



Management of Diabetes in Patients with Cancer

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Introduction

Cancer and diabetes are diagnosed within the same individual more frequently than would be expected by chance, even adjusted by age. Patients with cancer who have pre-existing diabetes have higher mortality; poorer glycemic control leads to poorer cancer outcomes.

Cancer & DM: Shared Characteristics

- Aging
- Diet
- Physical inactivity
- Obesity
- Hyperinsulinemia
- Insulin-like growth factor 1
- Hyperglycemia
- Dyslipidemia
- Adipokines
- Cytokines
- Gut microbiome

Type of Diabetes Increased Risk

Type 1 Diabetes increased risk for

- Stomach cancer
- Liver cancer
- Pancreas cancer
- Endometrial cancer

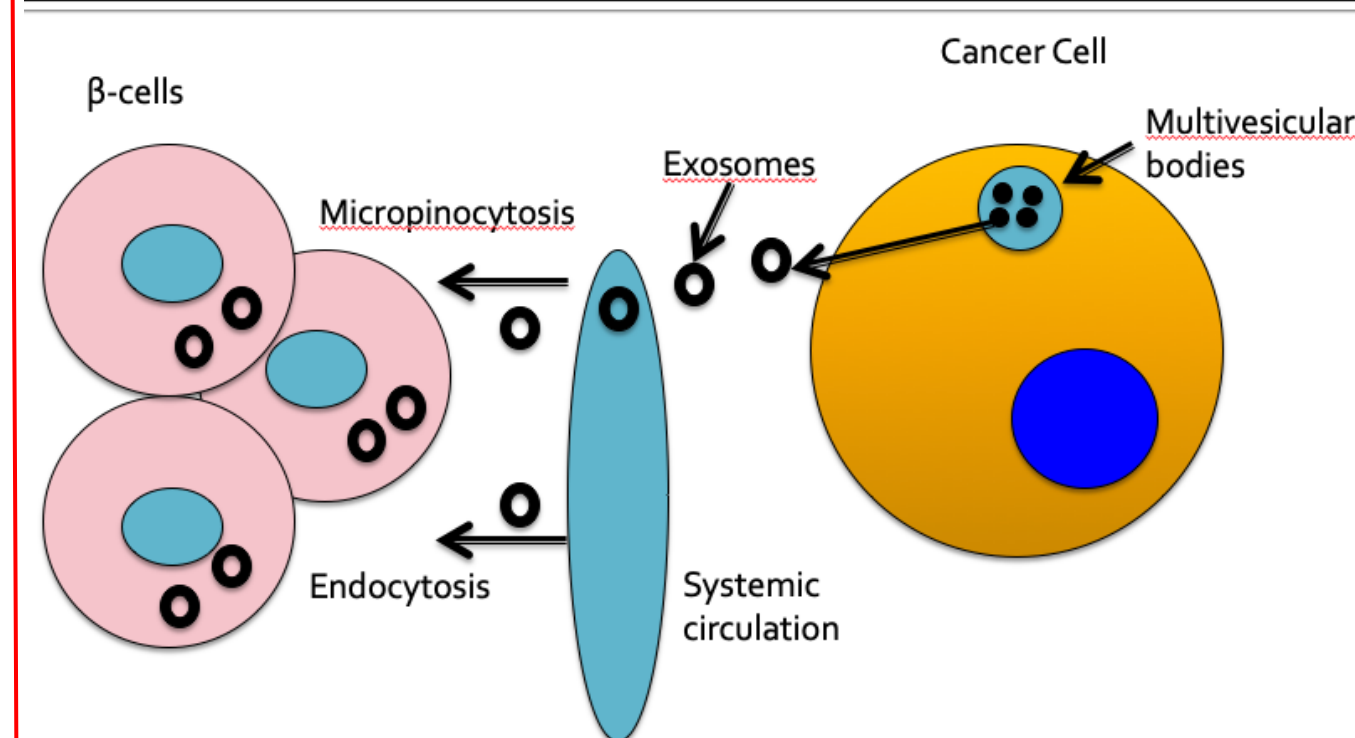
Type 2 DM increased risk for

- Liver cancer
- Pancreas cancer
- Endometrium cancer
- Colon cancer
- Rectum cancer
- Breast cancer
- Bladder cancer

Pancreaticogenic Diabetes: T3cDM

- Pancreatic cancer cells express and release adrenomedullin into circulation Adrenomedullin inhibits insulin secretion by β -cells
- Release of exosomes delivering to β -cells causing β -cell dysfunction / death
- DM dx can precede pancreatic Ca dx by weeks to 3 years

Exomes Cause β -cell Dysfunction



Drugs Causing Hyperglycemia

PI₃K-AKI-mTOR inhibitors

Act on mTOR signaling pathway which play a role in cell growth, lipid, and glucose metabolism

Associated with 13-50% incidence of hyperglycemia/new onset DM

- Everolimus, temsirolimus, Sorolimus

Treatment

- Therapeutic lifestyle
- Preferable: metformin, SGLT-2i or other non insulin treatment but if necessary sulfonylureas and insulin

