Diabetic Ketoacidosis Complicated by Untreated Comorbidities

UNC HEALTH®

01.28.2026

Objectives

- Gain a broad understanding of the patient by assessing their history, vitals, and labs
- Understand the pathophysiology, presentation, diagnosis, and treatment of diabetic ketoacidosis (DKA)
- Discuss primary literature related to an alternative approach of DKA management and how this is relevant to the patient
- Assess the patient's problem list and develop treatment plans

Patient Assessment

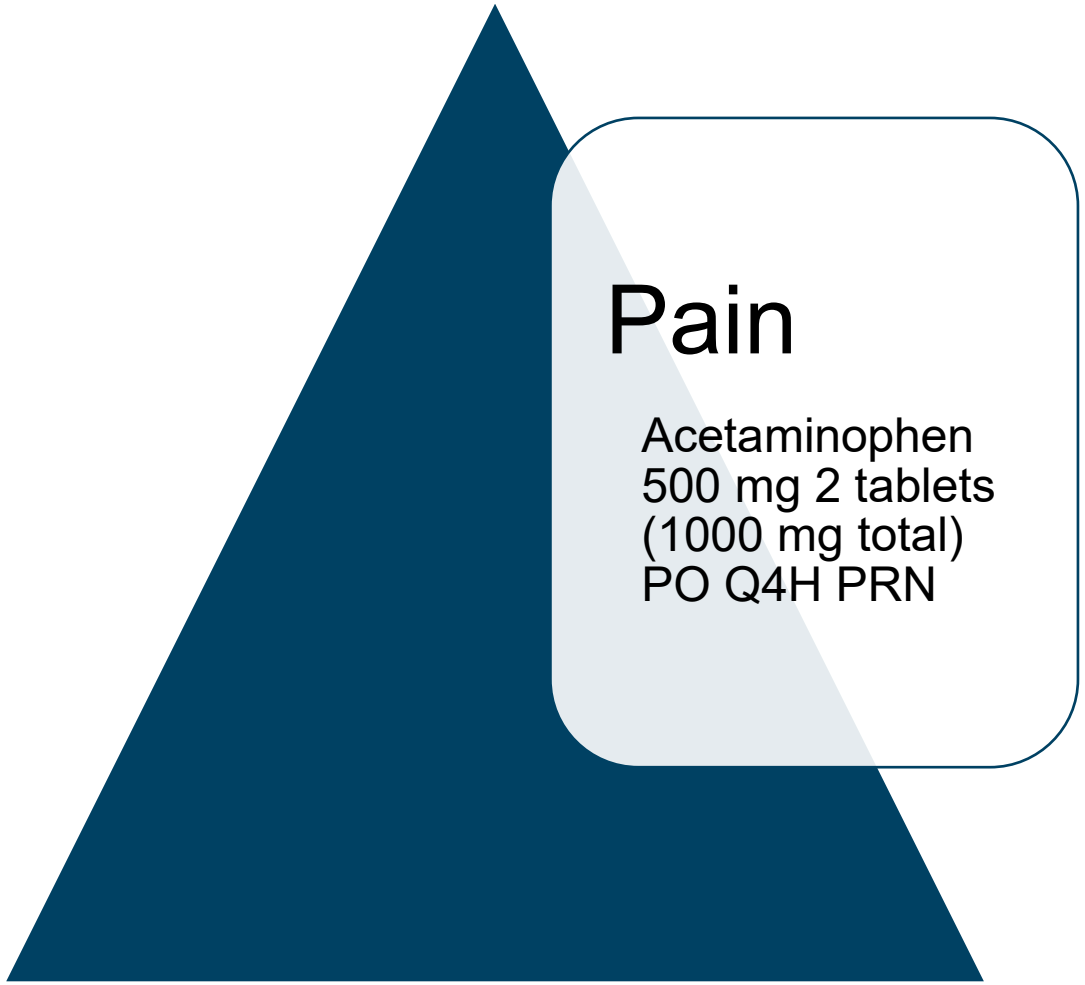
Chief Concern and History of Present Illness

- MR is a 25 YOM who presented UNC Chatham ED with 2 weeks of nausea, vomiting, and weight loss
- Reports being in a usual state of good health prior to admission
- Typically feels nauseated and bloated every morning
- Vomits 2-3 times per day and they do not contain blood or bile
- Lost ~30 lbs over the last 2 weeks
- Reports drinking more frequently and urinating more

