Heart Sci J 2020; 1(1): 1-3

Contents list available at www.heartscience.ub.ac.id

Heart Science Journal

Journal Homepage : www.heartscience.ub.ac.id

Editorial

Good Physician Adherence to Guideline-Directed Medical Therapy Associated with Lower Patient Mortality and Hospitalisation Rates Across The World

Mohammad Saifur Rohman [1,2]

[1] *Brawijaya Cardiovascular Research Center, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.*
[2] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia.*

ARTICLE INFO

Keywords:
Guideline-directed medical therapy;
Physician adherence;
Mortality

ABSTRACT

While the guidelines for the managements of heart diseases have been well-developed and updated periodically, they do not guarantee to reduce the number of heart disease morbidity and mortality. Since the holistic approach is not carefully applied, this morbidity rate may not be significantly reduced. The holistic approach to managing heart disease has broad aspects, but the most important aspect is regarding physician adherence to Guideline-Directed Medical Therapy (GDMT). This paper aimed to discuss the physician adherence to GDMT, and its role in reducing morbidity and in-hospitalization in heart disease patients. Several large scale studies have revealed that good adherence to heart failure treatment guidelines among physicians improved not only quality of life but also resulted in a better prognosis. On other hands, because the main target of physicians adherence to GDMT is to achieve maximally tolerated dose, it is also important that the understanding when and how to add, switch, and titrate all therapies to maximally tolerated doses and ideally target doses is important to reduce the morbidity and mortality of heart disease patients. However, in some points, this principle might not be applied properly due to several limitations. In this case, physicians may have to consider the balance between patients preferences, healthcare resources, and the risk of adverse outcomes. In conclusion, it should be noted that physician adherence to GDMT has an important role to reduce morbidity and mortality of heart disease patients.

The incidence of heart failure (HF) is steadily increasing with an estimated 26 million people afflicted world-wide. This increase can be attributed to several factors, including prompt and improved treatment for acute myocardial infarction, an increasing prevalence of hypertension, diabetes mellitus, and aging population.[1,2] HF management consumes significant health care resources, inflicts significant morbidity and mortality, and greatly impacts quality of life. Annually, HF is the primary reason for 12 million to 15 million office visits.[3] Hospitalization due to heart failure as a primary diagnosis is reported in over 1 million patients yearly as a first diagnosis with an additional 3 million hospitalizations as a contributing diagnosis.[4] Several studies suggested HF readmission rate at 30 days was 4.9 % while 90 day rehospitalisation rate was approximately 25%. Data from OPTIMIZE-HF, Euro-Heart Failure Survey II and other studies reported in-hospital mortality was vary from 3% to 9%. One year Mortality rates ranged across the different regions from 21.6 % to 36.5 %.[5]

Significant advances have been made in the pharmacologic treatment of HF in recent decades. The benefits of β-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, aldosterone antagonists, and isosorbide dinitrate or hydralazine have been supported by a large number of randomized clinical trials (RCT) showing improvements of symptoms, reduce burden of hospitalization, and/or provide survival benefit. Cardiac societies have published updated HF guidelines regularly, according to the recent RCTs.[6]

Previous studies also suggested that good adherence to HF treatment guidelines among physicians improved not only quality of life but also resulted in a better prognosis.[7] Therefore, understanding when and how to add, switch, and titrate all therapies to maximally tolerated doses and ideally target doses is important. To achieve the maximal benefits of Guideline-directed medical therapy (GDMT) in patients with HF therapies must be initiated and titrated to maximally

*Corresponding author at: Brawijaya Cardiovascular Research Center, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia
E-mail address: ippoenk@ub.ac.id (M.S Rohman).

https://doi.org/10.21776/ub.hsj.2020.001.01.1
Received 9 March 2020; Received in revised form 12 March 2020; Accepted 24 March 2020
Available online 1 April 2020

tolerated doses (See table1). Doses of GDMT higher than those studied in randomized clinical trials, even if tolerated, are not known to provide incremental benefits and are generally not recommended.[8]

Table 1. Starting and Target Doses of Select Guidline-Directed Medical Therapy for HF

