poldiak², Nancy Crossley¹, Shantae Jenkins¹

1- Internal Medicine Residency – Trident Health; 2 – HCA Healthcare

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Study Team

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**Dr. Curtis
Wong**
(IM-PGY1)



**Erica
Junqueira**
(Corporate Statistician)



**Dr. Nayda
Parisio-Poldiak**
(Division Research Director)



**Dr. Nan
Crossley**
(IM-Program Director)



**Dr. Shantae
Jenkins**
(IM-Faculty Mentor)

Our mission

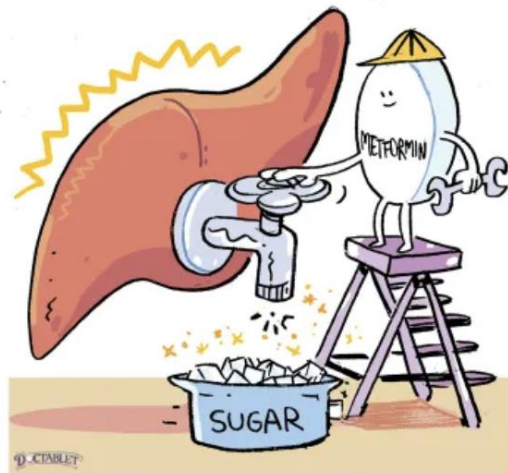
Above all else, we are committed to the care and improvement of human life.

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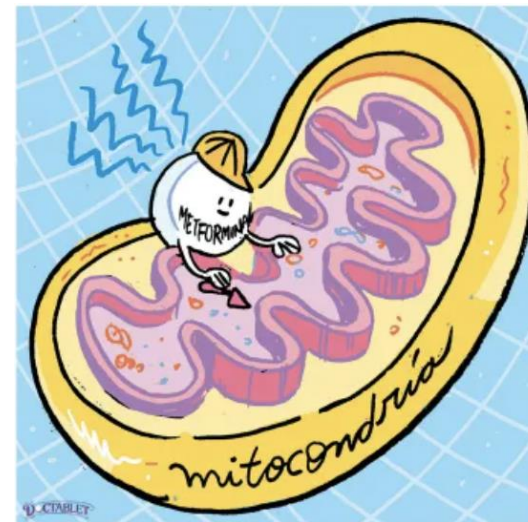
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Introduction

- **Diabetes Mellitus** (DM) is a prevalent comorbidity in patients with **heart failure** (HF) that can cause increased mortality and hospitalizations (1).
- The first-line oral medication for diabetes mellitus (DM) type II patients is **metformin**, which lowers the risk of complications, diabetes-related death, and myocardial infarction (2).



* Image Source: Does Metformin Cause Weight Loss?
Chirs Palmero, DO. MSc. Doctablets. Weight Loss.
<https://doctablet.com/weight-loss/metformin-weight-loss/#.ZEJ54HbMJPw>



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Introduction (cont.)

- Metformin was **originally** seen as **dangerous for people with heart failure** since it can produce lactic acidosis (3).
- Studies show that metformin can be administered safely in people with DM who are at risk of or already have heart failure as long as their estimated **glomerular filtration rate** (eGFR) is more than 30 ml/min/1.73 m² (4).
- Metformin has known to have cardioprotective effects (5). Individuals taking metformin experience **fewer hospitalizations** for heart failure exacerbations. Patients with diabetes and HF taking metformin have **lower overall mortality**. (6, 7).

Objective/Hypothesis

- It has not been determined whether discontinuing metformin in patients with heart failure results in changes in outcomes.
- Acute exacerbation of chronic heart failure contributes to substantial increases in **major adverse cardiovascular events (MACE)** (8). We **propose** a retrospective study of how discontinuing metformin in patients hospitalized with heart failure impacts the risk of mortality and readmission rates for MACE.
- We **hypothesize** that diabetic patients admitted with acute heart failure exacerbations who were discontinued from metformin therapy during hospitalization and no longer prescribed after discharge, will have a higher incidence of major adverse cardiac events and an impact on readmission rates.

