

SUPPLEMENTAL DIGITAL CONTENT

File S1: materials and methods

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1. Search strategies applied to the topic of transplantation.

Two independent search strategies (search strategy A and search strategy B) were used by two independent teams and resulted in the identification of the same references reporting transplantation of cells and organs from COVID-19 positive donors.

Detailed descriptions of the PICO questions, search strategy, information sources and results, is provided here.

a. Search strategy A.

The first search strategy was designed and executed June 18-21, 2020 and updated once August 22-28, 2020 and again Jan 9-10, 2021. This search sought to identify any publication reporting on outcomes of COVID-19 positive solid organ transplant recipients, regardless of the mode or source of infection. Multiple electronic databases were searched for references published since 2019 without language or publication type limits. A total of 1930 unique references were obtained from nine distinct databases. Title and abstract reviews identified 7 relevant articles addressing the question: “What are the outcomes of solid organ transplant recipients from COVID-19 positive donors?” Eventually, we selected 5 articles for review reporting 4 cases of solid organ transplantations from COVID-19 infected donors, or donors with one SARS-CoV-2 RTPCR positive test the day of transplantation or the day before.

The abbreviated PROSPERO protocol for systematic reviews was used.

Review questions:

Can we transplant organs recovered from COVID positive patients?

When is it safe to transplant an organ from a COVID positive donor? (living and deceased)

What are the outcomes of solid organ transplant recipients from COVID-19 positive donors?

Search methods:

A comprehensive search has been designed and executed between June 18-21, 2020 with text words and controlled vocabulary terms combining concepts for COVID-19/SARS-CoV-2 and organ transplantation. An update search in all sources was executed between August 22-28, 2020 and again between Jan 9-10, 2021. Search results were limited to references published since 2019. No language or publication type limits were applied to the search. Search results were managed, and duplicates removed in EndNote X9 (Clarivate). The complete search strategies are explicated below.

Search sources:

- MEDLINE Ovid (1946 to August 24, 2020 and then Jan 8, 2021), searched August 25, 2020 and Jan 9, 2021;
- Embase Ovid (1947 to August 24, 2020 and then Jan 8, 2021), searched August 25, 2020 and Jan 9, 2021;
- Cochrane COVID-19 Study Register (<https://covid-19.cochrane.org/>), searched August 25, 2020 and Jan 9, 2021;
- WHO COVID-19 Global literature on coronavirus disease (<https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/>), searched August 28, 2020 and Jan 9, 2021;
- Science Citation Index (1900 to August 25, 2020 and then Jan 8, 2021) Web of Science, searched August 25, 2020 and Jan 9, 2021;
- medRxiv and bioRxiv preprint server Cold Spring Harbor Laboratory, BMJ, Yale (<https://www.medrxiv.org/>; <https://www.biorxiv.org/>; current up to August 22 2020, searched August 22, 2020;
- Chinese translations of COVID-19 journal articles from Lanzhou University's Evidence-Based Medicine Center (current up to August 22, 2020), searched August 25, 2020;
- Google Scholar (<https://scholar.google.com/>), searched August 25, 2020 and Jan 10, 2021;
- NHS Blood and Transplant (<https://www.nhsbt.nhs.uk/news/coronavirus-update/>), searched August 28, 2020 and Jan 10, 2021

Condition or domain being studied:

Solid organ transplantation from COVID positive donors

Inclusion:

- All solid organ donors which proceeded to retrieval during the COVID-19 era
- All solid organ transplants which occurred during COVID-19 era
- Living and deceased donors

Exclusion: Other viral disease transmission

Intervention(s), exposure(s):

Inclusion:

- COVID positive donors which proceeded to donation including if they were COVID positive in the past.
- Living donor who were previously COVID positive.

Exclusion: Patients who were not proven to be COVID positive on laboratory findings according to local criteria

Comparator(s)/control:

Solid organ donors who were COVID-19 negative during COVID era

Types of study to be included initially:

No restrictions.

Context:

During the COVID-19 pandemic, there has been a substantial decrease in the number of solid organ transplants occurring globally. Currently, the risk of virus transmission from COVID-19 positive donors remains unquantified.

This review aims to collate the global experiences of using COVID-19 positive solid organ transplant donors, and the evidence found will be used to inform clinically relevant guidelines.

