LETTER TO THE EDITORS

COVID-19 in solid organ transplantation: an analysis of the impact on transplant activity and wait lists

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Dear Editors,

The limited knowledge about COVID-19, the disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), makes mortality figures hard to interpret in the undetermined prevalence of an asymptomatic infection.

Treatments are currently being tested, but without proof of an effective vaccination, the fear of further detrimental outcomes, as a result of a second wave, persists. One of the main differences in the death toll among the various countries seems related to the different response to the outbreak: early measures of containment as lockdown, revealed their effectiveness in mitigating the virus spread, with the earliest the lockdown, the lower the death toll [1].

We report individual activities for solid organ transplantation (SOT) in Italy during the first phase of the pandemic, with a further interregional analysis, in relation to the wait-listing activity, the hospitalization of symptomatic COVID-19-infected patients and those admitted to intensive care unit (ICU).

Figure 1 represents the overall transplant activity (black) and selective data for kidney (red), liver (green) and heart (blue). Since 2016, there has been a mean value of 70 transplants/week, progressively increasing by year in the pre-COVID-19 era (left plots Fig. 1).

The unforeseen and sudden consequences of the SARS-CoV-2 spread (right-sided plots in Fig. 1) determined an average drop to about 60 transplants/week (~16% less), with the lowest value of ~20 transplants/week (~70% less). This paralleled the rapid escalation of the patients affected by COVID-19 and for which the majority of healthcare resources were utilized: hospitalized, hospitalized with symptoms and in the worst scenario of severe acute respiratory distress, admission to intensive care unit (ICU) for ventilation support (Fig. 1, bottom-right plot).

During the pandemic, the total number of patients in the Italian waiting lists dropped only partially from >9000 to ~8500 (Fig. 1 right, second line).

The peak in the hospitalized patients and the ones requiring ventilation is mirrored by the activity drop for all SOT (Fig. 1).

COVID-19 impacted individual organs differently: in Fig. 1 the second row corresponding to kidney shows that this was the one mostly affected, with wait-listed candidates being almost constant around 7000 in the last five years and dropping to ~6000 (15% less) during the lockdown. This effect is not instead observed for two life-saving procedures, the heart and liver transplants, whereas their numbers remaining constant throughout the pandemic. For instance, at the end of 2019, wait-listed heart transplant candidates were 668, with the lowest number registered at the beginning of May (653) and again 660 at the end of June.

Table 1 summarizes wait-list trends during the pandemic by Italian regions in relation to the COVID-19 hospitalization rate and admission to ICU. The Italian most affected region, Lombardy (LO), had the same drop in the waiting list compared with other regions in the Centre and Southern area, as Lazio (LA) and Sicily (SI), despite the rate of COVID-19 hospitalized and ICU patients was significantly less in these latter regions. A similar trend was confirmed for the vast majority, with the statistically significant exception of Piedmont (PI) and Sardinia (SA), where on the contrary the number of wait-listed candidates for kidney transplantation increased. This last observation is striking as Piedmont and Lombardy are neighbour regions, although in this case the lockdown impacted with more patients not being transplanted, rather than because of the drop in referral.

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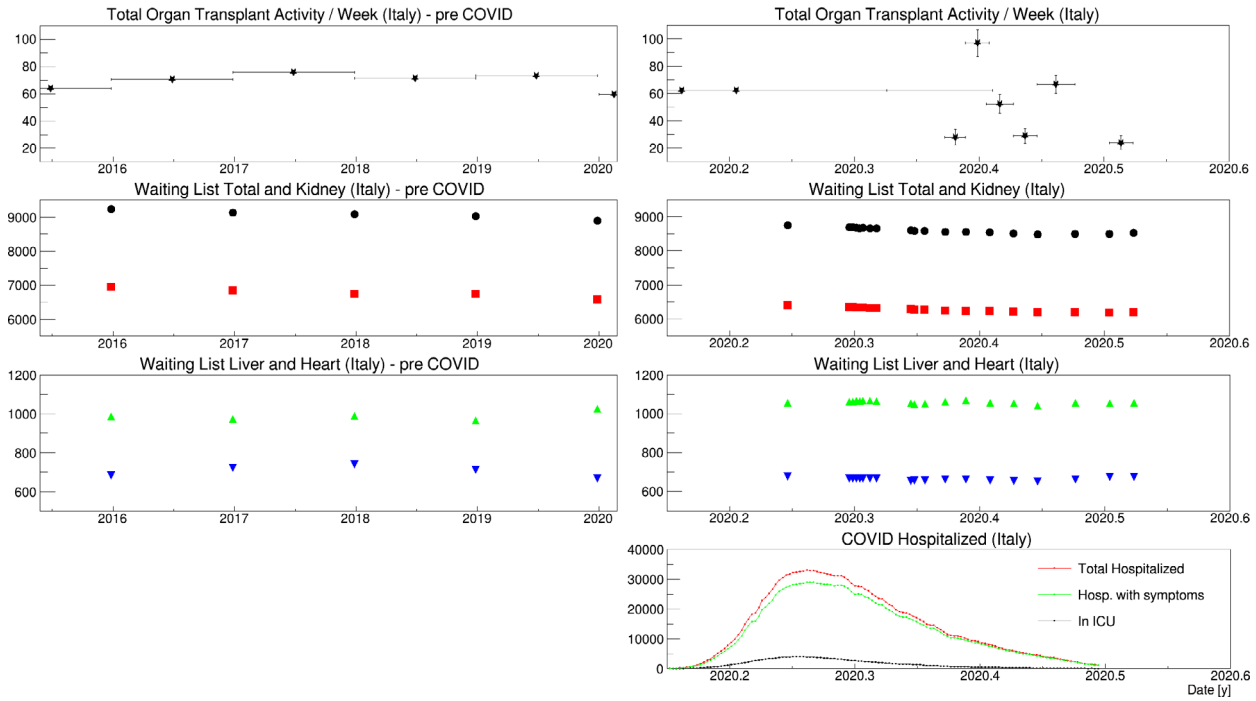

Figure 1 Total organ transplant activity, waiting list activity, and COVID hospitalised patients: kidney (red), liver (green), heart (blue).

