



COVID-19 incidence was initially associated with posttransplant graft failure rates

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Introduction

The emergence of COVID-19 severely disrupted the transplant system. Living donor kidney transplant was essentially halted, and waitlist mortality rates for kidney candidates increased. To better understand the effect of COVID-19 on kidney posttransplant outcomes, we estimated the association of county-level COVID-19 incidence with kidney posttransplant all-cause graft failure.

Methods

Study population

The study used a period-prevalent cohort of kidney recipients from March 13, 2019 to July 31, 2020, who received a transplant on or after January 1, 2000. Specifically, recipients were included if (1) transplanted on or after January 1, 2000, (2) transplanted on or before July 31, 2020, and (3) had graft function on March 13, 2019.

COVID-19 incidence

The county-level incidence of COVID-19 for each kidney transplant program was determined from the *New York Times* database and aggregated into cases per 1,000,000 for each week before and after the national emergency declaration for COVID-19.

For each week, recipients were given the county-level incidence of the transplant program during the previous week. For example, the association of COVID-19 incidence with posttransplant graft failure between March 13, 2020, and March 19, 2020 used the incidence of COVID-19 between March 6, 2020, and March 12, 2020.

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Methods (continued)

Modeling the effect of COVID-19 incidence

The effect of COVID-19 incidence could evolve over time because (1) COVID-19 testing was not widely available after the initial emergence of COVID-19, and (2) hospitals may have better handled COVID-19 outbreaks through, for example, better preventive care or better care of patients with COVID-19. In both situations, **COVID-19 may have a stronger association with posttransplant graft failure early in the pandemic compared to latter.**

A two-dimensional spline estimated the association of COVID-19 across calendar time and incidence, allowing for the effect of COVID-19 incidence to vary over time.

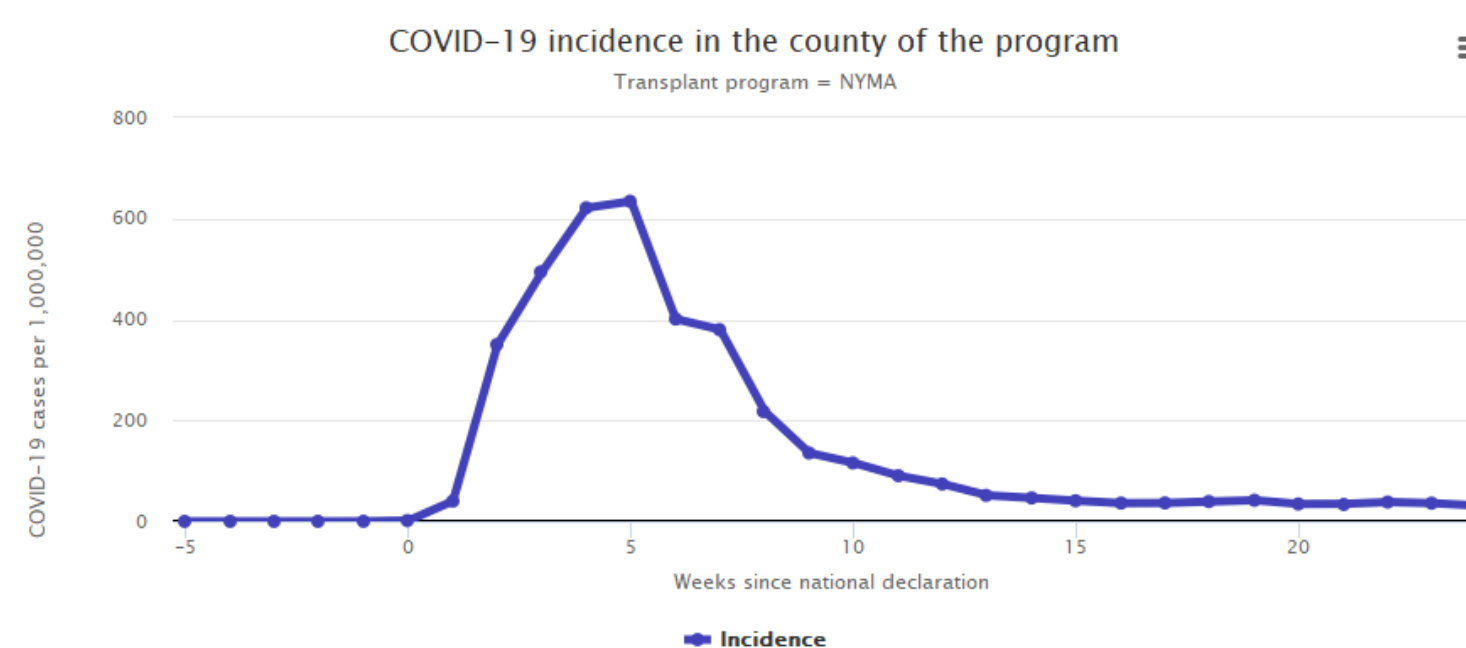
A piecewise exponential model (PEM) estimated the association of COVID-19 incidence with posttransplant graft failure. PEMs are proportional hazards models with a piecewise constant baseline hazard function. In contrast, the Cox proportional hazards model places no assumptions on the baseline hazard function. The baseline hazard was split into narrow intervals immediately after transplant and much wider intervals for recipients with long-term graft function.

