Indian Clinical Management Algorithm for Type-2 Diabetes Mellitus

An Atherosclerotic CVD Risk Perspective

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Sections

I. Classification and Screening of AS-CVD Risk in T2DM

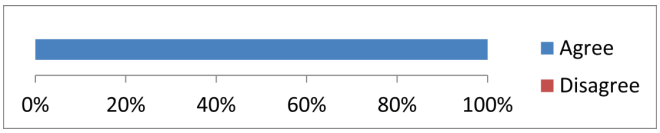
Principles

- Diabetes mellitus is a high-risk condition for CV Disease, but should not be considered as a CHD equivalent in all patients.
- Major risk-factors for AS-CVD:
  1. Age ≥ 45 years in males and ≥ 55 years in females
  2. Family history of premature ASCVD
  3. Current cigarette smoking or tobacco use
  4. High blood pressure
  5. Low HDL-C

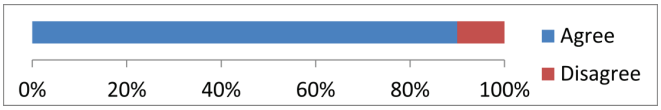
Classification of AS-CVD Risk in Patients of T2DM	
Presence of 0-1 additional major risk-factor for AS-CVD, without end-organ damage	High-risk for AS-CVD
Presence of 2 or more additional major risk-factors for AS-CVD **OR** end-organ damage	Very High-risk for AS-CVD

I. Classification and Screening of AS-CVD Risk in T2DM

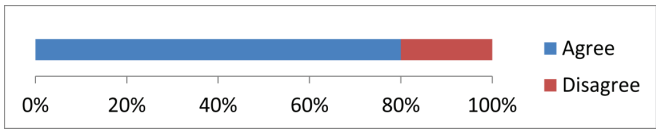
a. History of major risk-factors for ASCVD (Age, Family history of premature ASCVD, Tobacco use, BP, Lipid profile), should be assessed for all patients of T2DM.



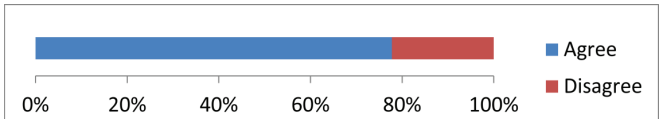
b. Noninvasive screening tests, including resting ECG, and albuminuria (assessed by urine albumin-creatinine ratio, UACR), may be considered for all patients of T2DM.



c. Tests for hsCRP, homocysteine levels, pulse-wave velocity, are not routinely recommended for all patients of T2DM.



d. Further assessment using risk-scores, preferably with greater relevance to Indian patients (e.g. QRISK3), may be optionally considered, based on personal preferences and familiarity.



Diagnostic Assessment Algorithm Recommended for all Patients of T2DM

Past h/o AS-CVD (Coronary / Cerebrovascular / Peripheral vascular disease) should be assessed for all patients of T2DM at initial visit.

Parameters for Assessment	Initial Assessment	Follow-up
H/o Smoking	At initial visit	Annually
Family h/o Premature CAD	At initial visit	Annually
Weight, Waist-circumference	At initial visit	At every visit
Blood-pressure	At initial visit	At every visit
Lipid Profile	At initial visit	At-least annually
UACR	At initial visit	At-least annually
eGFR	At initial visit	At-least annually
Resting ECG	At initial visit	Annually

Diagnostic Assessment Algorithm Recommended as Optional / for Reference to Specialist(s)

	Initial Assessment	Follow-up Assessments
AS-CVD Risk Calculator	Optional, based on personal preference of the healthcare provider	
Exercise ECG	Optional (if asymptomatic) Maybe considered if CVD is suspected	
Coronary artery calcium	Optional (if asymptomatic) Maybe considered if CVD is suspected	
Myocardial perfusion imaging	Maybe considered if CVD is suspected (maybe useful in patients not eligible for exercise)	
Stress echocardiography	Maybe considered if CVD is suspected (if exercise is not possible, pharmacological stress preferred)	

II. Treatment of T2DM from AS-CVD Risk Perspective

Principles

i. Holistic CVD Risk management in T2DM, should involve targeting multiple risk-factors for CV events.

ii. Therapeutic targets for Cardio-metabolic risk include Weight, BP, Lipids, HbA1c, overall CVD risk, albuminuria, and eGFR.

iii. Individualized therapeutic approach should be followed, for achieving optimum multi-factorial control for each patient.

iv. Early and sustained achievement of therapeutic goals should be attempted through possible intensified interventions.

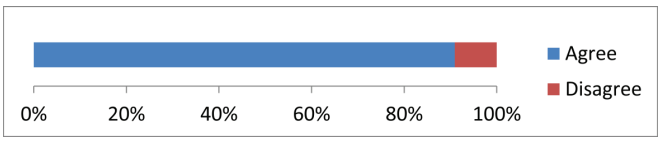
Recommended Therapeutic Targets:

Body-weight:

In Overweight / Obese patients, greater weight-loss maybe associated with better outcomes:

– Regular Target: Sustained loss of >5%

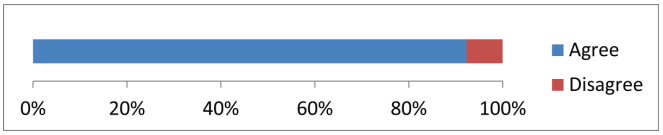
– Optimal Target: Sustained weight-loss of ≥7%