Pertinent Medical History

- History of tobacco use disorder, obesity, hypertension, hyperlipidemia, and prediabetes mellitus
- No past surgical history
- Mother and father have diabetes mellitus
- Lives with brother and is employed full-time
- Denies illicit alcohol and drug use
- Reports smoking 1-2 cigarettes per month
- Penicillin allergy (rash)

Medication History



Vitals

Vital	01/12/2026	01/15/2026
Height (cm)	170.2	-
Weight (kg)	115.078	-
Temperature (°C)	36.7 (36.3-37.1)	36.9 (36.6-37.6)
Heart Rate (bpm)	117 (107-127)	103 (86-108)
Blood Pressure (mmHg)	160/89 (142-177)/(62-116)	149/96 (126-171)/(57-115)
Respiratory Rate (breaths per min)	26 (18-26)	19 (15-23)
SpO_2 (%)	99 (97-100)	95 (93-98)

- Physical exam WNL except for tachycardia upon admission, which has since resolved

Labs

Lab	01/12/2026	01/15/2026
C-Peptide (ng/mL)	0.95	-
Hemoglobin A1c (%)	10.4**	-
POC Glucose (mg/dL)	247 (140-353)	192 (164-219)
ACETEST	SMALL	-
K^+ (mmol/L)	5.2	2.6
Venous pH	7.22 (7.20-7.24)	7.44 (7.43-7.44)
Venous pCO_2 (mmHg)	32.5 (31-33.9)	42 (40-43)
Serum CO_2 (mmol/L)	11.2 (10.7-11.6)	22.7 (19.6-25.8)
Venous HCO_3 (mmol/L)	14 (13-14)	29 (28-29)
Venous Base Excess (mmol/L)	-13.1 (-13.8 - -12.3)	3.6 (2.8-4.3)
Anion Gap (mmol/L)	27 (25-28)	16 (15-17)

** = Acquired on 01/13/2026

Labs cont.

Lab	01/12/2026	01/15/2026
BUN (mg/dL)	7 (6-8)	<5
SCr (mg/dL)	0.72 (0.90-0.53)	0.43 (0.40-0.45)
BUN/SCr	10 (9-11)	-
CrCl (mL/min)	>120	>120
eGFR (mL/min/1.73 m^2)	>90	>90

Lab	04/25/2025
Total Cholesterol (mg/dL)	188
Triglycerides (mg/dL)	282
HDL (mg/dL)	32
LDL (mg/dL)	107
VLDL (mg/dL)	49

Diagnostics

- A1c ≥6.5% (10.4%) → diagnostic of DM
- Age <35 YO (25 YO) → features of monogenic DM (both parents have DM) → features of T2DM (obesity) → C-peptide 0.6-1.8 ng/mL (0.95 ng/mL) → type of DM (T2DM vs LADA) is indeterminate
- Glucose ≥200 mg/dL (353 mg/dL), ketonemia (positive ACETEST), pH <7.3 (7.20), venous HCO_3 <18 mmol/L (13.1 mmol/L) → diagnostic of DKA
  - Glucose ≥200 mg/dL (353 mg/dL), pH 7.0-7.25 (7.20), ketonemia (positive ACETEST), alert → moderate severity
    - American Diabetes Association Professional Practice Committee for Diabetes*. 16. Diabetes Care in the Hospital: Standards of Care in Diabetes-2026. *Diabetes Care*. 2026;49(Supplement_1):S339-S355.
    - Umpierrez GE, Davis GM, ElSayed NA, et al. Hyperglycemic crises in adults with diabetes: A consensus report. *Diabetes Care*. 2024;47(8):1257-1275.
- SBP average ≥140 mmHg (160 mmHg and 149 mmHg) from ≥2 “in-office” BP readings on ≥2 separate instances → stage 2 hypertension
  - Writing Committee Members*, Jones DW, Ferdinand KC, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM guideline for the prevention, detection, evaluation and management of high blood pressure in adults: A report of the american college of cardiology/american heart association joint committee on clinical practice guidelines. *Circulation*. 2025;152(11):e114-e218.
- LDL ≥100 mg/dL (107 mg/dL) → hypercholesterolemia
- TG 150-499 mg/dL (282 mg/dL) → hypertriglyceridemia
  - Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139(25):e1082-e1143.
  - Management of Hypertriglyceridemia: Common Questions and Answers | AAFP.