Checkpoint inhibitor induced T1DM

PD-1 is immunoreceptor located on T-cells and pro-B cells inhibits T-cell activation and proliferation promoting self-tolerance

Anti-PD-1

- Nivolumab, pembrolizumab, cemiplimab

Anti-PD-L1

- Atezolimumab, avelumab, durvalumab
- CTLA-4
- Ipilimumab

Treatment

- Treat type 1 diabetes

Steroids

Steroid Potency Chart

- Hydrocortisone 20 mg
- Prednisolone 5 mg
- Prednisone 5 mg
- Methylprednisolone 4 mg
- Dexamethasone 0.75 mg

Treatment

Hydrocortisone affects BG ~ 8-12 hours

- NPH or 70/30

Prednisone affects BG 1 day

- Basal/bolus for 1-2 d

Dexamethasone affects BG 1-3 days

- Basal/bolus for 1-3 d

Enteral Nutrition

- Start with 1 unit rapid/short acting insulin per 10-15 gm CHO per 6 hours
- Adjust dose based on BG patterns
- Use correctional scale for hyperglycemia
- May need basal/prandial insulin

Parenteral Nutrition

- Start with 1 unit Regular insulin in the bag per 10 gm CHO
- Adjust based on BG patterns
- Use correctional scale for hyperglycemia
- May need basal/prandial insulin

Insulin Therapy

- Do not use "sliding scale" for prolonged period
- Use basal insulin if fasting hyperglycemia
- Use prandial insulin if postprandial hyperglycemia
- If needed a lot of correctional insulin, adjust the base doses

Starting Total Daily Insulin Dose

0.2-0.3 U/kg: age \geq 70, eGFR < 60 mL/min

- 0.4 U/kg: age < 70, eGFR 60+ BG 140-200 mg/dL

- 0.5 U/kg: age < 70, eGFR 60+ BG 201-400 mg/dL

- No steroids: 50% basal 50% bolus

- Steroids: low dose 40% basal 60% bolus, high dose 25% basal 75% bolus

Non insulin Medications

- Avoid metformin if patient prone to acidosis, has renal, liver, or heart failure, diarrhea, very poor appetite
- Avoid sulfonylurea/meglitinides if prone to hypoglycemia or eating poorly
- Do not use GLP-1 RA if has personal or family history of medullary thyroid cancer or MEN, or neuroendocrine tumors
- Avoid GLP-1 RA and DPP-4i if history pancreatitis
- Avoid SGLT-2i if prone to DKA ie low C-peptide

DM meds may decrease risk cancer

Metformin

- Reduces circulating insulin levels
- Activates immune system
- Activates LKB1/AMPK pathway
- Induces cell arrest and apoptosis
- Inhibits protein synthesis
- Reduces IGF1 and insulin-mediated signaling

Thiazolidinediones

- Restored adiponectin secretion and leptin sensitivity
- Reduces lipid droplets in hepatocytes and orexigen peptides in hypothalamus
- In cancer cells, reduced proliferation, production of reactive oxygen species, and inflammation by acting through the mTOR and FFKB pathways
- PPAR- γ activation may reduce tumor development through the arrest of cancer cell proliferation through effects on cell cycle checkpoints or growth factor inhibition,

Abbreviations

- CTLA-4 = cytotoxic T-cell associated antigen
- DKA = diabetic ketoacidosis
- DM = diabetes mellitus
- PD-1 = programmed cell death protein-1
- PD-L-1 = programmed cell death ligand-1

References

Bahrambeigi S, Badalzadeh R, et.al. Possible protective effects of thiazolidinediones antidiabetic drugs in colorectal cancer. Critical Reviews in Oncogenesis 24(3) 251-258. doi: 10.1615/CritRevOncog.2019031265

Biondo L, Teixeira A, et al. Pharmacological strategies for insulin sensitivity in obesity and cancer: thiazolidinediones and metformin. Current Pharmaceutical Design 26(9) 932-945
<https://doi.org/10.2174/1381612826666200122124116>

Carstensen B, Read S, et.al. Cancer incidence in perso s with type 1 diabetes: a five-country studey of 9,000 cancers in type 1 diabetic individuals. Diabetologia 2016; 59: 980-988. doi: 10.1007/s00125-016-3884-9.

Jacob P, and Chowdhury T. Management of diabetes in patients with cancer. QJM: An International Journal of Medicine 2014;108(6);
<https://doi.org/10.1093/qjmed/bcu218>

Giovannucci E, Harlan D, et. Al. Diabetes and cancer: a consensus report. Diabetes Care 2010 Jul; 33(7): 1674-1685 doi 10.2337/dc10-0666

Stamatouli A, Quandt A, et.al. Collateral damage: Insulin-dependent diabetes induced with checkpoint inhibitors. Diabetes 2018 Aug; 67(8): 1471-1480.
<https://doi.org/10.2337/dbi18-0002>.

Zhand K, Bai P, et.al. Metformin and risk of cancer amont patients with type 2 diabetes mellitus: A systematic review and meta-analysis. Prim Care Diab 2020.
<https://doi.org/10.1016/j.pcd.2020.06.001>