Primary (Critical) outcome(s):

COVID related morbidity and mortality in recipients

Secondary (Important) outcomes:

- Transplant related outcomes with a COVID-19 positive donor (examples: reduced immunosuppression, length of stay, acute rejection, delayed graft function, primary non function)
- Transmission to recipients
- Transmission to HCP and family members
- Morbidity and mortality associated with prolonged wait times prior to transplantation

Data extraction, (selection and coding):

Citation titles and abstracts have been scanned independently by two reviewers to identify any original or review articles. The full texts of retrieved articles have been independently reviewed to assess study eligibility.

Keywords:

(1) solid organ transplantation, (2) COVID-19, (3) disease transmission, (4) organ donation, (5) transplant outcomes

Search summary:

Source	Results (with duplicates) – baseline + update	June Baseline Results (unique)	August Update Results (unique)	Jan. (2021) Update Results (unique)	June and Jan. (2021) Results (unique)
MEDLINE		261	222	422	905
Embase		81	64	239	384
Cochrane COVID-19 Study Register		52	38	79	169
WHO COVID-19 Global literature on coronavirus disease		95	47	164	306
Science Citation Index		5	11	23	39
medRxiv & bioRxiv preprints		8	3	Not searched	11
Lanzhou Translations		7	10	Not searched	17
Google Scholar		26	63	0	89
NHS Blood and Transplant		1	3	6	10
Total:		536	461	933	1930

Search results:

6784 references were retrieved by the search, 1930 once duplicates were removed. A single screener (LH) reviewed all 1930 citations and removed those that were obviously unrelated to organ donation and transplantation and COVID-19.

This resulted in the removal of further 663 citations for a final result of 1267 that were reviewed in duplicate.

Search details (last update):

Database: Ovid MEDLINE(R) ALL 1946 to January 08, 2021

Date search conducted: January 9, 2021 Search

title: COVID-19_LSR_All-Groups_Update2

Strategy:

- 1 Coronavirus Infections/ (44311)
- 2 COVID-19/ (9731)

3 COVID-19 Nucleic Acid Testing/ (208)
 4 COVID-19 Serological Testing/ (124)
 5 COVID-19 Testing/ (438)
 6 SARS-CoV-2/ (6612)
 7 COVID-19.rs. (39012)
 8 severe acute respiratory syndrome coronavirus 2.os. (33013)
 9 (2019 nCov or nCov 2019 or nCov 19).tw,kf. (1468)
 10 (coronavir* or corona vir*).tw,kf. (49250)
 11 COVID.mp. (87442)
 12 COVID19.tw,kf. (1047)
 13 ("SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2").mp. (33517)
 14 ("SARS coronavirus 2" or "SARS-like coronavirus" or "Severe Acute Respiratory
 Syndrome Coronavirus-2").mp. (38862)
 15 or/1-14 [Set 1: COVID-19/SARS-CoV-2] (105294)
 16 Heart Transplantation/ (34797)
 17 Kidney Transplantation/ (96767)
 18 Liver Transplantation/ (57540)
 19 Lung Transplantation/ (15517)
 20 Organ Transplantation/ (13448)
 21 Pancreas Transplantation/ (7501)
 22 Transplantation/ (8959)
 23 ((allograft\$1 or donor\$1 or graft\$1 or recipient\$1 or transplant*) adj2 (cardiac or
 heart\$1 or heart-lung or hepatic or intestin\$ or kidney\$1 or kidney-pancreas or
 liver\$1 or lung\$1 or lung-heart or multiorgan or multi-organ or organ\$1 or pancreas
 or pancreaskidney or renal)).tw,kf. (247478)
 24 (transplant* not (cell* or faecal* or fecal*)).ti. (206029)
 25 or/16-24 [Set 2: Organ Transplantation] (347470)
 26 and/15,25 [Sets 1 & 2] (1024)
 27 limit 26 to yr="2020-Current" (980)
 28 remove duplicates from 27 (947)

Database: Ovid Embase 1974 to 2021 January 08

Date search conducted: January 9, 2021

Search title: COVID-19_LSR_All-Groups_Update2_2

Strategy:

1 exp coronavirus/ (22832)
 2 coronavirus infections/ (487)
 3 (2019 nCov or nCov 2019 or nCov 19).tw,kw. (1473)
 4 (coronavirus* or corona virus*).tw,kw. (48466)
 5 COVID.af. (80398)
 6 COVID19.tw,kw. (1124)
 7 ("SARS-CoV-2" or "SARS-CoV2" or SARSCoV2 or "SARSCoV-2").af. (28521)
 8 ("SARS coronavirus 2" or "SARS-like coronavirus" or "Severe Acute Respiratory
 Syndrome Coronavirus-2").af. (25301)

- 9 or/1-8 [Set 1: COVID-19/SARS-CoV-2] (107920)
- 10 exp heart transplantation/ (67511)
- 11 exp kidney transplantation/ (158915)
- 12 exp liver transplantation/ (120469)
- 13 exp lung transplantation/ (36612)
- 14 organ transplantation/ (36969)
- 15 exp pancreas transplantation/ (20715)
- 16 spleen transplantation/ (485)
- 17 transplantation/ (153776)
- 18 ((allograft\$1 or donor\$1 or graft\$1 or recipient\$1 or transplant*) adj2 (cardiac or heart\$1 or heart-lung or hepatic or intestin\$ or kidney\$1 or kidney-pancreas or liver\$1 or lung\$1 or lung-heart or multiorgan or multi-organ or organ\$1 or pancreas or pancreaskidney or renal)).tw,kw. (387986)
- 19 (transplant* not (cell* or faecal* or fecal*)).ti. (283338)
- 20 or/10-19 [Set 2: Organ Transplantation] (609379)
- 21 and/9,20 [Sets 1 & 2] (1402)
- 22 limit 21 to yr="2020-Current" (1263)
- 23 remove duplicates from 22 (1208)

Database: Cochrane COVID-19 Study Register

URL: <https://covid-19.cochrane.org/> (searched via the Cochrane Register of Studies: <https://crsweb.cochrane.org/>)

Date search conducted: January 9, 2021 Strategy:

1. ((allograft* or donor* or graft* or recipient* or transplant*) AND (cardiac* or heart* or hepatic* or intestin* or kidney* or liver* or lung* or multiorgan* or organ* or pancreas* or renal*)):TI,AB (662)
2. (transplant* not (cell* or faecal* or fecal* or microbiota*)):TI (451) 3. #1 OR #2 (680)

Database: WHO COVID-19 Global literature on coronavirus disease

URL: <https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/> Date search conducted: January 09, 2021 Strategy: transplant* (in: Title, abstract, subject) (n=1649)

Filter: Database filter – references from Medline/Embase are removed

Results: 491

Note: Content: The WHO Global COVID-19 Health literature database contains primarily research articles (published AND/OR pre-publication) journal articles. Major indexing databases, PubMed, Web of Science, Global Index Medicus, Embase as well as major health publishers' websites are searched Monday to Friday (excluding WHO Headquarter Official Holidays). The database is updated at 19:00 (Geneva local time). A working document of the search strategies is available upon request (email: library@who.int). In addition, Lanzhou University submits on a daily-basis citations from CNKI as well as a number of Chinese journal publishers.

Database: Science Citation Index Expanded (1900-present); Web of Science Clarivate
URL: <https://webofknowledge.com> Date
search conducted: January 09, 2021

Strategy:

```
# 687 #1 AND #5
6 Indexes=SCI-EXPANDED Timespan=2020-2021

# 17,989 #2 OR #3 OR #4
5 Indexes=SCI-EXPANDED Timespan=2020-2021

# 1,901 TS=((cadaver* OR dead OR deceased OR "heart beating" OR live OR living) NEAR/5 donor*)
4 Indexes=SCI-EXPANDED Timespan=2020-2021

# 10,753 TI=(transplant* NOT (fecal OR faecal OR cell* ) )
3 Indexes=SCI-EXPANDED Timespan=2020-2021

# 16,015 TS=((allograft* OR donor* OR graft* OR recipient* OR transplant*) NEAR/5 (cardiac* OR heart* OR hepatic* OR kidney* OR liver* OR lung* OR multiorgan* OR organ* OR pancrea* OR renal* ) )
2 Indexes=SCI-EXPANDED Timespan=2020-2021

# 57,666 TS=("2019nCov" OR "2019 nCov" OR "2019 novel CoV" OR COVID OR COVID19 OR coronavirus* OR "corona virus*" OR "nCoV 2019" OR "nCoV 19" OR "SARS-CoV-2" OR "SARS-CoV2" OR SARSCoV2 OR "SARSCoV-2")
1 Indexes=SCI-EXPANDED Timespan=2020-2021
```