	Starting dose	Target dose
Beta Blockers		
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25 mg twice daily for weight <85 kg and 50 mg twice daily for weight ≥85 kg
Metoprolol succinate	12.5–25 mg/d	200 mg daily
ARNI		
Sacubitril/valsartan	24/26 mg–49/51 mg twice daily	97/103 mg twice daily
ACEI		
Captopril	6.25 mg 3× daily	50 mg 3x daily
Enalapril	2.5 mg twice daily	10–20 mg twice daily
Lisinopril	2.5–5 mg daily	20– 40 mg daily
Ramipril	1.25 mg daily	10 mg daily
ARB		
Candesartan	4–8 mg daily	32 mg daily
Losartan	25–50 mg daily	150 mg daily
Valsartan	40 mg twice daily	160 mg twice daily
Aldosterone antagonists		
Eplerenone	25 mg daily	50 mg daily
Spironolactone	12.5–25 mg daily	25–50 mg daily
Vasodilators		
Hydralazine	25 mg 3× daily	75 mg 3× daily
Isosorbide dinitrate*	20 mg 3× daily	40 mg 3 × daily
Fixed-dose combination isosorbide dinitrate/ hydralazine†	20 mg/37.5 mg (one tab) 3× daily	2 tabs 3× daily
Ivabradine		
Ivabradine	2.5–5 mg twice daily	Titrate to heart rate 50– 60 bpm. Maximum dose 7.5 mg twice daily

Note; Digoxin remains indicated for HFrEF, but there are no contemporary data to warrant additional comment in this document. The reader is referred to already available guideline statements (2). *Isosorbide mononitrate is not recommended by the ACC/AHA/HFSA guideline. † The ACC/AHA/HFSA guideline considers either the fixed dose combination or the separate combination of isosorbide dinitrate and hydralazine as appropriate guideline directed therapy for HF. ACEI = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor neprilysin inhibitor; ARB = angiotensin receptor blocker; bpm = beats per minute; HF = heart failure; HFrEF = heart failure with reduced ejection fraction. (Source: Adapted from Yancy CW et al., 2017)

Achieving target or maximally tolerated doses of GDMT is the goal. β-blocker doses should be adjusted every 2 weeks in a patient with no evidence of decompensated HF and no contraindications to higher doses. Longer time periods may be needed for frail patients or those with marginal hemodynamics, whereas more rapid titration may be reasonable in clinically stable patients without hypotension. Following adjustment, patients should be cautioned that there may be a transient worsening of HF symptoms such as dyspnea, fatigue, or dizziness. ACEI and ARB may be titrated similarly to beta blockers with monitoring of renal function, potassium, and blood pressure; more rapid titration is also reasonable in clinically stable patients. In the absence of hypotension, electrolyte/renal instability, or angioedema on an ACEI or ARB, it is reasonable to change to ARNI.[8]

In some instances, it may not be possible to titrate GDMT to the target doses achieved in clinical trials. Patients in clinical practice may differ substantially from those enrolled in the trials; such differences may limit the ability to titrate therapies. For example, patients in clinical practice are typically older, may experience more side effects, and are likely to have more comorbidities that will limit titration. Social or economic barriers to care may also undermine ability to achieve GDMT.[8]

The optimal time-point for discharging hospitalised HF patients may be difficult to determine due to the need to balance patient preferences, healthcare resources and the risk of adverse outcomes. Indeed, the risk of death is high during hospitalisation for HF but is even higher during the immediate post-discharge period, which usually lasts 2–3 months and is known as the vulnerable phase.[9] Persistent subclinical congestion may contribute to the high rates of death and readmission observed after hospital discharge.[10] Indeed, despite a global improvement in symptoms during hospital stay, a relevant proportion of patients still display markedly elevated natriuretic peptides at discharge. Based on these data, titration of decongestive therapy based only on symptoms and signs may be insufficient and should include additional parameters, such as biomarkers and/or echocardiography.[11,12] Waranugraha Y. et all. reported the benefit of measuring ePCWP using echocardiography, similar to NT-proBNP sensitivity to assess hemodynamic congestion which present in 48% HF patients without appearance clinical congestion. Among 50% of hemodynamic congestion patients readmitted to hospital within 30 days.[13]

Underutilisation of heart failure therapies such as beta-blockers, renin–angiotensin system (RAS) inhibitors and mineralocorticoid receptor antagonists was prevalent and showed a 40–50 % relative risk reduction in 90-day mortality.[14,15] Additional 25–50 % relative risk reduction was shown after beta-blocker and RAS inhibitor combination therapy at hospital discharge compared to either treatment alone. The early benefits were present in both reduced and preserved ejection fraction and persisted at 1-year follow up.[15] Utomo YB. et all. has reported in this issue the role of GDMT during hospitalisation resulted in lower in hospital mortality. They also mentioned only 17% of HF patients receiving optimal angiotensin converting enzyme inhibitors (ACEi) suggesting low adherence of physician to GDMT in the study.

