COVID-19: Issues related to solid organ transplantation

Solid organ transplantation and SARS-CoV-2: Introduction

- 1. **Risk of infection**: It is not known whether solid organ transplant recipients are at higher risk for acquiring SARS-CoV-2 infection than the general population. However, chronic immunosuppression may lower the infectious dose needed to cause COVID-19 and impair adequate immune control once infection is established.
- 2. **Viral shedding:** Solid organ transplant recipients may shed greater amounts of virus for longer durations than otherwise healthy hosts. Thus, they may be more likely to spread infection to others.
- 3. **Severity of illness** : It is unclear if solid organ transplant recipients have a higher risk of severe disease compared with nontransplant patients if infected with SARS-CoV-2. Many solid organ transplant recipients have medical comorbidities (eg, hypertension, diabetes mellitus, chronic kidney disease, cardiovascular disease) that have been associated with more severe COVID-19 disease and mortality,
- 3. **Clinical features**: Clinical features of COVID-19 among solid organ transplant recipients are variable and similar to those in immunocompetent patients. However, fever appears to be less common

COVID-19 in immunocompromised patients: A systematic review of cancer, hematopoietic cell and solid organ transplant patients

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SUMMARY

Background: The clinical impact of severe coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in immunocompromised patients has not been systematically evaluated.

Methods: We reviewed current literature reporting on COVID-19 in cancer (CA), hematopoietic cell (HCT), and solid organ transplant (SOT) patients and compared their clinical data and outcomes to the general population. For adult CA, HCT and SOT patients, an extensive search strategy retrieved all articles published until July 20, 2020 by combining the terms *coronavirus, coronavirus infection, COVID-19*, and *SARS-CoV-2* in PubMed, Cochrane, and Web of Science, and following the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines. For the pediatric CA cohort, a global COVID-19 registry was used. For the general population cohort, a large meta-analysis was used to compare pooled prevalence estimates, and two large meta-analyses were utilized to serve as pooled comparators for hospitalized COVID-19 patients.

Findings: Compared to the general population, adult CA and SOT patients with COVID-19 had higher comorbidities, greater levels of inflammatory markers at diagnosis, and higher rates of intensive care and hospital mortality. Pediatric CA patients and HCT patients with COVID-19 tended to have clinical presentations and outcomes similar to the general population.

Interpretation: To our knowledge, this is the first systematic review evaluating COVID-19 phenotype and outcomes in immunocompromised patients and comparing them to the general population, which shows that hospital outcomes appear to be worse in adult CA and SOT patients, potentially due to their higher co-morbidity burden.

Funding: None

Management

- The approach to management (eg, use of antivirals, supportive care) is also similar to that for the general population, although careful attention should be paid to potential drug-drug interactions and effects on the immunosuppressive regimen

