Methods

Eligibility

Histopathologic data from autopsy, surgical and biopsy studies were collected based on 2009 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [25, 26]. Non-peer reviewed studies, duplicate articles, autopsy guideline consensus/review articles, studies, or cases with only macroscopic description or without confirmation of SARS-CoV-2 infection by real-time reverse-transcriptase polymerase chain reaction (RT-PCR) were excluded. Full texts article in English language and studies or cases with available microscopic description were included. The review focuses on histopathology. Laboratory, imaging and macroscopic findings were not included in this manuscript.

Search Strategy

PubMed and Medline (EBSCO and Ovid) were queried from June 4 to September 30, 2020, using the following key search terms: "(COVID-19 OR SARS-CoV-2)" AND (Pathology OR Pathological OR Postmortem OR Autopsy OR Biopsy)." The references of each included article were screened to identify additional potential studies.

Study Selection

Articles or the English abstract in Chinese language articles were independently screened by three authors (SC, MK, and GAG) to decide whether these met inclusion criteria (Supplementary Figure 1). The authors who screened and included manuscripts were not blinded to the manuscript's authors.

Evaluation of Manuscript Quality

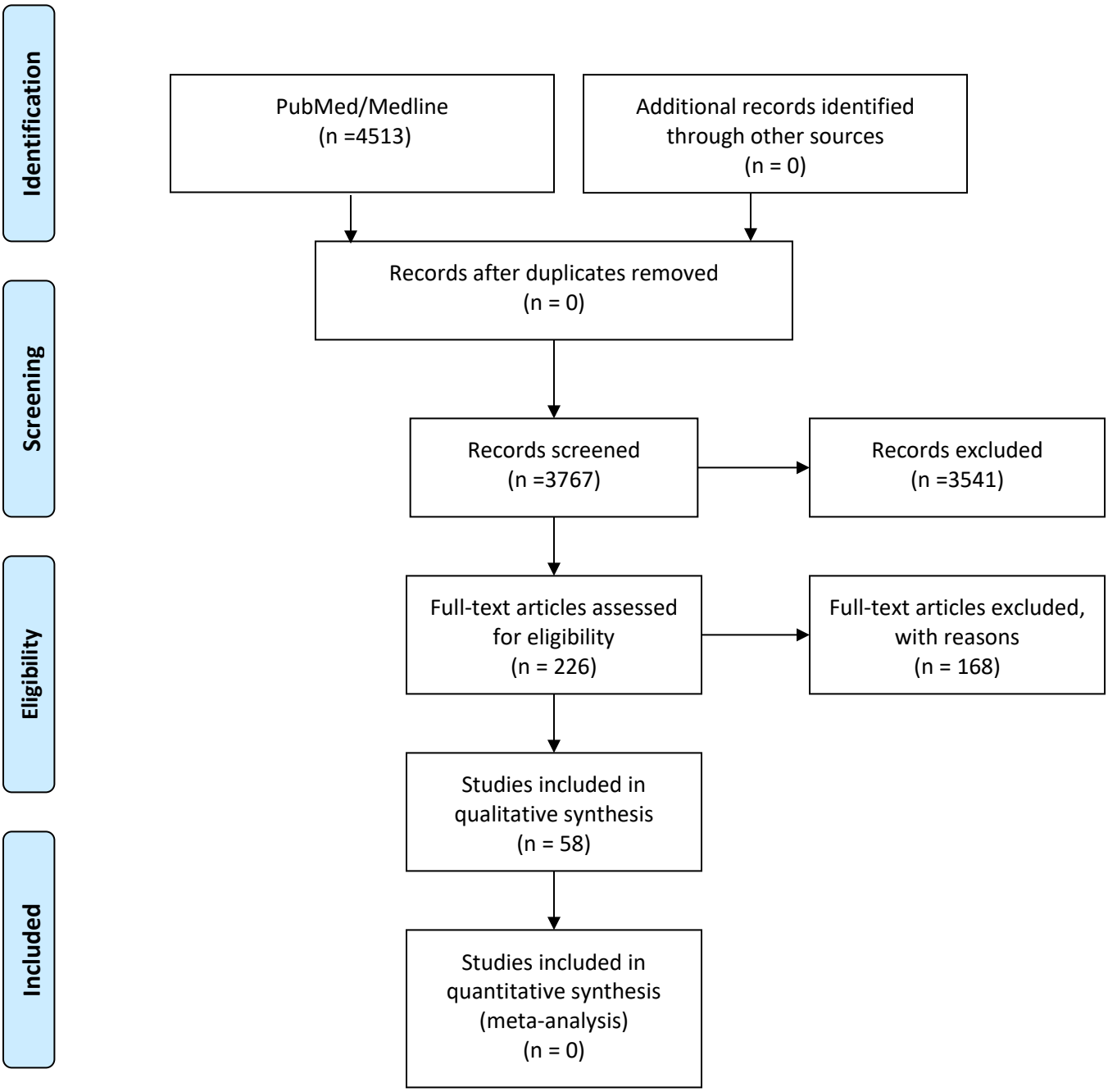
Quality analysis was performed based on previously reported pathology review criteria, including case series and case reports [27]. Articles were evaluated based on the availability of clinical, microscopic, and macroscopic data for each patient included in the article. Based on these criteria, articles were deemed high quality if all three data categories were available; moderate quality if macroscopic data were not available; and low quality if clinical or microscopic data were not available.

