Management of T2DM patients with Covid-19

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Underlying conditions among adults hospitalized with COVID-19


Source: MMWR. 2020 Apr 8;69(early release):1-7
Leading comorbidities among COVID-19 deaths in New York

As of midnight on April 6, 86.2% of the state’s 5,489 COVID-19 deaths involved at least one comorbidity.

Note: Data reported on a daily basis by hospitals, nursing homes, and other health care facilities.

Source: New York State Department of Health

<table>
<thead>
<tr>
<th>COPD</th>
<th>Diabetes</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>(n=1566)</td>
<td>(n=24)</td>
<td>(n=1460)</td>
</tr>
<tr>
<td>236/1566 (15.1%)</td>
<td>7/24 (29.2%)</td>
<td>218/1460 (14.9%)</td>
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<tr>
<td>1113/1566 (71.1%)</td>
<td>17/24 (70.8%)</td>
<td>1034/1460 (70.8%)</td>
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<tr>
<td>178/1321 (13.5%)</td>
<td>65/269 (24.2%)</td>
<td>926/1321 (70.1%)</td>
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<table>
<thead>
<tr>
<th>Severity</th>
<th>COPD No (n=1566)</th>
<th>COPD Yes (n=24)</th>
<th>Diabetes No (n=1460)</th>
<th>Diabetes Yes (n=130)</th>
<th>Hypertension No (n=1321)</th>
<th>Hypertension Yes (n=269)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite end point</td>
<td>239/1566 (15.3)</td>
<td>15/24 (62.5)</td>
<td>209/1460 (14.3)</td>
<td>45/130 (34.6)</td>
<td>166/1321 (12.6)</td>
<td>88/269 (32.7)</td>
</tr>
<tr>
<td>Death</td>
<td>119/1566 (7.6)</td>
<td>12/24 (50.0)</td>
<td>100/1460 (6.8)</td>
<td>31/130 (23.8)</td>
<td>78/1321 (5.9)</td>
<td>53/269 (19.7)</td>
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<td>Admission of ICU</td>
<td>44/1566 (2.8)</td>
<td>6/24 (25.0)</td>
<td>37/1460 (2.5)</td>
<td>13/130 (10.0)</td>
<td>22/1321 (1.7)</td>
<td>28/269 (10.4)</td>
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<td>Invasive ventilation</td>
<td>92/1566 (5.9)</td>
<td>7/24 (29.2)</td>
<td>80/1460 (5.5)</td>
<td>19/130 (14.6)</td>
<td>61/1321 (4.6)</td>
<td>38/269 (14.1)</td>
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<tr>
<td></td>
<td>45/1566 (2.9)</td>
<td>5/24 (20.8)</td>
<td>39/1460 (2.7)</td>
<td>11/130 (8.5)</td>
<td>28/1321 (2.1)</td>
<td>22/269 (8.2)</td>
</tr>
</tbody>
</table>
Fear from doctors & Lack of supplies → Clinical inertia → Not optimizing of glycemic control → Poor outcomes in patients with diabetes and COVID-19

Pasquel FJ, Umpierrez GE. Journal of Diabetes Science and Technology1–3.2020
Diabetes Technology Society. DOI: 10.1177/1932296820923045
Management of T2DM patients with Covid-19

• Out patients

• In hospital patients:
  • Non critically ill
  • Critically ill
T2DM out-patients with Covid-19

• Reducing the risk of COVID-19
  • Social distancing and hand washing.
  • Good glycaemic control to reducing the risk of infection and severity.
    • More frequent blood glucose self monitoring
    • Influenza and pneumonia vaccinations
    • Special care to stabilize their cardiac/renal status.

• Adequate control of blood pressure and lipids.

Lancet Diabetes Endocrinol 2020Published Online April 23, 2020 https://doi.org/10.1016/S2213-8587(20)30152-2
Management of health anxiety and diabetes-related distress during the COVID-19 pandemic

Distancing but still social – Therapeutic Recreation during COVID-19

Management of patients with COVID-19

Out-patient care

Prevention of infection in diabetes

• Sensitisation of patients with diabetes for the importance of optimal metabolic control
• Optimisation of current therapy if appropriate
• Caution with premature discontinuation of established therapy
• Utilisation of Telemedicine and Connected Health models if possible to maintain maximal self containment
Anti Diabetic Medications during Pandemic Covid-19

• SU, metformin and SGLT2 inhibitors should not be discontinued prophylactically in outpatients who don't have evidence of COVID-19.