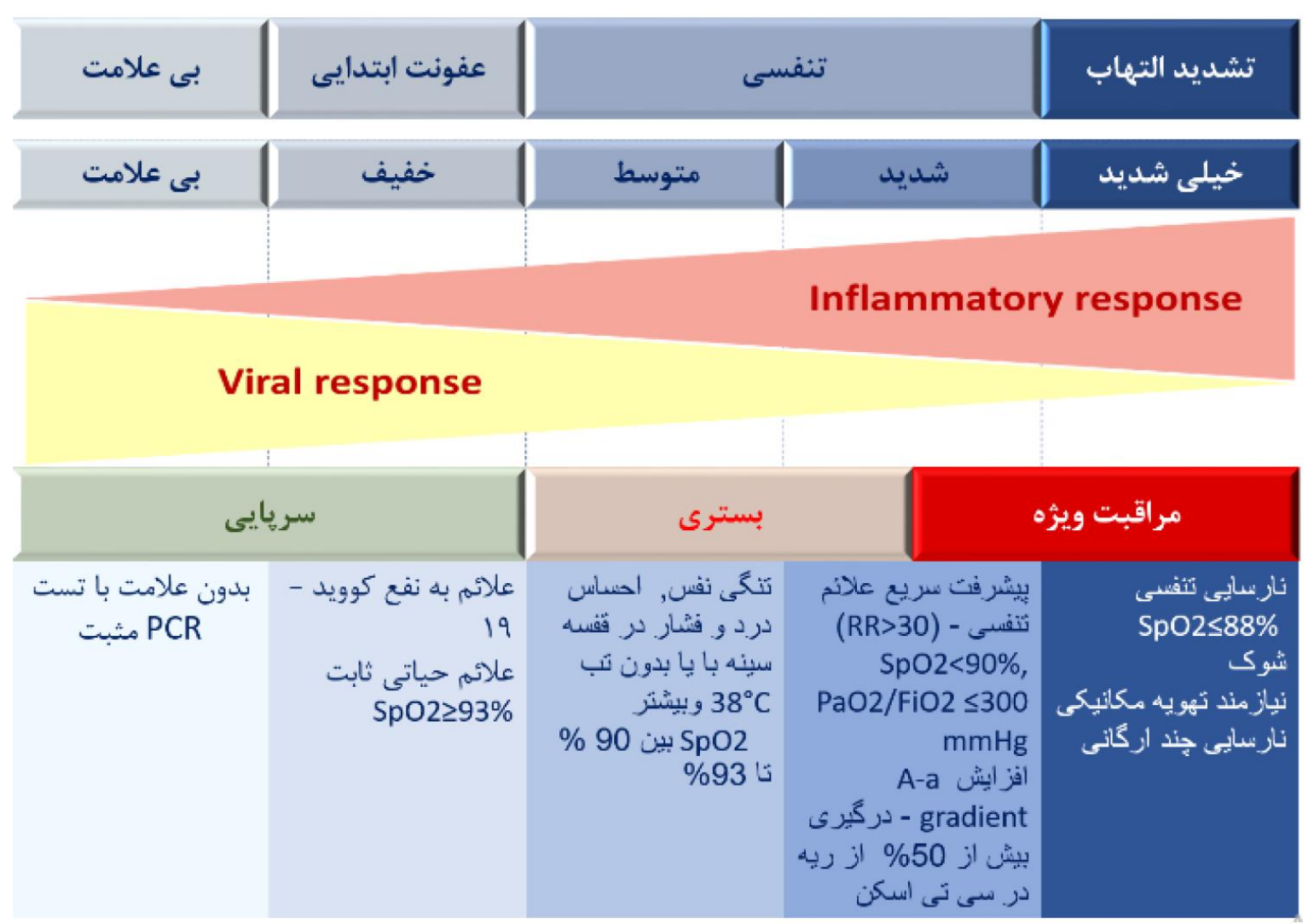
Maintenance immunosuppressive therapy

- A calcineurin inhibitor (Cyclosporine or Tacrolimus) or mTOR inhibitor (Rapamycin or Everolimus)
- An antimetabolite (Azathioprine, mycophenolate mofetil, or enteric-coated mycophenolate sodium)
- A Glucocorticosteroid (Prednisolone).

Adjustments to the immunosuppressive regimen are necessarily individualized, based upon:

- 1. **Disease severity**
- 2.**The risk of acute allograft rejection**: particularly high in transplant recipients who generally require high levels of maintenance immunosuppression (eg, first two months after transplantation, patients with second time transplantation, transplantation in sensitized patients, lung or heart recipients).
- 3.**The specific regimen used**
- 4.**Type of organ transplanted**

