

Empagliflozin role in the treatment of type 2 diabetes with cardiovascular disease and subclinical cardiovascular disease in outpatient setting: case reports

Abstract

SGLT2 inhibitors based on recent evidence have shown promising Cardio vascular benefits apart from Glycemic Control in T2DM management. ESC-EASD 2019 clearly suggest that All SGLT2i reduces CV risk (3P MACE), HHF, worsening of Nephropathy .Only Empagliflozin has been recommended for reducing the Risk of CV death in T2DM with ASCVD & the CV death remains independent of baseline HbA1c or control of HbA1c. Empagliflozin CV death is very unique because the consistency of Mortality benefit remains very significant in patients of T2DM with various CVD (like Single Vessel disease CAD, Multiple Vessel Disease CAD, Prior CABG, Prior MI, Prior Stroke, Prior HHF, PAD).

Keywords: type 2 diabetes, cardiovascular disease, subclinical cardiovascular disease, coronary artery disease, left ventricular mass index, peripheral arterial disease

Volume 7 Issue 3 - 2020

Rajesh Jain,¹ Mohammadreza Shoghli,² Muhammad Iqbal,³ Amit Chauhan,⁴ Rachna Jain⁵

¹Director Jain hospital, India

²Tehran Heart Center, Cardiovascular Diseases Research Institute, Tehran University of Medical Sciences, Iran

³Consultant Family Physician, UK/UAE

⁴Jain hospital, India

⁵Department of maternal health, Jain hospital, India

Correspondence: Jain R, Jain hospital, 108 B Gandhi gram, Vinobhanagar, Kanpur, 208007, India, Tel 09044034370, Email jaihospitals@gmail.com

Received: May 22, 2020 | **Published:** July 30, 2020

Abbreviations: LVMi, left ventricular mass index; T2DM, type 2 diabetes; CAD, coronary artery disease; SGLT2, sodium-glucose co-transporter-2; ASCVD, atherosclerotic-cardio vascular diseases; PAD, peripheral arterial disease; CV, cardio-vascular; CVD, cardiovascular disease; MACE, major cardiovascular event; PAD, peripheral arterial disease; MI, myocardial infarction

Case presentations

Case I: type 2 diabetes with hypertension with CVD

Clinical case: A 55-year old female patient with T2DM (5 yrs) and hypertension (12 yrs), presented with complaint of recent-onset chest-pain on cycling.

Current medication:

- Tab Metformin 1g BD
- Tab amlodipine 5 mg OD
- Tab Perindopril 4 mg OD
- Tab Rosuvastatin 10 mg OD

Examination Findings: BP: 128 / 84 mmHg HbA1c: 7.5%, FPG: 120 mg/dl; PPG: 192 mg/dl

Urine albumin-creatinine ratio: 200 mg/dL (microalbuminuria)

Serum creatinine: 0.8 mg/dL; eGFR CKD-EPI: 83 mL/min/1.73m²

Total-cholesterol: 193 mg/dl, LDLc: 110 mg/dl; HDLc: 50 mg/dl; TG: 167 mg/dl

Cardiac MR imaging report indicated ischemic heart disease; left ventricular (LV) mass-index was slightly increased; LV volumes, and ejection fraction were within normal range.

Changes Made to the Medication Regimen: Tab Rosuvastatin 20 mg OD, Empagliflozin 10mg OD was added, Tab Aspirin 75mg OD was added regarding this patient.

Among people with T2DM and CAD, SGLT2 inhibition with empagliflozin was associated with significant reduction in LVMi over 6 months, which may account in part for the beneficial cardiovascular outcomes observed in the EMPA-REG OUTCOME trial.¹ LVMi is strong and independent predictor of CV and all-cause mortality.² Based on precise quantitative myocardial perfusion, microvascular angina might more correctly be called “no stenosis angina” with 4 physiologically diverse, evidence-based subcategories or “primary” prototypes quantified objectively as follows: subendocardial ischemia due to diffuse epicardial atherosclerosis (most common),-overlooked epicardial stenosis, diffuse microvascular dysfunction or microvasculopathies and-nonischemic cardiac pain mechanisms (rare), or a mix of these prototypes, over 95% of which are associated with risk factors, and subclinical or clinically manifest coronary atherosclerosis needing vigorous risk factor treatment.³

Case II: Indian patient with T2DM and subclinical CAD

History: 52 yr old male, nonsmoker, K/c/o T2DM (3 yrs); HT (9 yrs)

Moderately active lifestyle

Weight 76 Kg; BMI 26 Kg/m²

Blood Pressure 130 / 86 mmHg

Present drug-regimen: Metformin 2.0g per day

- Perindopril 8 mg OD
- Amlodipine 5 mg OD

- Atorvastatin 10 mg OD

Investigation: HbA1c: 7.8%

FPG: 154 mg/dL; PPG: 238 mg/dL

eGFRCKD-EPI: 86 mL/min/1.73m²

UACR: 60 mg/gCr

Total-cholesterol: 191 mg/dLLDLc: 96 mg/dL; HDLc: 40 mg/dL;
TG: 156 mg/dL

Recent Exercise TMT +ve

Coronary CT angiography: 50% stenosis of Left-main coronary artery (s/o CAD)

Change in medication: adding 10 mg Empagliflozin and Statin dose changed to 20 mg Atorvastatin.