Database: medRxiv and bioRxiv preprint servers Cold Spring Harbor Laboratory, BMJ, Yale (<https://www.medrxiv.org/>; <https://www.biorxiv.org/>)

Note: COVID-19/SARS-CoV-2 results from medRxiv & bioRxiv identified by the Stephen B. Thacker CDC Library, exported results current to August 22, 2020 and searched via EndNote URL:

<https://www.cdc.gov/library/researchguides/2019novelcoronavirus/researcharticles.htm>

Date search conducted: August 22, 2020 Strategy:

Keyword used was 'transplant' (any field)

Results: 7

Database: Chinese translations of COVID-19 journal articles from Lanzhou University's Evidence-Based Medicine Center

Date search conducted: August 25, 2020

Note: COVID-19/SARS-CoV-2 Chinese translations identified by research project of Campbell UK & Ireland; translations provided by Evidence-Based Medicine Center Lanzhou University; 4046 translations current up to August 22, 2020 and searched via EndNote

Strategy: Keywords used: transplant, donation, donor, immuno*, allograft, graft, recipient (194; kept 17)

Source: Google Scholar

URL: <https://scholar.google.com/> Date search conducted: January 10, 2021

Strategy:

(coronavirus | COVID-19 | SARS-CoV-2) (transplant)

Searched the first 10 pages of results (100 records). All records already retrieved by the search. No new records added.

Source: NHS Blood and Transplant

URL: <https://www.nhsbt.nhs.uk/news/coronavirus-update/> ; <https://www.odt.nhs.uk/covid-19-advice-for-clinicians/>

Date search conducted: January 10, 2021

Strategy: Manual search of the COVID-19 section of the NHSBT website.

Results: 6

b. Search strategy B.

A second independent search strategy was designed to identify the literature on the transmission of SARS-CoV-2 to recipients following CTO transplantation. Despite the scope of this search being larger, the search strategy was designed to yield a more selective list of references. Searches were performed in *PubMed* (<https://pubmed.ncbi.nlm.nih.gov/>) on September 07th, 2020, on October 07th, 2020, and on January 04th, 2021. Results were limited to references published in English since 2020.

A search script provided by *PubMed* was used to perform searches dedicated to SARSCoV-2/Covid-19 topic as follows:

```
((wuhan[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND 2019/12[PDAT] : 2030[PDAT]) OR 2019-nCoV[All Fields] OR 2019nCoV[All Fields] OR COVID-19[All Fields] OR SARS-CoV-2[All Fields]
```

This script was simplified during our search period as indicated by the NCBI SARS-CoV2 resources web page giving a direct access to articles referencing SARS-CoV-2 and COVID-19 in *PubMed* (<https://www.ncbi.nlm.nih.gov/sars-cov-2/>). Ultimately this change had no consequences on our literature search results.

We combined the records obtained following *PubMed* interrogation with three different types of queries, using medical subject headings terms or different keywords.

The following table presents the search results obtained as of January 04th, 2021:

