

Peran Disfungsi Sel T Memori Spesifik SARS-CoV-2 pada Peningkatan Resistensi Insulin 12 Bulan Pasca COVID-19 = The Roles of Dysfunctional SARS-CoV-2 Memory T Cells in Increase Insulin Resistance within 12 Months Post-COVID-19

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Abstrak

Latar Belakang

Penelitian ini meneliti potensi peningkatan resistensi insulin dan obesitas dalam 12 bulan pasca COVID-19 pada penyintas COVID-19 dengan status glikemik beragam. Analisis retrospektif dilakukan untuk mengidentifikasi faktor metabolik dan respons inflamasi yang berkontribusi, termasuk proporsi sel T memori spesifik SARS-CoV-2 yang fungsional dan yang mengalami disfungsi, kadar sitokin, serta polarisasi makrofag. Metode

Penelitian kohort ini melibatkan 47 pasien terinfeksi SARS-CoV-2 yang dipantau selama lima periode: fase akut (baseline), bulan ke-1, ke-3, ke-9, dan ke-12 fase konvalesen. Partisipan dikelompokkan menjadi tiga berdasarkan status obesitas dan peningkatan HOMA-IR, yaitu non-obes (NO), obes tanpa peningkatan HOMA-IR (O), dan obes dengan peningkatan HOMA-IR (O-IR). Peningkatan HOMA-IR didefinisikan sebagai rasio HOMA-IR bulan ke-12/bulan ke-1 $\geq 1,21$. Pada setiap periode, dilakukan pengukuran komposisi tubuh, kadar kendali glikemik, serta isolasi PBMC. Identifikasi sel T CD4⁺ dan CD8⁺ memori spesifik SARS-CoV-2 dilakukan melalui inkubasi PBMC dengan antigen SARS-CoV-2 selama 24 jam. Supernatan hasil inkubasi PBMC dengan antigen digunakan untuk menilai kadar sitokin yang diproduksi dan kecenderungan polarisasi makrofag.

Hasil

Sebanyak 35,3% pasien non-DM, 75% pasien DM baru, dan 59,1% pasien DM mengalami peningkatan HOMA-IR $\geq 21\%$ dalam 12 bulan pasca COVID-19. Kelompok O-IR tidak mengalami penurunan total lemak tubuh, rasio lemak/otot, dan lingkar perut dalam 12 bulan follow up. Selain itu, kelompok O-IR memiliki proporsi sel T memori spesifik SARS-CoV-2 fungsional lebih rendah, sementara sel yang mengalami disfungsi lebih tinggi, kadar sitokin lebih rendah, tetapi rasio TNF-/IL-10 lebih tinggi dibandingkan dengan kelompok lain. Supernatan dari PBMC dari kelompok O-IR menurunkan ekspresi IL-10 pada makrofag M2. Sehingga ekspresi IL10 ini tidak mampu menekan ekspresi IL-6 makrofag M1.

Kesimpulan

Disfungsi sel T memori spesifik SARS-CoV-2 meningkatkan resistensi insulin 12 bulan pasca COVID-19 pada kelompok obes yang tidak mengalami penurunan kadar lemak dan obesitas sentral.

.....Background: A retrospective analysis to investigate the increased of insulin resistance and obesity within 12 months after COVID-19 was conducted to identify contributing metabolic factors and inflammatory responses, including the proportion of functional and dysfunctional SARS-CoV-2-specific memory T cells, cytokine levels, and macrophage polarization.

Methods:

This cohort study involved 47 SARS-CoV-2-confirmed patients, who were followed-up at five periods: the acute phase (baseline) and months 1, 3, 9, and 12 of the convalescent phases. Participants were categorized

into three groups based on obesity status and increased HOMA-IR: non-obese (NO), obese without HOMA-IR increase (O), and obese with HOMA-IR increase (O-IR). Increased of HOMA-IR was defined as a HOMA-IR ratio of 12th/1st month > 1.21 . At each period, body composition and glycemic indices were measure and PBMC was isolated. The PBMC was incubated with SARS-CoV-2 antigen for 24 hours to identify SARS-CoV-2-specific CD4⁺ and CD8⁺ memory T cells. The PBMC supernatant was used to evaluate cytokine production and macrophage polarization. Results:

A 35.3% of non-DM patients, 75% of newly diagnosed DM patients, and 59.1% of DM patients experienced increased of HOMA-IR $> 21\%$ within 12 months postCOVID-19. The O-IR group did not show a reduction in total body fat, fat-to-muscle ratio, or waist circumference over the 12-month follow-up. Additionally, the O-IR group had a lower proportion of functional SARS-CoV-2-specific memory T cells, a higher proportion of dysfunctional cells, lower cytokine levels, but a higher TNF-/IL-10 ratio compared to other groups. The PBMC supernatant from the O-IR group reduced IL-10 expression in M2 macrophages, which failed to suppress IL-6 expression in M1 macrophages.

Conclusion:

The dysfunctional SARS-CoV-2 memory T cells may increase the risk of elevated insulin resistance within 12 months post COVID-19, particularly in obese individual who do not experience body fat and central obesity reduction.