Disease State Background

Pathophysiology

- Increasing blood glucose triggers pancreatic β-islet cells to secrete insulin → decreased glycogenolysis, decreased gluconeogenesis, increased glucose uptake by skeletal muscle and adipose tissue
- Insulin deficiency shifts the body towards glucose-creating processes, leaving glycolysis behind → increased lipolysis releases fatty acids into the blood, which are oxidized into ketoacids β-hydroxybutyric acid and acetoacetic

Persistent hyperglycemia...

- Inhibits white blood cell function → delayed wound healing and blunted immune response
- Impairs blood flow → decrease perfusion in patients with ACS
- Increases mortality

Lizzo JM, Goyal A, Kaur J. Adult Diabetic Ketoacidosis. In: *StatPearls*. StatPearls Publishing; 2025.

Clinical Presentation

Symptoms of hyperglycemia

- Polyphagia
- Polyuria
- Polydipsia

Physical exam findings

- Tachycardia
- Tachypnea

Increased ketone production

- Fruity breath

Additional symptoms

- Nausea
- Vomiting
- Weight loss

Lizzo JM, Goyal A, Kaur J. Adult Diabetic Ketoacidosis. In: *StatPearls*. StatPearls Publishing; 2025.

Treatment Pathways for DKA

IV Fluids

- Mild hypovolemia → 500-1000 mL/h normal saline (or balanced crystalloid) x2-4 hours, then monitor hydration status
- At blood glucose <250 mg/dL → add 5% or 10% dextrose to normal saline (or balanced crystalloid)

Insulin

- Moderate DKA → 0.1 U/kg short-acting insulin IV bolus if delay in setting up infusion, then 0.1 U/kg/h short-acting insulin IV until blood glucose <250 mg/dL
- At blood glucose <250 mg/dL → 0.05 U/kg/h short-acting insulin IV to achieve and maintain blood glucose 150-200 mg/dL until resolution

Potassium

- K^+ <3.5 mmol/L → 10-20 mmol/L/h until K^+ >3.5 mmol/L
- K^+ 3.5-5.0 mmol/L → 10-20 mmol/L in each liter of IV fluid as needed to maintain K^+ 4-5 mmol/L
- K^+ >5.0 mmol/L → start insulin, but do not give K^+; check serum K^+ every 2 hours

Resolution Criteria

- Plasma ketone <0.6 mmol/L and
- Venous pH ≥7.3 or bicarbonate ≥18 mmol/L

Umpierrez GE, Davis GM, ElSayed NA, et al. Hyperglycemic crises in adults with diabetes: A consensus report. *Diabetes Care*. 2024;47(8):1257-1275.

Evaluation of an Alternative Approach to Managing Diabetic Ketoacidosis: Combination Rapid-Acting and Basal Subcutaneous Insulin (CRABI-DKA)

Ibarra F, Cruz M, Chinnock B, Sunde C, Campagne D, Uller M. Evaluation of an Alternative Approach to Managing Diabetic Ketoacidosis: Combination Rapid-Acting and Basal Subcutaneous Insulin (CRABI-DKA). *Ann Pharmacother*. 2026;60(1):15-22.

Background

- DKA management varies by institution, but most include rapid-acting IV insulin because of their predictable pharmacokinetics and familiarity to the providers
- Administering insulin via IV is associated with increased…
  - Resource utilization
  - ICU admission rates
  - Hospital costs
- Some studies have found SQ insulin to conserve costs and resources while preserving patient outcomes
- Strict staffing and lab testing requirements have prevented the implementation of rapid-acting SQ insulin into practice, but this may be addressed by co-administering SQ basal insulin
  - Providing sustained insulin concentrations via this method mimics IV insulin infusion and may reduce the number of SQ rapid-acting insulin injections and frequency of lab tests

Ibarra F, Cruz M, Chinnock B, Sunde C, Campagne D, Uller M. Evaluation of an Alternative Approach to Managing Diabetic Ketoacidosis: Combination Rapid-Acting and Basal Subcutaneous Insulin (CRABI-DKA). *Ann Pharmacother*. 2026;60(1):15-22.

Methods

- Retrospective cohort study conducted at a Central California academic level 1 trauma center
- Two order sets comparing SQ and IV insulin treatment

Insulin	SQ-DKA	IV-DKA
Initial	Glargine 0.2 U/kg x1 + lispro 0.2 U/kg x1	0.1 U/kg rapid-acting insulin bolus (optional)
Maintenance	- BG ≥250 → lispro 0.2 U/kg Q3H - BG <250 → lispro 0.1 U/kg Q3H	0.05-0.5 U/kg/h rapid-acting insulin

- The SQ-DKA order set was restricted to the ED observational (OBS) unit
- Both order sets contained initial normal saline and maintenance half-normal saline IVF, but only the SQ-DKA group had access to LR as an option
  - D5W was added to the order set when blood glucose <250 mg/dL and <200 mg/dL for SQ-DKA and IV-DKA, respectively
- Resolution was defined as blood glucose <200 mg/dL and at ≥2 of the following: pH >7.3, bicarbonate ≥15 mEq/L, or anion gap <12 mEq/L per the 2009 ADA guidelines

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Methods cont.