In EMPA-REG OUTCOME, >99% Patients had Established CVD
Established CVD in EMPA-REG OUTCOME⁴

Coronary artery disease / OR Prior MI / OR Prior Stroke

Coronary artery disease (any of)

- Multi-vessel disease or Left main disease ($\geq 50\%$ luminal narrowing), OR
- Single-vessel disease ($\geq 50\%$ luminal narrowing); plus
 - ☐ Provocable ischaemia, or
 - ☐ Unstable angina within 12 months prior

Peripheral arterial disease (any of)

- Presence of $\geq 50\%$ luminal narrowing on angiography or non-invasive method, OR
- Ankle brachial index < 0.9 , OR

- Limb angioplasty, stenting, bypass, OR
- Limb or foot amputation due to circulatory insufficiency

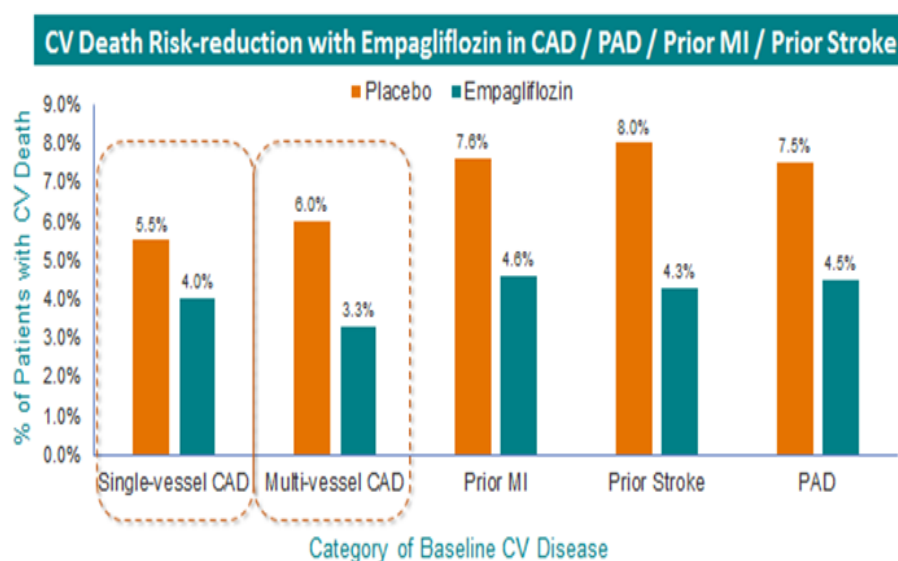
Conclusion

Case I: Empagliflozin use first of its kind among SGLT2 Inhibitors, for confirmatory evidence of LVMi regression with an SGLT2-I, LVMi regression was observed early, within 6 months of therapy, LVMi regression was greater in patients with higher baseline LVMi. The CV Death benefit is significant irrespective of HbA1c level at baseline means CV death benefit is observed in well controlled T2DM patients means HbA1c $< 7\%$, in uncontrolled T2DM patients means HbA1c $> 7-9\%$. The CV death benefit of Empagliflozin remains significant regardless of subclinical cardiovascular disease or MI, Stroke, HF, CKD at baseline.

Case II: Subclinical CVD remains a very important aspect in T2DM management. Symptomatic CVD can be easily classified on the basis of patient History but universal Screening for Asymptomatic/Subclinical CVD is not possible in 100% diabetic patients in country like India due to many reasons. So we can look for various Risk-factors of ASCVD (Asymptomatic Cardio Vascular Diseases) like LDL-cholesterol > 100 mg/dl, high blood pressure, smoking, chronic kidney disease, albuminuria, PAD and family history of premature CV death, and once we get the idea of CV risk then we can go for specific diagnostic tests for ruling out the ASCVD. Empagliflozin use in subclinical cardiovascular disease also results in significant all cause mortality and CV death reduction in future.