Methods

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Study Population



- IRB Exempt Determination: #2023-017
- Retrospective study within the HCA Healthcare System → Enterprise Data Warehouse
- Timeline: **2016** to **2022**
- **36,688 distinct encounters** with diabetes and heart failure present on admission

| Encounters removed | Reason |
|--------------------|---|
| 399 | missing sex and race data |
| 2,568 | removed for having renal disease |
| 4,972 | outcome present on admission (stroke, MI, Severe heart failure) |
| 20,543 | missing A1C, glucose or troponin lab |
| 466 | keep only one encounter per patient |

Final population: 7740

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Analysis Plan

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- Primary Endpoints: **30-, 60-, 90-day readmission rates**
- Independent Variables: **demographics – age, sex, race, etc., metformin therapy discontinuation**
- **Binary logistic regression** was performed to ascertain the association between predictor variables, metformin discontinuation and various control variables, and patients experiencing a MACE outcome.

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Results

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Descriptive Table

| | Total | Continue Metformin=No N=6,991 | Continue Metformin=Yes N=749 | P-value |
|-------------------------------|----------------|----------------------------------|---------------------------------|--------------------------|
| Sex | | | | |
| Female | 3,160 (40.83%) | 2,835 (40.55%) | 325 (43.39%) | 0.1330 |
| Male | 4,580 (59.17%) | 4,156 (59.45%) | 424 (56.61%) | Chi square |
| Age | | | | |
| Median (IQR) | 71.00 (16.00) | 71.00 (16.00) | 70.00 (16.00) | 0.0471 Mann Whitney * |
| Race | | | | |
| Black | 1,375 (17.76%) | 1,232 (17.62%) | 143 (19.09%) | 0.6041 |
| Other | 906 (11.71%) | 819 (11.72%) | 87 (11.62%) | Chi square |
| White | 5,459 (70.53%) | 4,940 (70.66%) | 519 (69.29%) | |
| HTN | 5,022 (64.88%) | 4,456 (63.74%) | 566 (75.57%) | <.0001 Chi square * |
| Asthma | 1,548 (20.00%) | 1,376 (19.68%) | 172 (22.96%) | 0.0329 Chi square * |
| CKD | 723 (9.34%) | 670 (9.58%) | 53 (7.08%) | 0.0250 Chi square * |
| Acute Kidney Failure | 3,300 (42.64%) | 3,103 (44.39%) | 197 (26.30%) | <.0001 Chi square * |
| Heart Failure Category | | | | |
| Combined | 1,297 (16.76%) | 1,194 (17.08%) | 103 (13.75%) | 0.0064 |
| Diastolic | 3,685 (47.61%) | 3,290 (47.06%) | 395 (52.74%) | Chi square * |
| Systolic | 2,758 (35.63%) | 2,507 (35.86%) | 251 (33.51%) | |
| Metformin Disch | 5,162 (66.69%) | 4,569 (65.36%) | 593 (79.17%) | <.0001 Chi square * |

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Patients Not Discharged With Metformin

MACE outcome

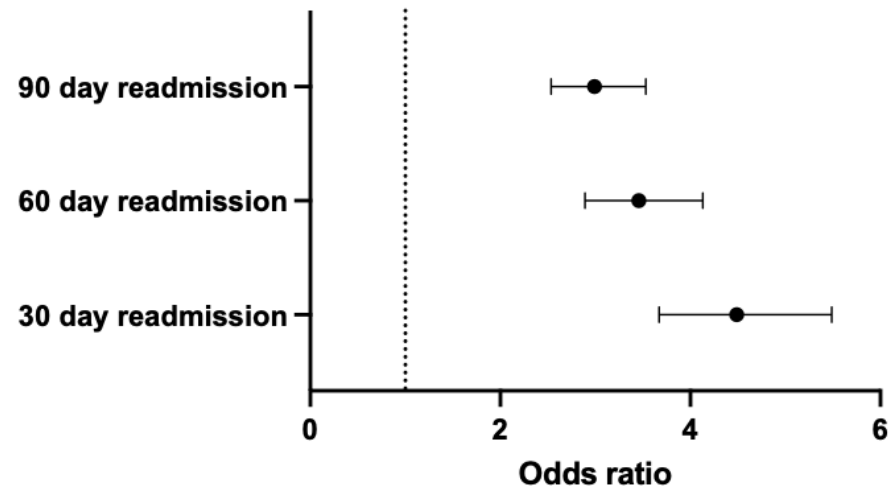
➔ 30 days readmission rate → 4.489 (95% CI 3.673-5.488, $p < 0.0001$)