• GLP-1 RA and DPP-4 inhibitors, continued. Patients taking GLP-1 RA should be carefully monitored for dehydration. Adequate fluid intake and regular meals encouraged.

• Insulin therapy should never be stopped, may need to be started in new-onset patients or those with hyperglycemia after being taken off other agents.
Outpatient Appointment Prioritisation for Specialist Diabetes Departments during the Coronavirus pandemic

- New diagnosis of type 1 diabetes
- Urgent Insulin start: symptomatic or HBA1c > 10% or ketones
- Teaching blood glucose monitoring for urgent reasons, e.g. during pregnancy
- Blood test monitoring, e.g. declining renal function, raised potassium, low sodium
- Where physical examination essential, e.g. monitoring of foot ulcer, infection, pregnancy
- Urgent training of other device, e.g. CGM

Follow-up of new diagnosis of type 1 diabetes
- Vulnerable patient: e.g. recent hospital admission, recurrent severe hypoglycaemia episodes, HBA1c >11%
- Intensive follow-up in high risk situation, e.g. pregnancy
- Risk of attending appointment face to face greater than benefits

Patient’s diabetes is stable and well managed
- All face to face group structured education courses (DAFNE, DESMOND)
- All flash glucose monitoring start sessions
- Risk of attending appointment greater than benefits
- Deferring appointment will not compromise clinical care

Date approved 26.03.20
Are some diabetes medicines better than others at fighting the virus?

• At this time, there is no rigorous scientific data from studies in people that highlights either a special benefit or a risk of a different outcome with COVID-19 for any of the common glucose-lowering medicines used to treat Type 2 diabetes.

The diagram illustrates the interaction between SARS-CoV-2 and the host cell. Key components include:

- **SARS-CoV-2**: Initiates infection by binding to receptors on the host cell.
- **ACE2**: A receptor targeted by SARS-CoV-2 for entry into the cell.
- **Anti-ACE2**: An anti-viral strategy to block ACE2 receptors.
- **Anti-APN**: Another anti-viral strategy targeting APN receptors.
- **Anti-DPP4**: A third receptor targeted for inhibition.
- **Immunocytes (Im Cell)**: The immune system responds to the virus.
- **Translation**: Viral proteins are translated within the cell.
- **Viral Proteins**: Include N7-MTase, which modifies the RNA cap.
- **RNA Synthesis**: Involves RdRp and N7-MTase activities.
- **Cell Stress** and **Membrane Stress**: Result in pH changes.
- **Chloroquine**: A drug that interferes with viral replication.
- **Vaccine**: A preventive measure against SARS-CoV-2 infection.

The diagram highlights potential targets and strategies for anti-viral therapies and immune responses.
Metformin

• Exerts anti-inflammatory actions in preclinical studies, ↓ circulating biomarkers of inflammation in people with T2D.

• Been used successfully in nonhospitalized subjects with stable hepatitis or HIV infections however,

• Scant information about the immunomodulatory actions of metformin in the context of coronavirus infection.
Metformin

• Caution in unstable hospitalized patients.
• Discontinued in people with concomitant sepsis or severe impairment of hepatic and renal function.

Drucker DJ. Coronavirus Infections and Type 2 Diabetes. Endocrine Reviews, June 2020, 41(3):1–13
Dipeptidyl peptidase-4 inhibitors

• Insufficient evidence to determine the impact of partial reduction of DPP4 activity, on clinical outcomes in humans with active coronavirus infection.

• DPP-4 inhibitors, or in combination with basal insulin, effectively control glucose in patients with mild to moderate hyperglycemia.

• In active SARS-CoV-2 infection, clinically significant volume depletion or systemic sepsis, ↓ renal function needed adjustment of the dose of some DPP4 inhibitors.