- Primary efficacy outcome defined as percentage of individuals whose DKA resolved within 12 hours
- Secondary efficacy outcomes included…
  - Time to DKA resolution
  - Hospital length of stay (LOS)
- Primary safety endpoints included…
  - Percentage of individuals who experienced hypoglycemia (blood glucose <70 mg/dL)
  - Percentage of individuals who experienced hypokalemia (serum K^+ <3.3 mEq/L)

Ibarra F, Cruz M, Chinnock B, Sunde C, Campagne D, Uller M. Evaluation of an Alternative Approach to Managing Diabetic Ketoacidosis: Combination Rapid-Acting and Basal Subcutaneous Insulin (CRABI-DKA). *Ann Pharmacother*. 2026;60(1):15-22.

Methods cont.

Inclusion Criteria	Exclusion Criteria
Mild-to-moderate DKA (blood glucose >250 mg/dL with a serum bicarbonate ≥10 mmol and/or pH >7.0) per 2009 ADA guidelines	• <18 YO • Pregnant • Euglycemic DKA (blood glucose ≤250 mg/dL) • Critically ill (acute congestive heart, liver, or renal failure; acute coronary syndrome; required vasopressors) • Severe edema on presentation • Weight >120 kg • Current use of high-dose corticosteroids • Use of insulin pump prior to admission • Discharged against medical advice • Diagnosed with alcoholic or starvation ketoacidosis • Patient already met serum bicarbonate and anion gap resolution goals prior to order set initiation

Ibarra F, Cruz M, Chinnock B, Sunde C, Campagne D, Uller M. Evaluation of an Alternative Approach to Managing Diabetic Ketoacidosis: Combination Rapid-Acting and Basal Subcutaneous Insulin (CRABI-DKA). *Ann Pharmacother*. 2026;60(1):15-22.

Methods cont.

- Sample size not driven by power → chart of patients who received SQ-DKA were reviewed up to 2 years after the order set was released until 50 patients were included and authors decided this number would be appropriate in determining if the order set should continue being available or retired
  - Chart of IV-DKA patients was reviewed until 50 patients were also included
- Patients who re-presented during the study period were included and counted as separate encounters
- Non-normally distributed continuous variables were compared using the Mann-Whitney *U* test
- Dichotomous variables were compared using the chi-square or Fisher exact tests
- $P<0.05$ established statistical significance

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Baseline Characteristics

Characteristic	SQ-DKA	IV-DKA	P-value
Male, n (%)	22 (44%)	28 (56%)	0.23
Age, years	32 (25–43)	40 (29–51)	0.083
Weight, kg	71.9 (58.7–83.2)	64.7 (58.7–77.1)	0.26

Reason for Admission	SQ-DKA	IV-DKA	P-value
Non-compliance	40 (80%)	35 (70%)	0.25
Infection	1 (2%)	8 (16%)	**0.031**
New diagnosis	0 (0%)	4 (8%)	0.12
Unknown	9 (18%)	4 (8%)	0.23

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Baseline Characteristics cont.

Lab Value	SQ-DKA	IV-DKA	P-value
Glucose, mg/dL	440 (374–545)	471 (371–559)	0.75
Bicarbonate, mEq/L	15 (12–16)	13 (11–16)	0.25
pH	7.30 (7.23–7.33)	7.26 (7.25–7.27)	0.34
Anion gap, mEq/L	18 (16–20)	17 (15–18)	**0.048**
β-hydroxybutyrate, mmol/L	7.3 (5.0–9.0)	7.2 (5.2–8.4)	0.97
Hemoglobin A1C, %	11.5 (10.4–13.3)	11.2 (10–12.8)	0.57
Creatinine, mg/dL	0.7 (0.6–0.9)	0.7 (0.6–1.0)	0.78
Potassium, mEq/L	4.7 (4.3–5.0)	4.6 (4.2–4.9)	0.51

Ibarra F, Cruz M, Chinnock B, Sunde C, Campagne D, Uller M. Evaluation of an Alternative Approach to Managing Diabetic Ketoacidosis: Combination Rapid-Acting and Basal Subcutaneous Insulin (CRABI-DKA). *Ann Pharmacother*. 2026;60(1):15-22.