Data Collection

Data were extracted independently by each author based on a common framework. Specifically, this included the following information: number of total cases, patient's age, gender, ethnicity, comorbidities, procedure performed (e.g., autopsy with type and methodology, biopsy, surgical resection), organs analyzed, histopathologic features characteristic of each specific organ analyzed, ancillary studies.

In some studies, pathologic findings were described only as present or absent, and the number of patients demonstrating these findings was not reported. In this case, the reference was cited, but the number of patients was not included in the total count. Although a full autopsy was performed in some studies, the description was limited to a single organ system.

Supplementary Figure 1. Flow-chart of systematic literature review methodology.



Supplementary Table 1: Quality assessment of the included reports.

Article	Procedure type	N. patients	Clinical data (per case)	Microscopic data (per case)	Macroscopic data (per case)	Quality
Ackerman M et al.	Autopsy	7	No	No	No	Low
Adachi T et al.	Autopsy	1	Yes	Yes	Yes	High
Aguiar D et al.	Autopsy	1	Yes	Yes	Yes	High
Barton LM et al.	Autopsy	2	Yes	Yes	Yes	High
Basso C et al.	Autopsy	21	No	No	No	Low
Bosmuller H et al.	Autopsy	4	Yes	Yes	Yes	High
Bradley BT et al.	Autopsy	14	Yes	Yes	No	Moderate
Borczuk A et al.	Autopsy	68	No	No	No	Low
Buja LM et al.	Autopsy	3	Yes	Yes	Yes	High
Carsana L et al.	Autopsy	38	No	No	No	Low
Craver R et al.	Autopsy	1	Yes	Yes	Yes	High
Dohlnikoff, M et al.	Autopsy	1	Yes	Yes	No	Moderate
Edler C et al.##	Autopsy	80	Yes	No	No	Low
Escher F et al.	Biopsy	5	Yes	No	No	Low
Fitzek A et al.	Autopsy	1	Yes	Yes	Yes	High
Fox S et al.	Autopsy	10	Yes	No	No	Low
Fox S et al.**	Autopsy	22	No	No	No	Low
Grimes Z. et al.	Autopsy	2	Yes	No	Yes	Low
Kantonen J et al.	Autopsy	4	Yes	Yes	No	Moderate
Kissling S et al.	Biopsy	1	Yes	Yes	No	Moderate
Kudose S et al.#	Biopsy	17	Yes	Yes	No	Moderate
Larsen CP et al.	Biopsy	1	Yes	Yes	No	Moderate
Lax SF et al.	Autopsy	11	Yes	Yes	Yes	High
Lindner D et al.*	Autopsy	39	No	No	No	Low
Magoon S et al.	Biopsy	2	Yes	Yes	No	Moderate
Matschke, J et al.	Autopsy	43	Yes	Yes	Yes	High
Menter T et al.	Autopsy	21	Yes	Yes	Yes	High
Nunes Duarte-Neto A	Autopsy	10	Yes	Yes	No	Moderate
Peleg Y et al.	Biopsy	1	Yes	Yes	No	Moderate

Pernazza A et al.	Surgical resection	1	Yes	Yes	No	Moderate
Rapkiewicz AV et al.	Autopsy	7	Yes	No	No	Low
Ross Reichard, T et al.	Autopsy	1	Yes	Yes	Yes	High
Rossi GM et al.	Biopsy	1	Yes	Yes	No	Moderate
Santoriello D et al.	Biopsy	42	No	No	No	Low
Sauter J et al.	Autopsy	8	Yes	Yes	No	Moderate
Schaefer IM et al.	Autopsy	7	Yes	Yes	No	Moderate
Schaller T et al.	Autopsy	10	Yes	Yes	No	Moderate
Sekulic M et al.	Autopsy	2	Yes	Yes	Yes	High
Sharma P. et al (J Am Soc Nephrol)	Biopsy	10	Yes	Yes	No	Moderate
Sharma Y. et al (Kidney Medl)	Biopsy	2	Yes	Yes	No	Moderate
Solomon, I et al.	Autopsy	18	Yes	Yes	Yes	High
Su H. et al.	Autopsy	26	Yes	Yes	No	Moderate
Suess C et al.	Autopsy	1	Yes	Yes	Yes	High
Tavazzi G. et al.	Biopsy	1	Yes	Yes	No	Moderate
The COVID-19 Autopsy	Autopsy	1	Yes	Yes	Yes	High
Tian S et al. (J Thor Oncol)	Surgical resection	2	Yes	Yes	No	Moderate
Tian S et al. (Mod Pathol)	Postmortem biopsy	4	Yes	Yes	NA	Moderate
Varga Z et al.	Autopsy/Surgical resection	3	Yes	Yes	No	Moderate
Wang Y et al.	Postmortem biopsy	2	Yes	Yes	No	Moderate
Wenz, P et al.	Biopsy	2	Yes	No	No	Low
Wichmann D et al.	Autopsy	12	Yes	Yes	Yes	High
Von Weyhern CH et al.	Autopsy	6	Yes	Yes	No	Moderate
Xu X et al.	Postmortem biopsy	10	No	No	No	Low