Search number	Query	Number of hits
1	((wuhan[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND 2019/12[PDAT] : 2030[PDAT]) OR 2019-nCoV[All Fields] OR 2019nCoV[All Fields] OR COVID-19[All Fields] OR SARS-CoV-2[All Fields]	88,941
2	covid-19	88,940
3	("2020/01/01"[Date - Publication] : "2021/01/01"[Date - Publication]) AND (((tissue donors[MeSH Terms]) OR (tissue and organ procurement[MeSH Terms])) OR (tissue and organ selection[MeSH Terms]))	1,547
4	("2020/01/01"[Date - Publication] : "2021/01/01"[Date - Publication]) AND ((donor OR donat*) AND (identifi* OR detect* OR graft* OR infect* OR transmi* OR receiv* OR contaminat*) AND (cell* OR tissue OR organ* OR kidney OR renal OR lung OR pancrea* OR liver OR hepato* OR heart OR cardio* OR endothelial OR cord blood OR hematopoietic OR cornea OR conjonctiv* OR stem OR "stem cells" OR "bone marrow" OR intestine))	8,898
5	("2020/01/01"[Date - Publication] : "2021/01/01"[Date - Publication]) AND (("donor-derived" OR "SARS-Cov-2infected" donor OR "infected SARS-COV-2 donor" OR "infected donor" OR "asymptomatic donor" OR "COVID-19positive donor" OR "donor with unknown" OR "COVID-19associated") AND (identifi* OR detect* OR graft* OR infect* OR transmi* OR receiv* OR contaminat* OR cell* OR tissue OR organ* OR kidney OR renal OR lung OR pancrea* OR liver OR hepato* OR heart OR cardio* OR endothelial OR "cord blood" OR hematopoietic OR cornea OR conjonctiv* OR stem OR "stem cells" OR "bone marrow" OR intestine))	2,100
6	#2 AND #3	254
7	(#2 AND #4) AND transplant*	259
8	(#2 AND #5) AND transplant*	230
9	#6 OR #7 OR #8	437
10	#6 OR #7 OR #8 Filter: Journal article	311
11	#6 OR #7 OR #8 Filters: Case Reports, Comment, Letter, Preprint	132

We obtained 437 references for analysis among journal articles, case reports, letters, comments and preprints.

When cross-referencing the results from the 2 search strategies, we identified 7 publications; three of which discussed transplantation of organs from COVID-19 positive donors with 2 of those 3 reporting on the same clinical case. Two other articles discussed

transplantation of hematopoietic stem cells from COVID-19 positive donors. The last two articles reported transplantation of organs from donors with one SARS-CoV-2 RT-PCR positive result the day of the transplantation or one day before. There was an overlap of the references of interest obtained using search strategy B and search strategy A. No additional references on tissues or cells transplanted from COVID-19 positive donors were identified among the references arising from search strategy A.

2. Search strategies applied to the topic of viral detection.

This review was extended to identify references related to the detection of viral genomic material, proteins and infectious SARS-CoV-2 virus in clinical samples, cells and tissue specimens collected from different organs in COVID-19 positive patients. Searches were performed in *PubMed*.

Search number	Query	Number of hits
1	("2020/01/01"[Date - Publication]: "2020/10/08"[Date - Publication]) AND covid-19	63,054
2	("2020/01/01"[Date - Publication] : "2020/10/08"[Date - Publication]) AND (((isol* OR infect*) AND (presence OR identifi* OR detect* OR replicat* OR tropism) AND (cell OR tissue OR organ) AND (specimen OR biopsy OR sample)) OR (post-mortem OR postmortem OR autopsy)) AND (kidney OR renal OR lung OR pancrea* OR liver OR hepato* OR heart OR cardio* OR endothelial OR cord blood OR hematopoietic OR ocul* OR cornea OR conjonctiv* OR stem OR "stem cells" OR "bone marrow" OR intestine)	4,451
3	#1 AND #2	582

Titles of 582 references were screened resulting in a final list of 39 selected references reporting on SARS-CoV-2 detection in clinical samples, cells, tissues and organs.

3. Search strategies applied to the topic of ACE2 and TMPRSS2 detection in cells and tissues.

We conducted a non-exhaustive search on *PubMed* to review evidence regarding the presence of key host factors, angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2), in cells and tissues that could explain potential susceptibility to SARS-CoV-2 infection.

Search number	Query	Number of hits
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1	("2020/01/01"[Date - Publication]: "2020/09/03"[Date Publication]) AND covid-19	53,906
2	("2020/01/01"[Date - Publication]: "2020/09/03"[Date Publication]) AND ((cell OR tissue OR organ) AND (kidney OR renal OR lung OR pancrea* OR liver OR hepato* OR heart OR cardio* OR endothelial OR cord blood OR hematopoietic OR ocul* OR cornea OR conjonctiv* OR stem OR "stem cells" OR "bone marrow" OR intestine))	113,687
3	("2020/01/01"[Date - Publication]: "2020/09/03"[Date Publication]) AND (ACE2 OR TMPRSS2)	1,755
4	#1 AND #2 AND #3	588