Results

Outcome	SQ-DKA (n = 50)	IV-DKA (n = 50)	P-value
Insulin ordered to administration, minutes	57.5 (26.2–104)	74.5 (57.5–99.5)	0.075
DKA resolved ≤ 12 hours, n (%)	45 (90%)	39 (78%)	0.1
Time to resolution, hours	5.83 (3.13–8.28)	6.16 (4.02–9.95)	0.12
Hospital length of stay, hours	19.6 (15.7–27.3)	63.2 (42.1–94.3)	**<0.001**
Hypoglycemia, n (%)	4 (8%)	3 (6%)	1
Hypokalemia, n (%)	5 (10%)	5 (10%)	1

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Discussion

- Treatment groups were well-balanced with no clinically significant differences, but sample size is small
- Proportion of patients whose DKA resolved within 12 hours after receiving the SQ-DKA set was comparable to those receiving the IV-DKA set
- Primary safety outcomes and time to DKA resolution did not have any statistically significant differences
- The median hospital length of stay was 43.6 hours (1.8 days) shorter for patients who received the SQ-DKA set compared to those who received the IV-DKA set
  - The authors note the ED OBS unit was developed to provide high quality care for select patients who could be discharged within 24 hours of admission, so this finding may be due to the care team rather than the intervention
- The authors determined DKA severity via 2009 ADA guidelines, which did not utilize serum ketone levels to distinguish severities. Since 2024, a serum ketone >6.0 mmol/L has been considered severe DKA
  - 44% of the patient population had serum β-hydroxybutyrate >6.0 mmol/L, which would have excluded them from this study

Ibarra F, Cruz M, Chinnock B, Sunde C, Campagne D, Uller M. Evaluation of an Alternative Approach to Managing Diabetic Ketoacidosis: Combination Rapid-Acting and Basal Subcutaneous Insulin (CRABI-DKA). *Ann Pharmacother*. 2026;60(1):15-22.

Problem Assessment and Plans

Problem 1 Assessment: Diabetes Mellitus (DKA)

- A1C 10.4% is diagnostic of diabetes, but type (T1DM vs. LADA vs. T2DM) is unclear at the moment
- Meets criteria for DKA with moderate severity
- Presentation of polydipsia, polyuria, vomiting, and recent unintended weight loss suggests patient could be mildly hypovolemic
- Hyperkalemic on presentation (K^+ 5.2), but this was overcorrected and patient is now hypokalemic (K^+ 2.6)
- Family history of diabetes
- Currently not on any medications for diabetes

Problem 1 Plan: Diabetes Mellitus (DKA)

IV Fluids

- Lactated ringers 500-100 mL/h with D5W and adjust rate to maintain adequate volume status until resolution

Insulin

- Insulin lispro 12 U SQ Q3H to maintain blood glucose 140-180 mg/dL until resolution
- If blood glucose ≥250 mg/dL, increase to insulin lispro 24 U SQ Q3H until goal range is achieved

Potassium

- KCl 10-20 mmol/L/h IV until K^+ >3.5 mmol/L
- When, K^+ 3.5-5.0 mmol/L, give KCl 10-20 mmol/L IV in each liter of IV fluid as needed to maintain K^+ 4-5 mmol/L until resolution
- If K^+ >5.0 mmol/L → start insulin, but do not give K^+ and check serum K^+ every 2 hours

Umpierrez GE, Davis GM, ElSayed NA, et al. Hyperglycemic crises in adults with diabetes: A consensus report. *Diabetes Care*. 2024;47(8):1257-1275.

Problem 1 Plan: Diabetes Mellitus (DKA) cont.

