Digoxin Initiation and Outcomes in Patients with Heart Failure with Preserved Ejection Fraction

Background

- Digoxin has been proven to have clinical efficacy and effectiveness in patients with heart failure with reduced ejection fraction (HFrEF)
- The Digitalis Investigation Group (DIG) trial showed digoxin reduced risk heart failure hospitalization in patients with HFrEF but had no effect on all cause mortality.
- DIG trial showed digoxin did not influence all-cause mortality in patients with heart failure with preserved ejection fraction (HFpEF)
- Limited data is available on the association between digoxin use and outcome in hospitalized patients with HFpEF in clinical practice

Objective

- Determine if there was an association between digoxin use and outcomes in hospitalized patients with HFpEF

Methods

- Design: Retrospective study that used the Organized Program to initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OMPIMIZE HF), a national hospital based registry of patients hospitalized with decompensated heart failure (HF) to find patients who had heart failure and had or didn't have digoxin initiated during their stay. Total 26,376 patients were found with HF which was reduced to 1,026 by following the criteria listed in Figure one. The patients were matched by prosperity scores which looked at baseline characteristics between the groups who had digoxin initiated and those who did not.
- Inclusion: HF with ejection fraction ≥ 50% and were not receiving digoxin on admission
- Exclusion: had to be discharged alive, ejection fraction < 50%, were on digoxin pre admission, discharge heart rate > 50 beats /min, had in hospital dialysis, estimated glomerular filtration rate < 30
- Primary outcome measure: heart failure readmission for 30 days, 2 years, and 6 years of follow-up starting from the date of hospital discharge
- Secondary outcome measures: all-cause readmission, all-cause mortality, the combined endpoint of HF readmission or all-cause mortality, and the combined endpoint of all-cause readmission or all-cause mortality at all 3 time periods.
- Data was analyzed using Pearson's chi-squared and Wilcoxon rank-sum tests

Results:

- Primary outcome measure: heart failure readmission rates were found to be not statistically significant with or without digoxin in the 30 day and 6-year groups. The 2-year group was significant for heart failure readmission rates with a hazard ratio (HR) 0.80 with 95% CI: (0.64-0.99) with p = 0 .041.
- Important baseline characteristics: 46% and 48% of the patients were on warfarin in the non-digoxin initiation and digoxin initiation groups respectfully. Patients' mean ages were 79 and 80. 7% and 8% of the study populations without and with digoxin were African American and 66% of both groups were female. Patients had similar medical history and similar discharge medications in the non-digoxin and digoxin initiation groups. There were no statistically significant differences between the two groups at baseline after propensity score matching
- Authors did not mention how other discharge medications or conditions could influence the results.
- Authors could not assess adherence to the digoxin as the data was pulled from a database and were limited to what was reported
- Secondary outcome measures: heart failure readmission, all-cause readmission, all-cause mortality, heart failure readmission or all-cause mortality, and all cause readmission or all cause mortality were found to be not statically significant between groups for the 30 day and 6-year time periods. For the 2-year time period, all cause readmission and all cause mortality were found to be statistically significant with HR: 0.79 with

95% CI: (0.65-0.96) and p = 0.020 and 0.83 with 95% CI: (0.70-0.97) with p = 0 .020 respectfully. Heart failure readmission, heart failure readmission or all-cause mortality, and all-cause readmission or all-cause mortality were not statistically significant in the 2-year time period for the groups with or without digoxin.

- **Authors' conclusion**: Hospitalized patients with HFpEF who were initiated on digoxin prior to hospital discharge had 30-day and 6-year outcomes similar to those who were not initiated on digoxin.

Strengths:

- Participants in each group, with or without digoxin had similar backgrounds and similar ages with no statistically significant differences between them

Limitations:

- Study was retrospective study design relying on data from a database that was Medicare fee for service which limited the age ranges the investigators could look at. This does not represent the overall population of people with heart failure as it frequently occurs in people 65 or older, and the mean ages in study were 79 and 80. Authors also had to rely on the information being entered into the database accurately by other individuals.
- Digoxin dose was not mentioned and was not mentioned how or if the dose was adjusted for the patients.
- Authors did not mention how patients' past medical conditions or discharge medications could have influenced results

Conclusion:

In conclusion, digoxin was found to significantly reduce all cause mortality after 2 years and reduce HF readmission; however, digoxin did not reduce HF readmission and all cause mortality in the 30 days and 6-year groups. The results should be taken with caution as it is unknown if there is a benefit at the 2-year mark with digoxin and how long the benefits last. Retrospective and prospective studies should be conducted with digoxin dosing and dosing changes reported along with a wider range of ages to confirm the results of this study.

Reference:

Lam PH, Packer M, Gill GS, et al. Digoxin Initiation and Outcomes in Patients with Heart Failure with Preserved Ejection Fraction. *Am J Med*. 2020;133(10):1187-1194. doi:10.1016/j.amjmed.2020.02.040

Zachary Bryner, PharmD Candidate

11-01-2021