Xu Z et al.	Postmortem biopsy	1	Yes	Yes	No	Moderate
Yan L et al.	Autopsy	1	Yes	Yes	Yes	High
Yao XH et al.	Autopsy	3	Yes	No	No	Low
Youd A et al.	Autopsy	3	Yes	Yes	Yes	High
Zhang H et al.	Postmortem biopsy	1	Yes	Yes	No	Moderate

* Cohort included in Edler at al.

** 22 patients including 10 from Fox SE et al. Pulmonary and cardiac pathology in African American patients with COVID-19: an autopsy series from New Orleans. Lancet Respir Med 2020; 8: 681–86.

1 patient also reported in Peleg et al. Acute Kidney Injury Due to Collapsing Glomerulopathy Following COVID-19 Infection. Kidney Int Rep. 2020;5:940-45.

##Cases 2-13 also included in Wichmann et al. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. Ann Intern Med. 2020;173:268-77.

Supplementary Table 2. Putative virus or virus-like particles reported by transmission electron microscopy in recent literature.

Organ	Cell/Site of Identification	Reclassification	Reference
Bowel	Enterocyte	Unidentified – not virions	Bradley BT et al. Lancet, 2020
Heart	Endothelium	Unidentified – not virions	Fox SE et al. Circulation, 2020
	Interstitial cell	Clathrin-coated vesicles	Tavazzi G et al. Eur J Heart Fail, 2020
	Endothelial cell	Rough endoplasmic reticulum	Dolhnikoff M et al. Lancet Child Adolesc Health, 2020
	Fibroblast	Rough endoplasmic reticulum	Dolhnikoff M et al. Lancet Child Adolesc Health, 2020
	Myocardiocyte	Unidentified – not virions	Dolhnikoff M et al. Lancet Child Adolesc Health, 2020
	Neutrophils	Unidentified – not virions	Dolhnikoff M et al. Lancet Child Adolesc Health, 2020
Kidney	Tubular epithelial cell	Clathrin-coated vesicles	Su H et al. Kidney Int, 2020
	Tubular epithelial cell	Clathrin-coated vesicles	Farkash EA, et al. JASN, 2020
	Endothelial cells	Clathrin-coated vesicles	Bradley BT et al. Lancet, 2020
	Podocytes	Clathrin-coated vesicles	Su H et al. Kidney Int, 2020
	Glomerular endothelium	Multivesicular bodies	Menter T et al. Histopathology, 2020
	Podocyte	Multivesicular bodies	Menter T et al. Histopathology, 2020
	Podocyte	Multivesicular bodies	Kissling S et al. Kidney Int., 2020
	Tubular epithelial cells	Multivesicular bodies	Farkash EA, et al. JASN, 2020
	Glomerular endothelium	Multivesicular bodies	Buja ML et a;. Cardiovasc Pathol, 2020
	Glomerular endothelium	Rough endoplasmic reticulum	Varga Z et al. Lancet, 2020
	Tubular epithelial cell	Clathrin-coated vesicles	Fox SE et al. Circulation, 2020
	Glomerular endothelium	Unidentified – not virion	Buja ML et a;. Cardiovasc Pathol, 2020
	Tubular epithelial cell	Unidentified – not virion	Menter T et al. Histopathology, 2020
	Tubular epithelial cell	Unidentified – not virions	Bradley BT et al. Lancet, 2020
Lung	Pneumocyte	Clathrin-coated vesicles	Grimes Z, et al. Cardiovasc Pathol, 2020
	Endothelium	Unidentified – not virion	Bosmuller H et al. Virchows Archiv, 2020
	Pneumocyte	Clathrin-coated vesicles	Borczuk et al.
	Pneumocyte	Multivesicular bodies	Bradley BT et al. Lancet, 2020
	Pneumocyte	Multivesicular bodies	Grimes Z, et al. Cardiovasc Pathol, 2020

	Endothelium	Rough endoplasmic reticulum	Borckzuk et al.
	Endothelium	Unidentified – not virions	Ackermann M, N Engl J Med, 2020
	Pneumocyte type 1	Unidentified – not virion	Bosmuller H et al. Virchows Archiv, 2020
	Pneumocyte	Unidentified – not virion	Bradley BT et al. Lancet, 2020
	Pneumocyte	Unidentified – not virion	Fox SE et al. Circulation, 2020
	Unspecified	Unidentified – not virion	Fox SE et al. Lancet Resp Med, 2020
Trachea	Epithelial cell	Unidentified – not virions	Bradley BT et al. Lancet, 2020
	Epithelial cell	Clathrin-coated vesicles	Bradley BT et al. Lancet, 2020