Impact of Pharmacy-led Congestive Heart Failure Medication Titration Clinic

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BACKGROUND

- Congestive heart failure (CHF) remains a large national burden, affecting 6.5 million people and contributing to one of the leading causes of hospitalizations. [1]
- 2013 ACCF/AHA Guideline for the Management of Heart Failure and 2017 ACC/AHA/HFSA Focused Update of the 2013 Guideline recommend the use of selected beta blockers, renin-angiotensin system inhibitors and aldosterone antagonists, if indicated. [2, 3]
- These efficacious therapies exist to reduce morbidity and mortality in patients with reduced ejection fraction, however, delaying guideline-directed medical therapy (GDMT) by one year can increase risk for worsening survival by 12%. [4]
- At Olive View-UCLA Medical Center (OVMC), limited provider access remains a barrier to this timely optimization. Pharmacist-led CHF medication titration services were developed in January 2019 to enhance the existing CHF clinic.

STUDY OBJECTIVES

OBJECTIVES: This was an IRB-approved therapeutics study to determine the impact of integration of pharmacist-led heart failure medication titration services to the congestive heart failure medication titration clinic at Olive View-UCLA Medical Center (OVMC) on acute care utilization, mortality and time to optimization of guideline-directed medical therapy (GDMT).

Primary endpoints were to determine:

- The number of acute care hospital services (i.e. urgent care, emergency department and hospitalizations) utilized for congestive heart failure, cardiac-related causes and all-causes at 30 days and 6 months post-initial visit
- The rate of mortality for congestive heart failure, cardiac-related causes and all-causes 6 months post-initial visit

Secondary endpoints were to determine:

- Time to reach maximum tolerated GDMT
- The average time between clinic visits

METHODS

- This is a retrospective cohort study conducted at Olive View-UCLA Medical Center (OVMC).
- Cohort 1 includes patients referred to the CHF clinic prior to pharmacist integration who had an initial visit between July 2017 and April 2018.
- Cohort 2 includes patients referred to the CHF clinic following pharmacist integration who had an initial visit between February 2019 to November 2019.
- The time gap between data collection periods minimized overlap among the patient population.
- *Inclusion Criteria*: Adult patients ≥ 18 years old with left ventricular ejection fraction (LVEF) ≤ 40%
- *Exclusion Criteria*: Adult patients ≥ 18 years old with left ventricular ejection fraction (LVEF) > 40% or who are lost to follow up
- Baseline patient demographics, acute care service utilization including urgent care, emergency department and hospitalizations within 6 months of initial clinic visit, time between clinic visits and time to optimization of GDMT were collected and analyzed.
- Optimization is defined as reaching maximum tolerated doses of GDMT which include beta blockers, afterload reduction medications (renin angiotensin aldosterone system inhibitors or hydralazine and nitrates) and if indicated, aldosterone antagonists.
- Reasons why patients did not reach GDMT were documented.
- Unpaired t-tests were utilized for secondary outcomes of time to optimization and average time between clinic visits between the two cohorts.
- Chi-square tests were utilized for the primary outcome of hospital service utilization and mortality between the two cohorts.
- GraphPad R Prism® with two-tailed p-values was used to calculate descriptive statistics which considered significance if the p-value was <0.05.

DEFINITIONS

A. **Congestive heart failure (CHF) patients**: For the purposes of this study, CHF patients will refer to those with a diagnosis of heart failure with left ventricular ejection fraction (LVEF) ≤ 40%
B. **Guideline-directed medical therapy (GDMT):** CHF therapy consisting of beta blockers, renin angiotensin aldosterone system inhibitors or hydralazine and nitrates, and aldosterone antagonists.
C. **Beta blockers**: Carvedilol 25 mg twice daily or Metoprolol succinate 200 mg daily
D. **Renin-angiotensin aldosterone system inhibitors**: Lisinopril 40 mg daily, Benazepril 40 mg daily, Losartan 150 mg daily, or Hydralazine 100 mg three times daily plus Isosorbide mononitrate 30 mg daily or Isosorbide dinitrate 40 mg three times daily.
E. **Aldosterone antagonists**: Spironolactone 12.5 to 25 mg daily.
F. **Optimization**: Reaching maximum tolerated doses of GDMT which may have been limited by individual patient's heart rate, symptomatic hypotension, renal function, elevated potassium, compliance or mortality.

RESULTS

Table 1. Baseline Demographics

	Cohort 1	Cohort 2	p-value
Total Number of Patients	60	93	
Average age	54.95	54.32	
Male	45	74	0.44
Female	14	19	
Non-binary	1	0	
NYHA Functional Class			
Class I	26	45	0.54
Class II	20	34	0.68
Class III	6	4	0.19
Class IV	0	0	>0.99
Unknown	8	10	0.63
Etiology of CHF			
Ischemic	17	25	0.18
Non-ischemic	26	44	
Mixed	6	2	
Unknown	11	22	
Past medical history			
Diabetes	30	41	0.47
Obesity	32	46	0.64
Hyperlipidemia	21	26	0.36
Hypertension	39	63	0.73
CKD/ESRD	18	23	0.47
Atrial fibrillation	21	26	0.36
CVA/TIA	4	10	0.57
CAD	29	42	0.70
Hyperthyroidism	2	2	0.65