Disease severity



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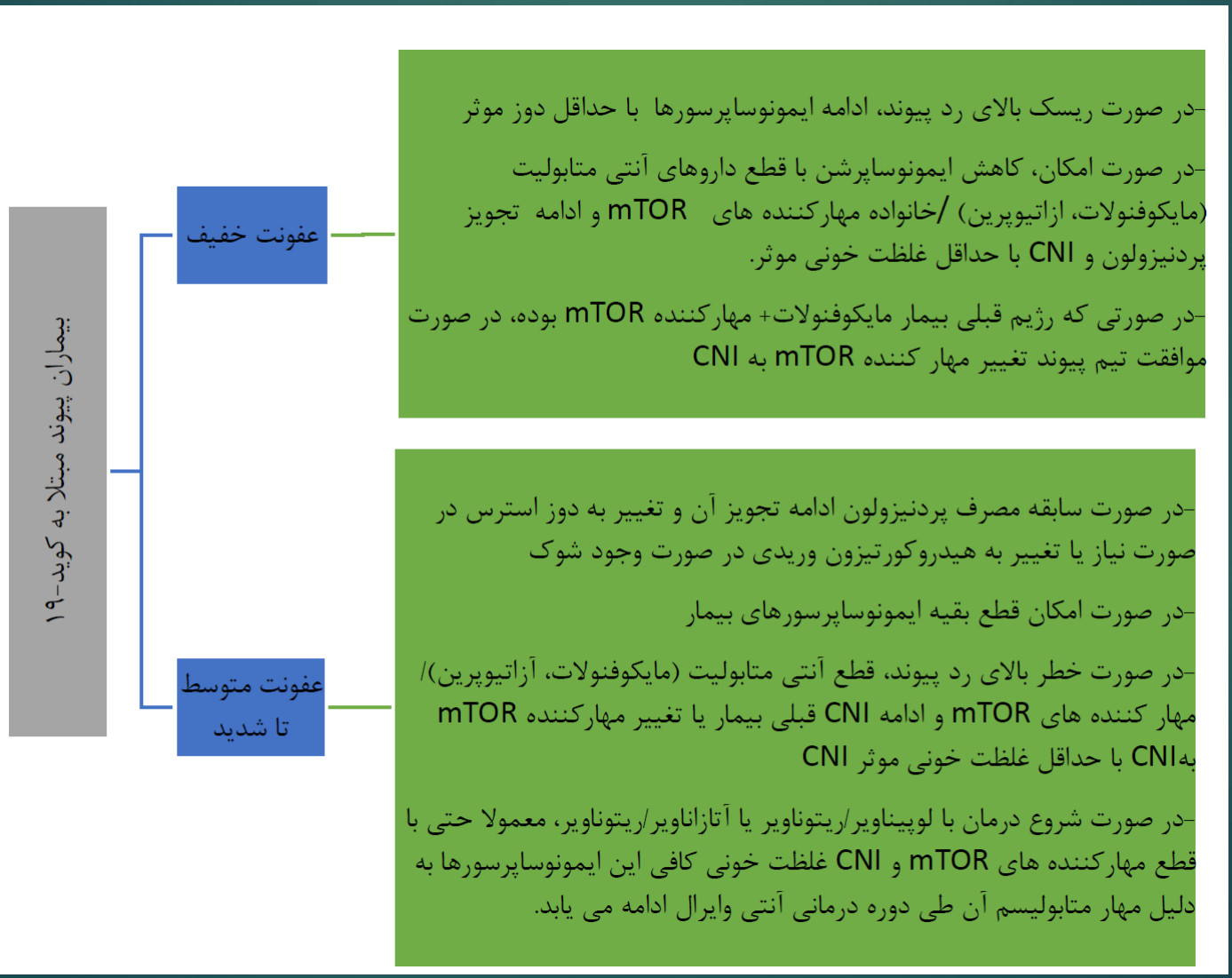

Potential Importance of Drug–Drug Interactions Between Immunosuppressive Drugs and Investigational COVID-19 Treatments

	(Hydroxy)chloroquine	Lopinavir/Ritonavir (Kaletra)
Tac		
Risk level	Moderate—major	Major
Outcome	QT-interval prolongation.	Increased Tac concentrations; may result in an increased risk of Tac toxicity
Our recommendations	QT interval monitoring (required)	Consider a Tac dosing regimen of 0.5–1 mg once weekly and close TDM (highly recommended)
CsA		
Risk level	Moderate	Moderate-major
Outcome	Increase the concentration of CsA may result in an increased risk of CsA toxicity	Increased CsA concentrations; may result in an increased risk of CsA toxicity
Our recommendations	QT interval monitoring (required)	Consider a CsA dosing regimen of 25 mg every 1–2 days and close TDM. ! possible delay in Tmax (highly recommended)

vaccination

- All transplant recipients are eligible for vaccination, . Although the immunogenicity and efficacy COVID-19 vaccines are uncertain in solid-organ transplant recipients [21], the potential for benefit from vaccination likely outweighs this uncertainty.

- When possible, we delay vaccination for at least one month from the time of transplantation and for at least three months after use of T cell-depleting agents (eg, anti-thymocyte globulin) or specific B cell-depletion agents (eg, rituximab) [22].
- For transplant recipients outside of the early posttransplantation period, we do not adjust maintenance immunosuppressive medications around the time of vaccination to avoid rejection.