- Despite MR's classification of diabetes being unknown, 2026 ADA guidelines suggest adults with T1DM be treated with continuous insulin and adults with T2DM be treated with insulin if A1C >10% or blood glucose ≥300 mg/dL
  - 60 U/day → insulin lispro 10 U SQ before breakfast, lunch and dinner + insulin glargine 30 U SQ QHS
- MR is also obese; 2026 ADA guidelines suggest semaglutide as a highly efficacious agent for weight loss and glycemic control
  - Semaglutide also has proven CVD benefit, which could be useful if MR's hyperlipidemia leads to ASCVD
  - Initiate semaglutide 0.25 mg SQ once weekly x4 weeks, then increase to 0.5 mg SQ once weekly.
    - May sequentially titrate from 0.5 mg SQ once weekly → 1 mg SQ once weekly → 2 mg SQ once weekly as needed for glycemic goals every 4 weeks
- Have MR consult with a nutritionist to encourage a diet that will help him reach his glycemic goals
- Counsel MR to engage in ≥60 min/day moderate-to-vigorous-intensity aerobic activity, with muscle-strengthening and bone-strengthening ≥3 days/week

American Diabetes Association Professional Practice Committee for Diabetes*. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2026. *Diabetes Care*. 2026;49(Supplement_1):S183-S215.

Problem 2 Assessment: Hypertension

- Stage 2 hypertension is likely as evidenced by inpatient SBP measurements
  - Acknowledge that BP measurements can be elevated due to comorbidities and hospital stay
- Currently does not take any medications for hypertension

Problem 2 Plan: Hypertension

- Initiate two first-line antihypertension medications of different classes (excluding ACEi and ARB) at lowest effective dose
  - Example regimen: lisinopril 5 mg PO daily + hydrochlorothiazide 25 mg PO daily
- Monitor and record blood pressure twice daily (ideally 12 hours apart) upon discharge
- Have MR consult with a nutritionist, placing emphasis on blood pressure-friendly diets like DASH
  - DASH diet's mean change in SBP is ~5 to ~8 mmHg
- Assess readiness to quit smoking and work towards complete tobacco cessation → long-term blood pressure reduction

Writing Committee Members*, Jones DW, Ferdinand KC, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM guideline for the prevention, detection, evaluation and management of high blood pressure in adults: A report of the american college of cardiology/american heart association joint committee on clinical practice guidelines. *Circulation*. 2025;152(11):e114-e218.

Problem 3 Assessment: Hyperlipidemia

- MR has elevated cholesterol and triglyceride levels
- Not on any cholesterol- or triglyceride-lowering medications

Problem 3 Plan: Hyperlipidemia

- In adults aged 20-39 YO with long duration diabetes, eGFR <60 mL/min/1.73 m^2, albuminuria, retinopathy, neuropathy, or ankle-brachial index <0.9, it may be reasonable to initiate a statin
  - A moderate-intensity statin (atorvastatin 20-40 mg or rosuvastatin 10-20 mg) should be initiated at around 40 YO for MR, barring LDL-C <190 mg/dL, no ASCVD events occur, or no risk-enhancing factors precipitate
    - If such events occur, then strongly consider initiating high-intensity statin (atorvastatin 40-80 mg or rosuvastatin 20-40 mg) regardless of age or control of diabetes
- Since triglycerides 150-499 mg/dL (282 mg/dL), but no ASCVD risk score, initiate intense lifestyle modifications and routine surveillance
- MR's hyperlipidemia can be managed by lifestyle modifications for now
  - Assess readiness to quit smoking and work towards complete tobacco cessation → lowers ASCVD risk
  - Consult with a nutritionist → limit refined carbohydrates and added sugar, increase foods lower on glycemic index and foods containing omega-3 fatty acids
  - Implement moderate-to-high intensity aerobic and resistance exercises

Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139(25):e1082-e1143.

Problem 4 Assessment: Tobacco Use Disorder

- Smokes 1-2 cigarettes monthly → approximately 0.02 to 0.04 pack-years by 40 YO
- Any bit of smoking will contribute to progression of comorbidities and introduction of new ones

Problem 4 Plan: Tobacco Use Disorder

- Provide tobacco cessation education packet on discharge → make MR aware of the consequences (e.g., cancer, reproductive, ophthalmic, cardiovascular, respiratory, etc.)
  - 5 A's Framework (Ask, Advise, Assess, Assist, Arrange)
- If pharmacologic treatment is necessary, use a combination of nicotine gum/lozenge and patch
  - Gum/lozenge: 2 mg Q1-2H x6 weeks → 2 mg Q2-4H x2 weeks → 2 mg Q4-8H x2 weeks (12 weeks total)
    - Gum maximum = 24 pieces/day
    - Lozenge maximum = 20 pieces/day or 5 pieces/6 hours
  - Patch: 14 mg/day x6 weeks, then 7 mg/day x2 weeks
    - This regimen is chosen because MR is not a "heavy smoker" (≤10 cigarettes daily)

Gaddey HL, Dakkak M, Jackson NM. Smoking Cessation Interventions. *Am Fam Physician*. 2022;106(5):513-522.