To adjust for recipient and donor risk factors, an initial model was estimated without an effect for COVID-19 incidence. The final model with an effect for COVID-19 incidence included the linear predictor for recipient and donor risk factors from the initial model.

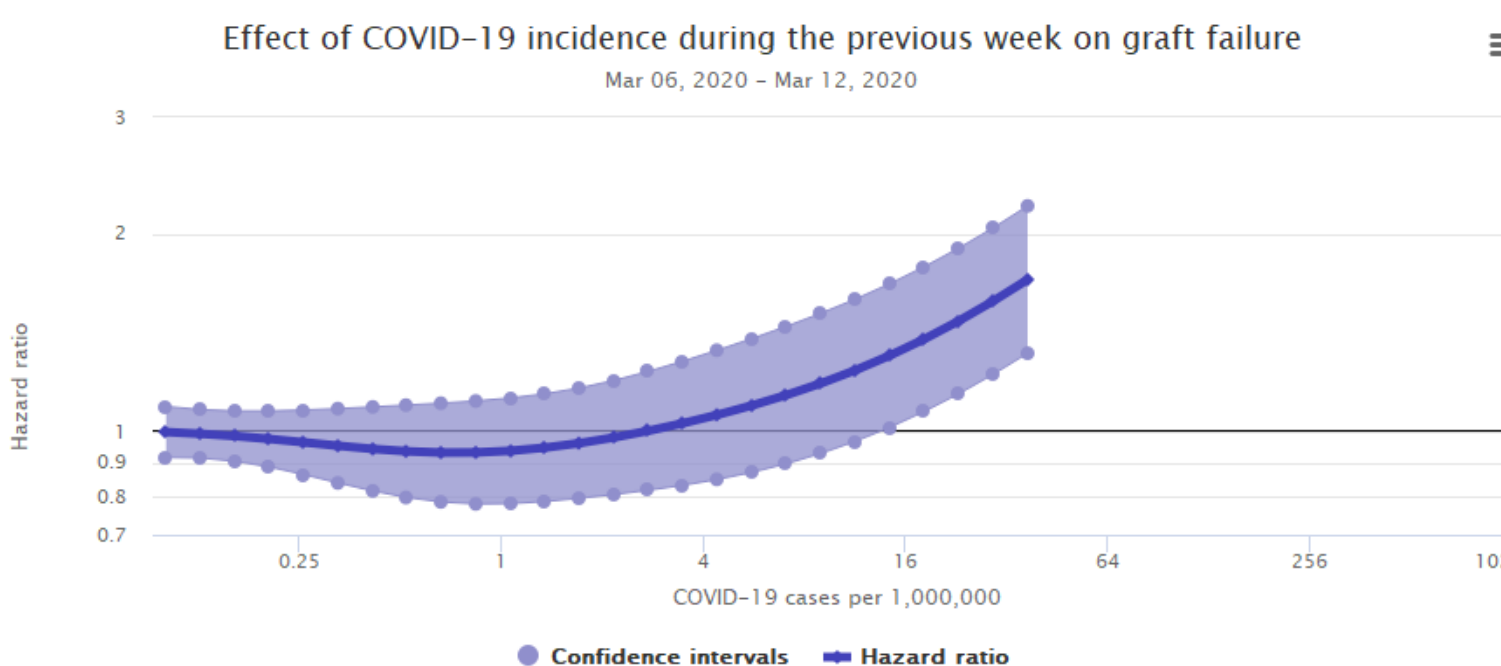
All analyses were performed in R v3.5.4, and the mgcv package estimated the two-dimensional spline for the effect of COVID-19 incidence.