Drucker DJ. Coronavirus Infections and Type 2 Diabetes. Endocrine Reviews, June 2020, 41(3):1–13
SGLT2 inhibitors

- SARS-CoV-2 infection associated with anorexia, dehydration, and rapid deterioration in clinical status.
- T2D with active SARS-CoV-2 infection, heightened risk for volume depletion and euglycemic ketoacidosis.
- Re-evaluation of or discontinuation of these agents in very unwell ambulatory individuals.
- Routinely discontinued in unstable patients with severe SARS-CoV-2 infection upon admission to hospital
GLP-1R agonists

- Although GLP-1 safely lowers blood glucose in short-term studies of perioperative period and in the ICU ventilated patients with critical illness, there is insufficient experience with the safety and use of GLP-1R agonists in critically ill subjects to make therapeutic recommendations for use of these agents in the context of coronavirus infection.
The current approach to manage inpatient diabetes with COVID-19/suspects

- Urgent need to implement effective glycemic control treatment approaches aiming at conserving the supply of PPE and reducing HCW exposure.
  - The use of noninsulin agents in selected groups of patients
  - Novel algorithms for hyperglycemic crises management
  - The use of diabetes technology.

Management of diabetic in-patient or ICU with COVID-19

In-patient or intensive care unit

Monitor for new onset diabetes in infected patients (in-patient care)

Management of infected patients with diabetes (intensive care unit)

- Plasma glucose monitoring, electrolytes, pH, blood ketones, or β-hydroxybutyrate
- Liberal indication for early intravenous insulin therapy in severe courses (ARDS, hyperinflammation) for exact titration, avoiding variable subcutaneous resorption, and management of commonly seen very high insulin consumption
Tatalaksana DMT2 pada Pasien Non-Kritis di Rumah Sakit dengan COVID-19 atau ODP

1. Hiperglikemia ringan atau pasien yang lemah
   - Insulin: 0.1 u/kg/hari atau 10U Detemir atau Glargine (sesuaikan jika perlu)
   - DPP4-i: mulai dengan dosis renal sitagliptin atau linagliptin
   - Koreksi: insulin regular/rapid
     A) Jumlah APD memadai: setiap 12 jam
     B) Kekurangan APD: sebelum makan pagi saja

2. Hiperglikemia sedang
   - Insulin: 0.2-0.3 u/kg/hari Detemir atau Glargine (sesuaikan jika perlu)
   - DPP4-i: mulai dengan dosis renal sitagliptin atau linagliptin
   - Koreksi: insulin regular/rapid
     A) Jumlah APD memadai: setiap 12 jam
     B) Kekurangan APD: sebelum makan pagi saja

3. Hiperglikemia berat
   - Insulin: turunkan TDH di rumah sebesar 20% atau mulai dengan 0.5 u/kg/hari
   - TDH ½ basal, ½ bolus (sesuaikan jika perlu)
   - Tunda pemberian insulin prandial apabila asupan makan buruk

Intensifikasi Terapi Apabila Target Glikemik Tidak Tercapai: Gula Darah 100-180mg/dl

APD, alat pelindung diri; DMT2, diabetes melitus tipe 2; DPP-4i, dipeptidyl peptidase-4 inhibitor; ODP, orang dalam pengawasan; TDH, total dosis harian
Insulin therapy has been the considered regimen of choice in the hospital

- Standardized basal-bolus regimen for most non critically ill patients.
  - Complex
    - Multiple injections, frequent point-of-care (POC) glucose testing.
    - Associated with iatrogenic hypoglycemia.

- In the intensive care unit (ICU), insulin therapy is even less convenient.
  - Continuous insulin infusion (CII) → needing hourly POC testing

Critically Ill Patients

• Glycemic target range for ICU patients: 140 - 180 mg/dL.

• Patients with mild to moderate DKA:
  - Subcutaneous insulin / 2-4 hours

• Severe DKA, HHS, or combined DKA-HHS:
  - CII is recommended.
Critically Ill Patients (cont.)

• This current approach with hourly POC glucose testing is clearly impractical.

• → urgent need to systematically learn novel approaches utilizing diabetes technology (ie, continuous glucose monitoring [CGM] and artificial pancreas).
Diabetes and COVID-19

• Higher case-fatality
• Prolonged length of stay
• Higher resource utilization
To reduce the barriers of optimizing glycemic control

- Individualized care strategies
- Novel therapeutic regimens
- Use of diabetes technology:
  - Prevent healthcare workers’ exposures
  - Reduce the waste of invaluable PPE
Graphical Abstract