Table 2. Primary Outcomes: Rate of Mortality

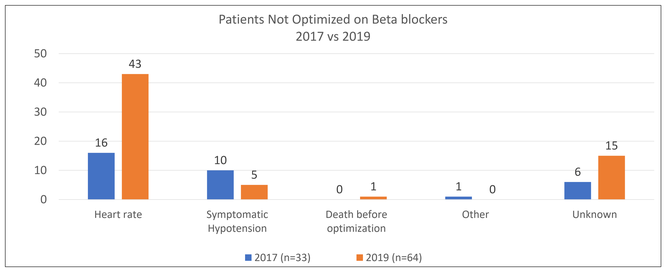
	Cohort 1	Cohort 2	p-value	RR	OR
30 days post-initial visit					
All-cause events	18.3%	15.1%	0.59	1.28 (0.60-2.45)	1.27 (0.55-3.06)
Cardiac-related events	6.7%	10.8%	0.60	0.62 (0.21-1.77)	0.59 (0.20-1.90)
Heart failure-related events	6.7%	9.7%	0.57	0.69 (0.23-2.00)	0.67 (0.22-2.28)
6 months post-initial visit					
All-cause events	45.0%	43.0%	0.81	1.05 (0.72-1.49)	1.08 (0.55-2.11)
Cardiac-related events	26.7%	24.7%	0.79	1.08 (0.62-1.84)	1.11 (0.52-2.24)
Heart failure-related events	20.0%	21.5%	0.82	0.93 (0.49-1.73)	0.91 (0.40-2.05)

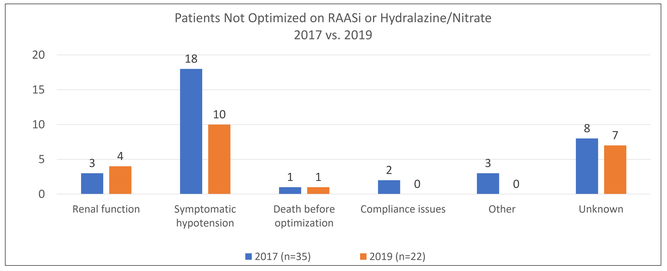
Table 2. Primary Outcomes: Rate of Mortality

	Cohort 1	Cohort 2	p-value	RR	OR
6 months post-initial visit					
All-cause deaths	13.3%	2.2%	0.01	6.20 (1.55-25.23)	7.00 (1.60-33.95)
Cardiac-related deaths	10.0%	2.2%	0.06	4.65 (1.11-19.70)	5.06 (1.20-25.08)
Heart failure-related deaths	8.3%	2.2%	0.11	3.88 (0.89-16.92)	4.14 (0.83-21.16)

Table 3. Secondary Outcomes

	Cohort 1	Cohort 2	p-value
Time to reach maximum tolerated GDMT (days)	87.6 ± 89	44.6 ± 44.9	0.0015
Average time between clinic visits (days)	13.6 ± 9.9	26.0 ± 18.5	<0.0001





DISCUSSION

- The number of acute care services utilized in Cohort 1 versus Cohort 2 for all-cause, cardiac-related and heart failure-related events at 30 days post-initial visit was not significantly different. Similarly, there was no significant difference between Cohort 1 and Cohort 2 at 6 months post-initial visit.
- In Murphy et al. 2019, heart failure or myocardial infarction 30-day readmission rates were not statistically significant with pharmacist transitions of care service involvement. [5] In contrast, Neu et al. 2020 displayed a significant decrease of ~7% in heart failure 30-day readmissions under the care of a pharmacy-led heart failure transition of care program. [6]
- Our findings are consistent with previous research; however, there is variability among current studies. The small population size may have been an influencing factor on the statistical significance.
- All-cause mortality was found to be lower in Cohort 2 compared to Cohort 1, suggesting that a pharmacist-led heart failure medication titration clinic could reduce the number of deaths due to all-cause events, though further studies may be needed to confirm these findings.
- Though cardiac-related and heart-failure related deaths were lower in Cohort 2 compared to Cohort 1, there was no statistically significant difference.
- The average time to reach maximum tolerated GDMT was 44.6 days in Cohort 2 and 87.6 days in Cohort 1 concluding that pharmacists can aid the patient care team in reaching maximum tolerated doses in a timely manner.
- There was also a shorter average time of 13.62 days between clinic visits in Cohort 2 compared to 26.04 days in Cohort 1 showing that pharmacist integration contributes to the adherence to current recommended guidelines of a 2-week follow-up after initiation or dose changes of heart failure medications to detect potential adverse side effects.[2]
- Further data was collected describing the reasons why patients were not optimized on guideline-directed medical therapy. Based on this study, most patients were not optimized on beta blockers after the implementation of pharmacists due to heart rate. Though patients were not maximized to the guideline recommended doses, one explanation of this is that pharmacists were more cautious in order to avoid the risk of adverse events due to bradycardia and potential acute care service utilization.
- Recently published studies found that pharmacist integration can improve the outcomes of CHF patients. However, considering the limited provider access to physicians at Olive View-UCLA Medical Center, the integration of pharmacists could lead to timelier optimization, closer follow-up periods while producing similar outcomes as physician management alone.

LIMITATIONS

- These results were based on a small study population.
- The OVMC CHF clinic with pharmacist integration was newly developed in January 2019.
- The collected data between each cohort was 10 months opposed to the intended 12 months to minimize overlap of patients.
- Data was not available for collection prior to July 2017.
- The follow-up period was within the following 6 months of reaching maximum tolerated GDMT. A longer study period may show underlying differences of acute care utilization and mortality between cohorts.

CONCLUSION

- A pharmacist-led CHF medication titration clinic is a promising strategy to facilitate care for CHF patients.
- Pharmacist-led care can improve provider access and time to optimization of GDMT, which is already proven to reduce morbidity and mortality.
- Acute care services utilized was unchanged following pharmacist integration, supporting that pharmacists can help produce similar patient outcomes while providing timely care for higher risk CHF patients.
- Future studies with a larger population, a longer, study period, and a more established heart failure pharmacy service may help further elucidate these findings.

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