Respiratory multiplex PCR could predict morbidity and mortality in solid organ transplant patients

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Introduction and Methods

Respiratory tract infections are commonly seen and compose a great burden of healthcare. The causing pathogens might be either bacteria or viruses and since the treatment is different for each, prompt diagnosis and early treatment is crucial especially in immunocompromised patients like solid organ transplant (SOT) recipients who often present with obscure findings. The aim of this study is to compare the respiratory multiplex PCR results of solid organ transplant recipients with the other hospitalized patients and analyze if it plays a role in morbidity and mortality prediction.

Material and Methods

The study was approved by the ethical committee of Başkent University (KA23/233) and included all the hospitalized patients from 1 January 2023 to 31 December 2023, who underwent a multiplex PCR for the respiratory tract infections diagnosis.

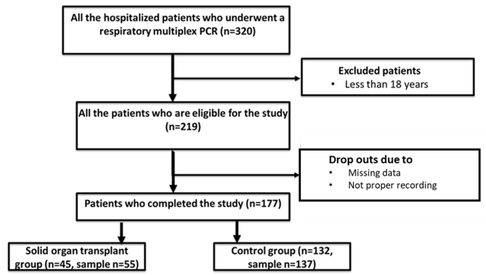


Figure 1. The consort chart summarizes the recruitment of patients for both solid organ transplant patients and the control group.

The characteristics of patients included in the study.

The average age for the SOT patients was 48.8 years, which was statistically significantly lower when compared to the control group with an average of 67.6 years. There were 30 kidney (66.6%), 9 liver (20%) and 6 heart (13.4%) transplant patients included. The gender distribution, smoking status, comorbidities and symptoms present at the time of PCR sampling were similiar for both groups with an exception of a higher prevalence of cancer, COPD or asthma, neurological and rheumatological diseases in control group. Whereas renal and liver diseases and diarrhea were more frequent in the SOT group while fever was slightly higher in the control group. Regarding the overall findings hypertension and cardiac diseases were the most common comorbidities, whereas dyspnea, cough and fever the most common symptoms for both groups of patients. There was no difference in between the groups regarding the clinical presentation, whereas the laboratory results showed some significant differences. Levels of alkaline phosphatase (ALP), total bilirubin, creatinine and procalcitonin were higher, whereas sodium, hemoglobin, leucocyte and lymphocyte total counts, lactate and bicarbonate level in blood gas values were lower in SOT group when compared to controls (Table 2).

Results-1

Table 1. The clinical and laboratory features for both groups.

Variables (unit)	Control (n=137)			SOT (n=55)			P*
	Median	Min.	Max.	Median	Min.	Max	
Heart rate (beats per minute)	86.00	40.00	200	90.50	70.00	128	,408
Systolic blood pressure (mmHg)	117.98	16.65	120.00	127.00	74.00	200	,094
Fever (^{0}C)	37.53	1.00	37.60	36.75	35.70	39	,101
SpO_2 (%)	93.37	3.60	94.00	95.00	75.00	100	,558
C-Reactive Protein (mg/L)	101.15	2.00	373.80	128.80	2.00	368.70	,319
ALT (U/L)	21.00	5.00	1,761.00	19.00	5.00	1,761.00	,641
AST (U/L)	21.50	7.00	3,643.00	24.00	6.00	3,643.00	,913
ALP (U/L)	80.00	13.00	495.00	111.00	57.00	544.00	**,004**
GGT (U/L)	42.50	6.00	881.00	53.00	16.00	556.00	,156
Total bilirubin (mg/dL)	.70	.20	15.80	.80	.30	41.00	**,015**
Creatinine (mg/dL)	.96	.31	9.01	2.04	.30	6.26	**,000**
Sodium (mmol/L)	138.00	124.00	153.00	136.00	122.00	146.00	**,001**
Potassium (mmol/L)	4.00	1.90	5.90	4.01	2.09	30.30	,369
Procalcitonin (μg/L)	.22	.02	12.69	.97	.03	77.21	**,001**
Hemoglobin (g/dL)	11.50	7.50	19.50	10.00	3.09	16.50	**,001**
Leucocyte x1000/μL	10.10	.12	33.10	8.18	1.01	60.90	**,038**
Platelet x1000/μL	205.00	13.00	998.00	158.00	22.00	463.00	**,000**
Erythrocyte xM/μL	3.78	2.47	5.99	3.38	1.29	6.49	**,041**
Lymphocyte x1000/μL	1.07	.03	5.43	.61	.13	3.31	**,001**
Neutrophils x1000/μL	7.49	.06	27.60	6.58	.12	51.50	,117
Monocyte x1000/μL	.68	.01	1,172.00	.55	.00	6.29	,083
Eosinophil x1000/μL	.02	.00	1.64	.01	.00	1.91	,567
LDH (U/L)	268.00	105.00	4,973.00	285.00	139.00	2,071.00	,389
Ferritin (U/L)	402.00	1.48	33,511.00	310.00	19.00	8,582.00	,803
D-dimer (mg/L)	1.87	.19	35.20	2.81	.24	16.48	,187
CK (U/L)	34.00	25.00	43.00	108.00	108.00	108.00	,221
CK_MB (μg/L)	1.30	.30	126.40	1.07	.30	15.00	,866
Troponin (ng/L)	57.00	2.00	35,557.00	52.50	3.00	16,046.00	,726
pH	7.42	7.22	7.61	7.39	7.17	7.50	,233
PCO_2 (mmHg)	38.90	21.00	97.60	35.30	21.08	62.50	,104
PO_2 (mmHg)	45.35	15.00	298.00	40.00	26.07	220.00	,461
SO_2 (%)	79.90	10.20	99.20	80.10	39.60	99.40	,444
HCO_3 (mEq/L)	24.90	14.80	35.20	22.40	12.50	29.40	**,002**
Lactate (mmol/L)	1.60	.50	11.70	1.05	.40	12.03	**,002**