Results

Example of county-level incidence (New York City)

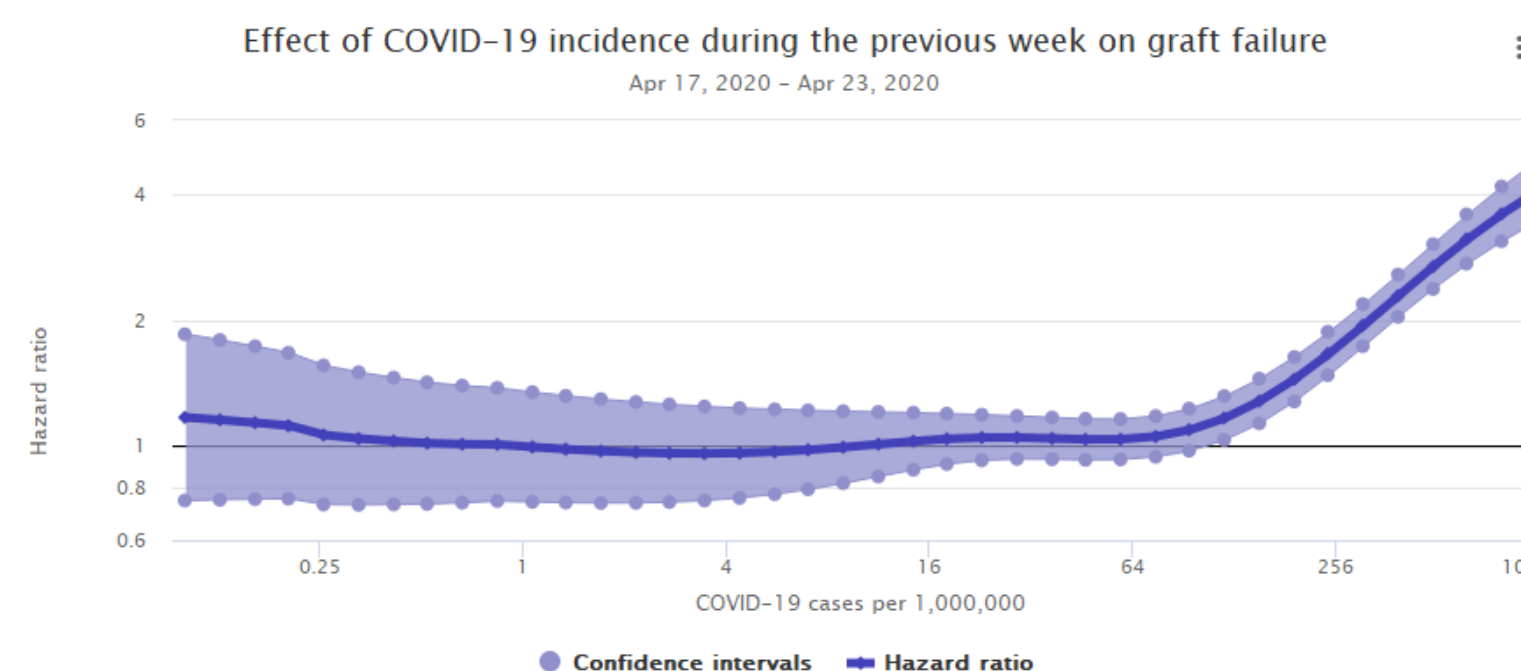


Effect of COVID-19 incidence: March 6, 2020 – March 12, 2020

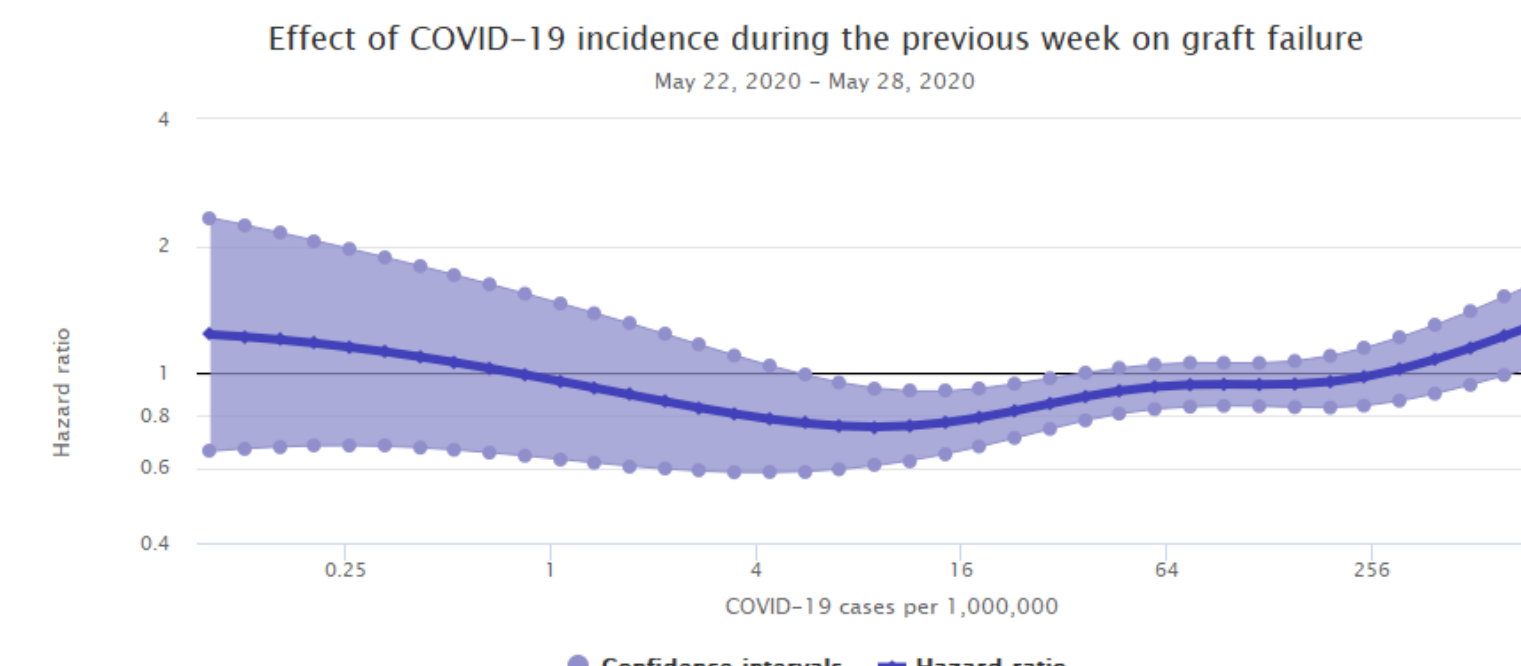


Results (continued)

Effect of COVID-19 incidence: April 17, 2020 – April 23, 2020



Effect of COVID-19 incidence: May 22, 2020 – May 28, 2020



Discussion

The association of COVID-19 incidence was particularly strong in mid-April but significantly attenuated by the end of May. Thus, the emergence of COVID-19 coincided with a significantly higher rate of kidney graft failure, potentially from COVID-19 infection or patients not seeking for-cause medical care. However, after the initial disruption, COVID-19 incidence had a weaker association with kidney graft failure rates.

The association may have attenuated because (1) kidney recipients and/or transplant programs adapted to the new conditions imposed by COVID-19 and/or (2) the availability of COVID-19 testing was different and the implied severity of, for example, an incidence of 64 cases per 1,000,000 was worse in March than May 2020.

The observed effect of COVID-19 incidence aligns with previous research into kidney waitlist mortality immediately following COVID-19. Specifically, the hazard of waitlist mortality was significantly elevated during the two months immediately after the emergence of COVID-19 before a notable attenuation. Because kidney candidates and recipients have different interactions with the medical system, the alignment early in the pandemic may represent an effect of community transmission on outcomes.

References

Miller J, Wey a, Musgrave D, Ahn YS, Hart A, Kasiske BL, Hirose R, Israni AK, Snyder JJ, "Mortality among solid organ waitlist candidates during COVID-19 in the United States," *American Journal of Transplantation*, In press.

No conflicts of interest to report.