Acta Cardiologia Indonesiana
Web page: jurnal.ugm.ac.id/v3/jaci
pISSN:2460-5700
eISSN:2579-4345

T2D as an Important Starting Point of Heart Failure – Early Intervention for Heart Failure Patients

Vina Yanti Susanti*

Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada – Sardjito General Hospital Yogyakarta, Indonesia

ARTICLE INFO

*Corresponding author
Email:
vinayantisusanti@ugm.ac.id

Address:
Jalan Farmako Sekip Utara, Yogyakarta 55281 Indonesia

Manuscript submitted: December 10, 2021
Revised and accepted: March 15, 2022

ABSTRACT

SGLT2i has shown benefit in T2D patients. Several studies have also shown its benefit for cardiovascular complication, such as heart failure. Heart failure is an often-missed complications in T2D patients. Dapagliflozin has shown benefit to reduce the hospitalization rate of heart failure in the T2D population, with several guidelines backing up the usage of SGLT2i in patients with high risk and heart failure complications.

Narrative

Diabetes patients are usually accompanied by few other comorbidities, such as hypertension, dyslipidemia, and obesity. It is therefore important for the management of type 2 diabetes to be more holistic and comprehensive, paying attention to the comorbidities and possible future cardiovascular complication, especially heart failure.

SGLT2 inhibition blocks the proximal reabsorption of sodium and glucose, resulting in urinary glycosuria and changes in several risk factors.[1-4]

It is found that Dapagliflozin 10 mg has a 0.89% HbA1c decrease from baseline at 24 weeks,[1] beside the decrease of HbA1c, Dapagliflozin also showed ~3kg weight loss[2] and 5.1 mmHg systolic blood pressure decrease,[3] both at 24 weeks.

T2D, Heart Failure and Chronic Kidney Disease are closely connected. T2D is responsible for increasing the risk of patients to develop heart failure up to five times[5]. Heart failure develops early and frequently in T2D patients, up to 14.1% incidence in a cohort study of ~1.9 million study population, beating NFMI (11.5%) and ischaemic stroke (5.1%).[6]

Heart failure is also the most common cause of hospitalization, in comparison to ACS, Ischaemic stroke, and cardiac dysrhythmia, in both male and female population.[7]

DECLARE TIMI 58 Study is the SGLT2i study looking at the benefit of Dapagliflozin 10 mg addition on top of standard care.[8] It has a total population of 17,160 patients, with a long duration of follow up time up to 4.2 years.

The DECLARE TIMI 58 Study enrolled patients early in the disease continuum, including those without ASCVD.[8] DECLARE study had 59% patients with multiple risk factors patients, CANVAS program with 34% population of multiple risk factors.[10,11] While both EMPAREG Study[9] and Vertis.[12,13] enrolled a population of >99% ASCVD populations.

DECLARE Study showed a significant primary outcome of hHF/CV death at 17% relative risk reduction, with statistical significance p-value <0.05. However, DECLARE Study didn't show statistical significance for its other primary outcome of MACE, numerical relative risk reduction was found at 7% reduction of the event of MACE. This insignificance is likely due to the amount of multiple risk factors patients in the DECLARE Study, lowering the MACE event, thus not showing the statistical significance.[8]

A meta-analysis between DECLARE, EMPA REG and CANVAS showed that as a class, SGLT2i shows benefit for ASCVD patients, both for the outcome of hHF or MACE.[14] However, only comparison between DECLARE and CANVAS can be made in the said meta-analysis, due to the unavailability of multiple risk factors population in the EMPA REG study.

DECLARE Study had several sub analysis which showed benefits in patients with prior myocardial infrarction,[15] and heart failure with reduced ejection fraction.[16] Both subanalysis showed statistical benefit for MACE and composite of hHF/CV death respectively.

The safety profile of Dapagliglozin were there confirmed in the DECLARE TIMI 58 Study.[8] It was showed that there is no concern regarding the aforementioned adverse

events, though the case of genital infection is showing 0.9% compared to the placebo group 0.1%, the percentage of event itself showed that it is actually a rare thing to happen to the broad sample of patients.[8]

All guidelines, including the local PERKENI 2019[17] and both ESC/EASD 2019[18] and ADA 2021[19] showed that SGLT2i is a preferred agent for T2D patients, for ASCVD patients, and high risk population. The ADA 2021 guideline further separate that SGLT2i is a preferred agent for high risk population/ASCVD population, as well as HF and CKD population.[19]

References

1. Ferrannini E, et al. *Diabetes Care.* 2010;33: 2217-2224.
2. Henry RR, et al. *Int J Clin Pract*. 2012;66: 446-456.
3. Bailey CB, et al. *Lancet*. 2010;375: 2223-2233.
4. Heerspink HJ et al. *Diabetes Obes Metab*. 2016;18: 590-597
5. Nichols GA, et al. *Diabetes Care* 2004;27:1879–1884
6. Shah AD, et al. *Lancet Diabetes Endocrinol* 2015;3:105–113; 2. Seferović PM, et al. *Eur J Heart Fail* 2018;20:853–872
7. Burrows NR, et al. *Diabetes Care* 2018;41:293–302
8. Wiviott SD, et al. *N Engl J Med*. 2019;380:347–357; 2
9. Zinman B et al. *N Engl J Med*. 2015;373: 2117-2128;
10. Neal B et al. *N Engl J Med*. 2017;377: 644-657;
11. Neal B et al. *Diabetes Obes Metab*. 2017;19: 387-393;
12. Cannon CP et al. *Am Heart J*. 2018;206: 11-23;
13. Cannon CP et al. *N Engl J Med*. 2020;383: 1425-1435
14. Zelniker TA et al. Article and supplementary appendix. Lancet. 2019;393: 31-39;
15. Furtado RHM et al. Online ahead of print. *Circulation.* 2019.
16. Kato ET et al. Online ahead of print*. Circulation*. 2019
17. Pedoman Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 Dewasa-2019
18. Cosentino F et al. *Eur Heart J.* 2020;41(2):255-323
19. American Diabetes Association. *Diabetes Care*. 2021;44(suppl 1): S1-S232.