This is a Type 2 DM with subclinical CAD and therefore as per the evidence from EMPA REG trial adding SGLT2 Inhibitor Empagliflozin will reduce CAD in future Figure 1, all-cause mortality, CV death and 3 MACE.⁵ Over 2/3rd of Asymptomatic patients of T2DM have CAD.⁶ Figure 2 Over Half of which may have Significant Obstruction in South Asia population.⁷ Framingham offspring study shows Findings over 2/3rd of patients of DM have Subclinical CVD DM sees the Risk of Subclinical CVD by 4.3-fold.⁸

Empagliflozin Consistently Reduced CV Death in Patients of T2DM and CVD with / without Prior Event



Zinman B et al. AHA 2016; abstract 16903; Fitchett D et al. J Am Coll Cardiol 2018;71:364

Figure 1 Empagliflozin consistently reduced CV death in patients of T2DM and CVD with/without prior event.

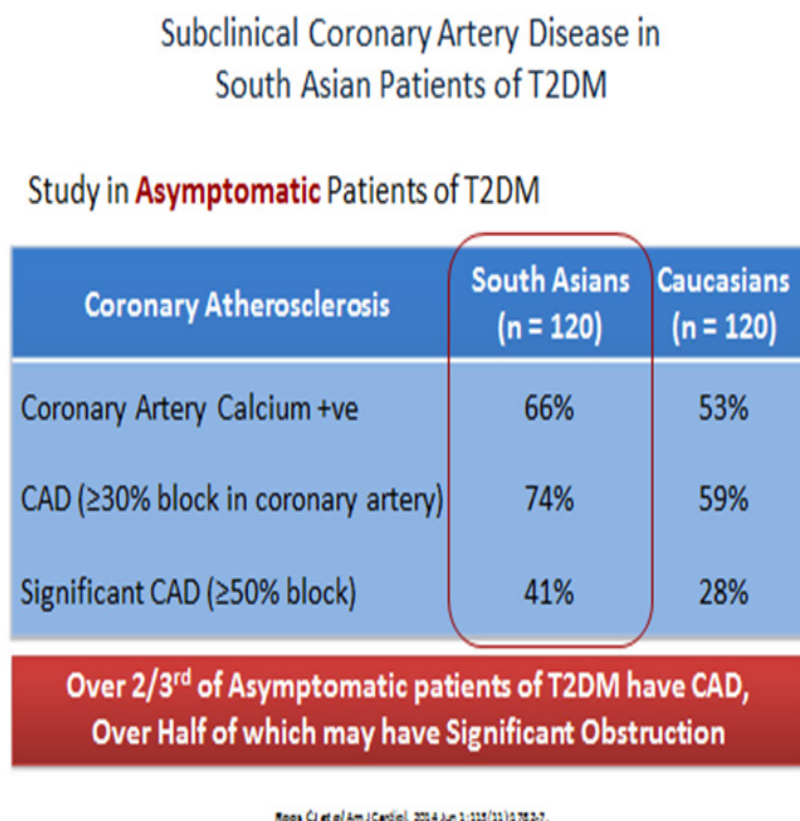


Figure 2 Subclinical coronary disease in South Asian patients of T2DM.

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Funding

None.

References

1. Verma S, Mazer CD, Yan AT, et al. Effect of empagliflozin on left ventricular mass in patients with type 2 diabetes and coronary artery disease: the EMPA-HEART cardioliNK-6 randomized clinical trial. *Circulation*. 2019;140(21):1693–1702.
2. Tsao CW, Gona PN, Salton CJ, et al. Left ventricular structure and risk of cardiovascular events: a Framingham heart study cardiac magnetic resonance study. *J Am Heart Assoc*. 2015;4(9):e002188.
3. Gould KL, Johnson NP. Coronary physiology beyond coronary flow reserve in microvascular angina: JACC State-of-the-Art Review. *J Am Coll Cardiol*. 2018;72(21):2642–2662.
4. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015;373(22):2117–2128.
5. Zinman B, Sullivan LM, Murabito JM, et al. Consistent effect of empagliflozin on cardiovascular death in subgroups by type of cardiovascular disease: results from EMPA-REG OUTCOME. *AHA*. 2016;134(Suppl 1):A16903.
6. Fitchett D, Inzucchi SE, Lachin JM, et al. Cardiovascular mortality reduction with empagliflozin in patients with type 2 diabetes and cardiovascular disease. *J Am Coll Cardiol*. 2018;71(3):364–367.
7. Roos CJ, Kharagitsingh AV, Jukema JW, et al. Comparison by computed tomographic angiography—the presence and extent of coronary arterial atherosclerosis in South Asians versus Caucasians with diabetes mellitus. *Am J Cardiol*. 2014;113(11):1782–1787.
8. Ingelsson E, Sullivan LM, Murabito JM, et al. Prevalence and prognostic impact of subclinical cardiovascular disease in individuals with the metabolic syndrome and diabetes. *Diabetes*. 2007;56(6):1718–1726.