QUALIFY (Quality of Adherence to guideline recommendations for LIFe-saving treatment in heart failure surveY) has demonstrated also that good physician adherence to guideline recommendations for key heart failure medication (angiotensin converting enzyme inhibitors/angiotensin receptor blockers, beta blockers, mineralocorticoid receptor antagonists and ivabradine) is associated with lower patient mortality and hospitalisation rates across the world. It underlines the importance of physicians' adherence to recommended drugs and drug dosages in improving clinical outcomes for patients with heart failure.[7]

Conflict of interest

There is no conflict of interest.

References

1. Brown SB, Shannon RP. Improving Medication Compliance in

Patients With Heart Failure [Internet]. Am. J. Cardiol. 2008 [cited 2020 Apr 16];101(2):274–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18178422

2. Ponikowski P, Anker SD, AlHabib KF, et al. Heart failure: preventing disease and death worldwide. ESC Hear. Fail. 2014;1(1):4–25.

3. Rosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics - 2007 Update: A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2007;115(5).

4. Sueta C. Editorial (Thematic Issue: The Life Cycle of the Heart Failure Patient). Curr Cardiol Rev 2014;11(1):2–3.

5. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. Card Fail Rev 2017;03(01):7.

6. McMurray J, Cohen-Solal A, Dietz R, et al. Practical recommendations for the use of ACE inhibitors, beta-blockers, aldosterone antagonists and angiotensin receptor blockers in heart failure: Putting guidelines into practice [Internet]. Eur. J. Heart Fail. 2005 [cited 2020 Apr 16];7(5):710–21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16087129

7. Cowie MR, Komajda M. Quality of Physician Adherence to Guideline Recommendations for Life-saving Treatment in Heart Failure: an International Survey. Card Fail Rev 2017;3(2):130.

8. Yancy CW, Januzzi JL, Allen LA, et al. 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With ReducedEjection Fraction: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol 2018;71(2):201–30.

9. Greene SJ, Fonarow GC, Vaduganathan M, Khan SS, Butler J, Gheorghiade M. The vulnerable phase after hospitalization for heart failure [Internet]. Nat. Rev. Cardiol. 2015 [cited 2020 Apr 16];12(4):220–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25666406

10. Ambrosy AP, Pang PS, Khan S, et al. Clinical course and predictive value of congestion during hospitalization in patients admitted for worsening signs and symptoms of heart failure with reduced ejection fraction: findings from the EVEREST trial. Eur Heart J [Internet] 2013 [cited 2020 Apr 16];34(11):835–43. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23293303

11. Arrigo M, Truong QA, Onat D, et al. Soluble CD146 Is a Novel Marker of Systemic Congestion in Heart Failure Patients: An Experimental Mechanistic and Transcardiac Clinical Study. Clin Chem [Internet] 2017 [cited 2020 Apr 16];63(1):386–93. Available from: https://academic.oup.com/clinchem/article/63/1/386/5612824

12. Kubena P, Arrigo M, Parenica J, et al. Plasma levels of soluble CD146 reflect the severity of pulmonary congestion better than brain natriuretic peptide in acute coronary syndrome. Ann Lab Med 2016;36(4):300–5.

13. Waranugraha Y, Rohman MS, Anjarwani S. Hemodynamic Congestion at Hospital Discharge Predicts Rehospitalization during Short Term Follow Up in Acute Heart Failure Patients. Indones J Cardiol 2019;40(3).

14. Shah KS, Xu H, Matsouaka RA, et al. Heart Failure With Preserved, Borderline, and Reduced Ejection Fraction: 5-Year Outcomes. J Am Cardiol 2017;70(20):2476–86.

15. Gayat E, Arrigo M, Littnerova S, et al. Heart failure oral therapies at discharge are associated with better outcome in acute heart failure: a propensity-score matched study. Eur J Heart Fail 2018;20(2):345–54.