*; <0.05, Mann-Whitney U test

SpO_2: oxygen saturation by pulse oxymetry; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: gamma glutamyltransferase; LDH: lactic acid dehydrogenase; CK: creatine kinase; CK-MB: Creatine kinase-MB; PCO_2: partial pressure of carbon dioxide; PO_2: partial pressure of oxygen; SO_2: oxygen saturation , HCO_3:bicarbonate.

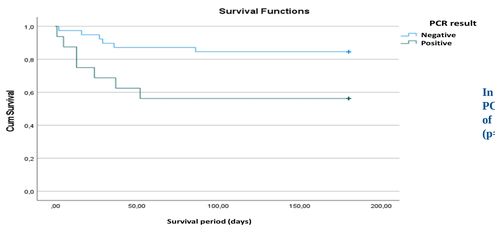
Results-2

Table 2. The PCR results for both SOT and controls.

	Groups				P*
	Controls (n=137)		SOT (n=55)		
	n	%	n	%	
At least one positive PCR result	28	20.44	18	32.72	0,071
Parainfluenza virus 4	3	10.71	-	-	0.106
Influenza A H3	3	10.71	4	23,53	
RSV	2	7.14	1	5.88	
Rhinovirus/enterovirus	9	32.14	7	41.18	
Parainfluenza virus 3	3	10.71	-	-	
Bocavirus	-	-	1	5.88	
Human metapneumovirus A/B	-	-	1	5.88	
SARS-CoV-2	7	25.00	2	11.76	
Influenza B	1	3.57	-	-	
Adenovirus	-	-	1	5.88	
Coronavirus HKU1	-	-	1	5.88	

Table 3. Morbidity and mortality regarding the result of PCR for both controls and SOT patients. Mortality was higher in PCR+ SOT patients

		Control patients (n=132)					SOT patients (n=45)				
		Negative PCR n=104		Positive PCR n=28		P*	Negative PCR n=29		Positive PCR n=16		P*
		n	%	n	%		n	%	n	%	
ICU admission	Yes	44	42,30	9	32,14	0,330	14	48,27	10	62,50	0,359
	No	60	57,70	19	67,86		15	51,73	6	37,50	
Re-hospitalization	Yes	21	20,19	8	28,57	0,341	14	48,27	5	31,25	0,268
	No	83	79,81	20	71,43		15	51,73	11	68,75	
Mortality	Yes	29	27,88	8	28,57	0,942	4	13,79	7	43,75	**0,025***
	No	75	72,12	20	71,43		25	86,21	9	56,25	



In SOT patients a positive PCR result increased the risk of mortality by 4.28 fold (p=0.03, %95 CI 1.15-15.95).

Figure 2. Survival data for the 6-month period in SOT group. (Log Rank (Mantel-Cox) p value=0.016).

Conclusion

Viral infections, remain a clinical challenge that negatively impact both patient and graft outcomes in SOT patients. Early initiation of specific antiviral therapy may reduce mortality and be life-saving in these patients. The respiratory multiplex PCR is a tool for fast diagnosis and targeted treatment in solid organ patients. The presence of a positive result was associated with a 4.28 fold higher mortality.