Recommended Therapeutic Targets

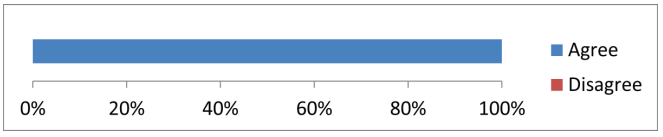
Blood-pressure

- Regular Target: SBP <140 mmHg, DBP <90 mmHg
- Optimal Target: SBP <130 mmHg, DBP <80 mmHg
- In CKD (Stages 1-4): SBP <130 mmHg, DBP <80 mmHg



Lipid Profile

- LDL-c level:
  - Regular goal: <100mg/dL
  - In T2DM with Very High CV risk*: <70mg/dL
- Non HDL-c level:
  - Up-to 30mg/dL greater than LDL-c goal

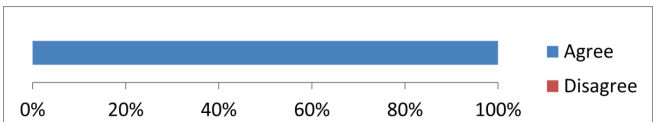


*In patients with extremely high CV risk (established AS-CVD): <50mg/dL (majority agreement)

Recommended Therapeutic Targets

HbA1c:

- Regular target: <7%
- Optimal target: <6.5% (if achievable without increased risk of hypoglycemia, or other adverse effects; in younger patients, with shorter duration of diabetes, with no established CVD)
- Less stringent target: <8% (Long-standing poorly controlled DM, Old-age, Frailty, Comorbidities)



Recommendations and Therapeutic Algorithm

Antidiabetic Therapy for T2DM

- Metformin should be considered as the first agent for glycemia control, unless contraindicated.
- In patients with AS-CVD, preferential use of empagliflozin and/or liraglutide to be considered, for reduction in risk of major adverse CV events as well as CV mortality, if clinically appropriate.
- In patients with AS-CVD, the preferential use of canagliflozin should be considered, for reduction in risk of major adverse CV events, if clinically appropriate.
- The existing evidence for a particular class of anti-diabetic agent is insufficient to recommend it for primary prevention of AS-CVD beyond glycemia control. Clinical judgment should be based on the known risks and benefits of individual agents.

Antihypertensive Therapy

- ACE-i, ARB, diuretics, or dihydropyridine CCBs may be considered as first-line therapy.
- In patients with CKD, ACE-i or ARBs should be preferred.
- Combination of ACE-i and ARB is not recommended.
- In patients being treated with ACE-i, ARB or a diuretic, eGFR, serum electrolyte levels should be monitored. Care must be observed when combining with SGLT2-i agents.
- Diuretics may cause hypokalemia, which may result in QT-interval prolongation. Caution must be observed in patients prone to QT-interval prolongation.

Lipid Management

- Choice of statin therapy should primarily depend on extent of LDL-C reduction targeted, rather than any individual agent.
- Atorvastatin may have benefit in renal outcomes over rosuvastatin, particularly in patients of T2DM with CKD.
- Depending on the intended therapeutic goal, moderate or high intensity statin therapy should be considered[#]:
  - **Moderate-intensity statin therapy**: Dose expected to reduce LDL-C by approximately 30 to <50%.
    - Atorvastatin 10-20 mg/day
    - Rosuvastatin 5-10 mg/day
    - Simvastatin 20-40 mg/day
    - Pitavastatin 2-4 mg/day
    - Pravastatin 40-80 mg/day
    - Lovastatin 40 mg/day

[#]Contra-indications and/or mandatory dosing requirements of the respective agents must be followed for each patient. If the intended statin dose is not tolerated, the maximally tolerated statin dose should be used.

  - **High-intensity statin therapy**: Dose expected to reduce LDL-C by ≥50% from baseline.

- Atorvastatin 40-80 mg/day
- Rosuvastatin 20-40 mg/day

In case the Non HDL-C or Triglyceride levels remain high:

- Intensification of lifestyle measures and statin therapy should be considered as next step.
- Non-statin drug (fibrate or ezetimibe) should be considered as the next alternative option, or in statin intolerance.
- In Triglyceride levels of >500mg/dL:
  - Avoidance of an event of pancreatitis must be the primary consideration. Fibrates, omega-3 fatty-acids should be initiated for priority control of Triglyceride levels.
  - Control LDL-C and Non HDL-C is the next goal; statin therapy should be initiated accordingly.

Antiplatelet Agents:

- Aspirin should not be used in all patients of T2DM.
- In patients of T2DM with Very-high CVD-risk, but without target-organ damage: low-dose aspirin (75-150 mg/day) may be used, after ruling out bleeding tendency.
- In patients with T2DM and established CVD, low-dose aspirin therapy (75-150 mg/day) should be used. Clopidogrel (75 mg/day) may be considered in patients intolerant to aspirin.
- Following an event of acute coronary syndrome, dual antiplatelet therapy may be considered.

Additional Considerations:

- In patients with known ASCVD, ACE-i / ARB should be used to reduce the risk of CVD event.
- In patients with prior myocardial infarction, β-blockers should be continued for at least 2 years after the event.
- Normotensive people with T2DM and macroalbuminuria should be treated with an ACE-i / ARB.
- Normotensive people with T2DM and microalbuminuria may be treated with an ACE-i / ARB.
- RAS-inhibitors should not be used in pregnancy.