For life-saving organs as liver, heart and lung, the waiting lists were not significantly affected, as expression of the urgency of these procedures, therefore considered not to be postponed.

To understand more in details the Italian situation, it is important to highlight that the lockdown was imposed on the 8th March in Northern Italy and only 24 h later (9th March) in the Southern macro-area, despite the latter not being affected as badly as the first and therefore without apparently an obvious reason to adopt such a radical measure. This decision contributed to maintain the overall COVID-19-hospitalized patients lower for regions in the Southern macro-area and confirmed the general principle of the earlier the lockdown, the better for the healthcare system.

Indeed, this seems already a valid point to take, as in the unfortunate event of a new pandemic, hospital will need to be COVID-19-free areas, with strict hand washing hygiene, physical distancing and full personal protection devices for staff, in order to avoid uncontrolled virus spread [2].

In the case of transplantation, to learn from the lessons the COVID-19 pandemic is of utmost importance: immunosuppressed patients face the burden of an increased infection risk because of the nature of their anti-rejection drugs [3–5]. Preliminary registry analyses show that liver transplant candidates, but also those being transplanted, are at higher risk compared with the general population [6] with a prevalence of 0.3% and a mortality rate of 20–25% in hospitalized patients. This increased risk is faced also by dialysis patients [7], for which there is a 30% increased mortality, a similar value to that of hospitalized kidney transplant patients [4]. We also know that surgery in patients affected by SARS-CoV-2 is associated with 50% risk of pulmonary complications [8] and an overall 30% risk of lethality. In view of the above, transplantation has been postponed if an alternative replacement therapy existed, such as dialysis [9] or insulin injection. The suspension of some transplant programs explain partially the significant drop we have described in SOT activity; to this, we need also to add the unprecedented crisis following the sudden hit of the pandemic impacting staff and personnel working in ICU (Fig. 1).

In conclusion, the strategy adopted from transplant centres to overcome the emergency circumstance and its effect result from the individual organ type and local hospital policy, but also from the government response and thus impacting the national healthcare system. Dialogue between providers to offer alternative strategies on how to improve safety in solid organ transplantation with limited health care resources is encouraged to prevent non-COVID-19 deaths related to the lack of the necessary care treatment [10].

Table 1. Organ transplant activity and wait-list cross-correlations for each region with Lombardy, the epicentre of the pandemic.

	Wait-list cross-correlations between Italian regions and Lombardy																
Organ/region	PI	VE	FVG	LI	ER	TO	UM	MA	LA	AB	CAM	PU	BA	CAL	SI	SA	LO
Kidney	−0.88	0.72	0.03	0.94	0.97	−0.22	0.48	0.94	0.81	0.52	0.83	0.86	−0.88	−0.01	0.97	−0.94	1
Lung	−0.44	0.32			0.78	0.57			0.39						0.72		1
Heart	−0.47	0.26	0.24		−0.68	0.64			0.21		0.09	0.21			−0.13	−0.82	1
Liver	−0.69	−0.16	0.68	0.79	0.69	0.69		0.77	0.42	0.25	−0.53	−0.71	−0.86	−0.87	−0.01	−0.8	1
Pancreas	0.82	0.56			0.53				0.34								
Max. hospitalized per day	3985	2068	296	1332	4310	1437	220	1168	1607	437	717	780	76	200	637	151	13328
FWHM hospitalized	56	46	58	46	46	40	36	46	69	57	57	43	47	41	45	62	50
Max. ICU per day	453	356	61	179	375	297	48	169	203	76	181	159	19	23	80	31	1381
FWHM ICU	39	34	22	37	51	41	32	38	37	33	19	15	25	27	31	41	44
Inhabitants (millions)	4.393	4.908	1.218	1.565	4.449	3.742	0.889	1.538	5.898	1.322	5.839	4.064	0.57	1.965	5.057	1.653	10.019
ICU/hospitalized (%)	11.37	17.21	20.61	13.44	8.70	20.67	21.82	14.47	12.63	17.39	25.24	20.38	25.00	11.50	12.56	20.53	10.36
Max. hospitalized per day per million population	907.2	421.4	243	851	968.8	384	247.5	759.4	272.5	330.5	122.8	191.9	133.2	101.8	126	91.34	1330.3

AB, Abruzzo; BA, Basilicata; CAL, Calabria; CAM, Campania; ER, Emilia Romagna; FVG, Friuli Venezia Giulia; FWHM, Full Width Half Maximum; ICU, Intensive Care Unit; LA, Lazio; LI, Liguria; Lo, Lombardy; MA, Marche; PI, Piedmont; PU, Puglia; Sa, Sardinia; SI, Sicily; TO, Tuscany; UM, Umbria; VE, Veneto.

Red: northern regions, yellow: centre regions, green: southern regions.

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Conflict of interest

The authors have declared no conflict of interest.

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