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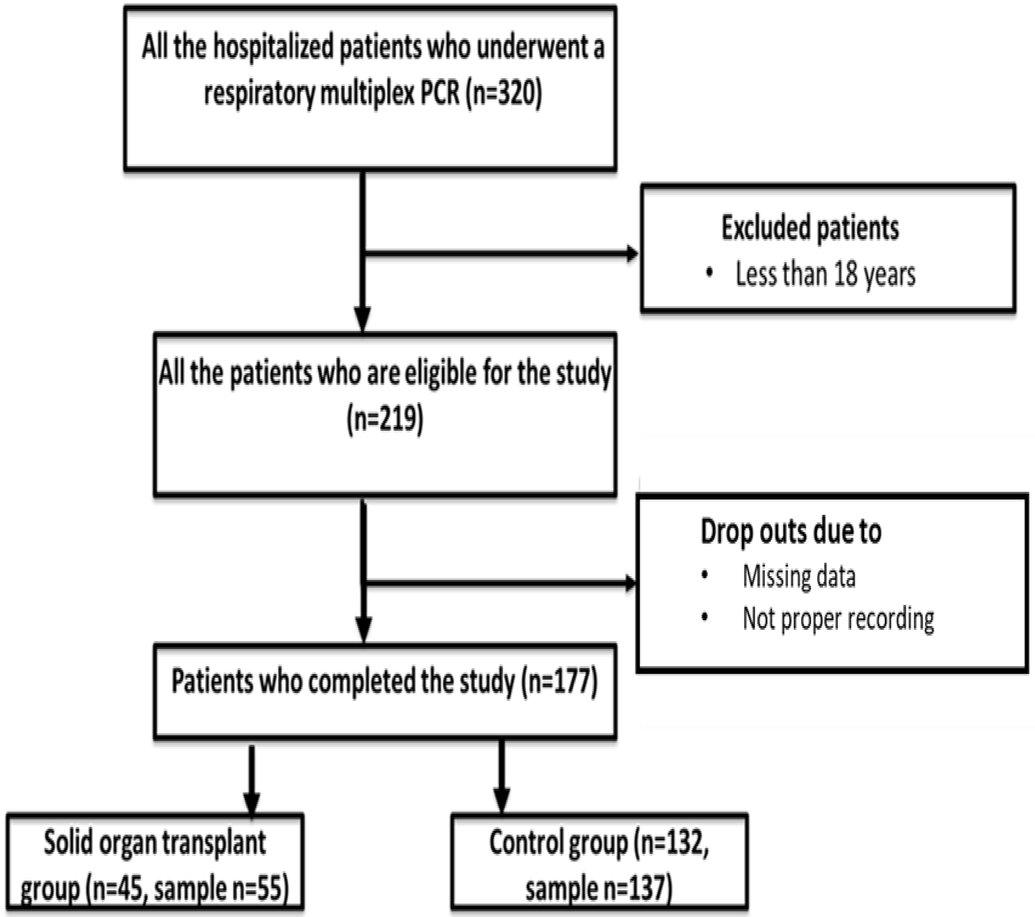

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	No	75	72.12	20	71.43		25	86.21	9	56.25	

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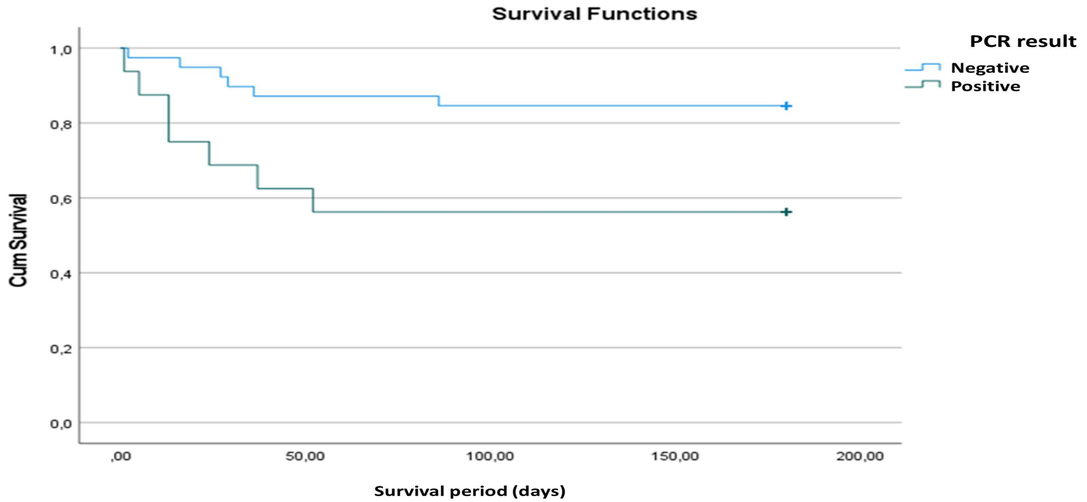

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