➔ 60 days readmission rate → 3.457 (95% CI 2.893-4.131, $p < 0.0001$)

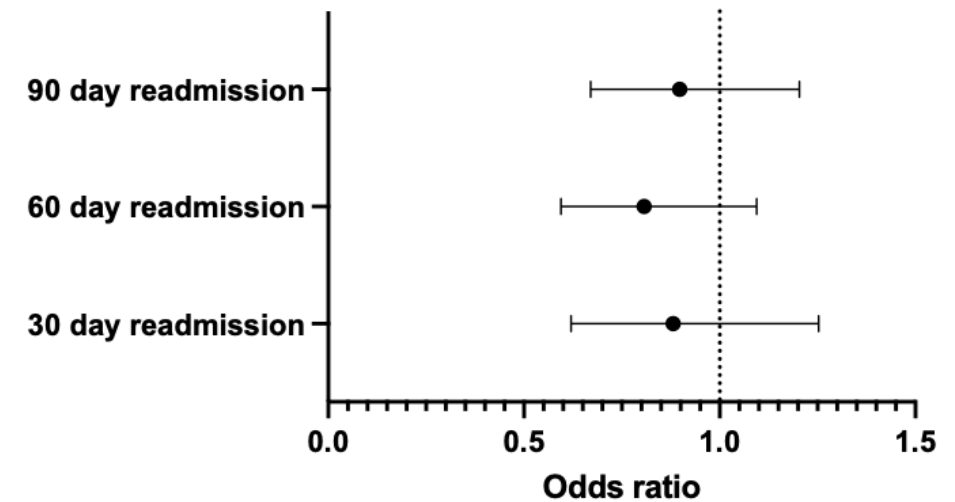
➔ 90 days readmission rate → 2.992 (95% CI 2.534-3.533 $p < 0.0001$)

- **6,991** patients did not continue metformin and **749** patients did
- Continuation of metformin during hospital stay was found to not be statistically significant.

Discontinuation of Metformin on Discharge



Discontinuation of Metformin Inpatient



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Discussion

- This study showed that discontinuation of metformin on discharge in patients with heart failure may have a **higher incidence of major adverse cardiac events** and an **impact on readmission rates**.
- Discontinuation of metformin while in the hospital did not increase the chance of having a major adverse cardiac event.
- This information helps **support other studies** that have shown metformin to have cardioprotective effects (5).
- Unless contraindicated or not tolerated, metformin can be continued in people with type 2 diabetes and heart failure. Metformin should be temporarily withheld if renal function acutely worsens.
- Possible future studies include comparing metformin and SGLT-2s with regard to cardiac outcomes, and metformin's potential to improve myocardial function in chronic HF.

Conclusion

Diabetic patients admitted with acute heart failure exacerbations who were no longer prescribed metformin after discharge, appear to have a higher incidence of major adverse cardiac events and an impact on readmission rates

Limitations

- This study has several limitations, including a large difference in numbers between the group that continued metformin and the group that discontinued metformin.
- This study cannot account for metformin being restarted by the primary care physician after discharge. It's unclear if the patients who fared poorly didn't see their PCP shortly after leaving the hospital, potentially resulting in a longer avoidance of metformin.
- This study selected patients who had a hemoglobin A1C, glucose, and troponin testing in hospital. It is possible that this group of patients was sicker than the 20,543 patients who were excluded.

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