

COVID-19 and Testis: A Systematic Review

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Received: 04 Dec 2020
Accepted: 23 Dec 2020
Published: 28 Dec 2020

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Citation:

Li B, COVID-19 and Testis: A Systematic Review. Clinics of Surgery. 2020; 4(4): 1-2.

Keywords:

Corona Virus Disease 2019 (COVID-19); Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2); Testis, Angiotensin-Converting Enzyme 2 (ACE2)

#Author Contributions:

Chai S. These authors have contributed equally to this article.

1. Abstract

Corona Virus Disease 2019 (COVID-19), triggered by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), has created a global pandemic. As of November 20, 2020, SARS-CoV-2 is known to have 56,623,643 persons infected globally, and 1,355,963 deaths have been reported worldwide. Angiotensin-Converting Enzyme 2 (ACE2) has been found to be one of the major receptors that modify the entry of SARS-CoV-2 into human cells, and ACE2 is expressed in multiple organ systems including the lungs, intestine, heart, kidney, and the testis. SARS-CoV-2 has been detected in multiple organs. However, whether the virus exists in the testis remains controversial. In this report we looked at the SARS-CoV-2 test outcomes of semen samples from COVID-19 male patients, we found that outcome was controversial in different literature. We conclude that SARS-CoV-2 does not exist in the test is most likely, but it causes damage to testicular tissue instead.

2. Introduction

Since the discovery of COVID-19 caused by SARS-CoV-2 at the end of December 2019, it has rapidly swept the world. As of November 20, 2020, there have been 56,623,643 confirmed cases of COVID-2019, including 1,355,963 deaths, reported to WHO

(<https://covid19.who.int/>). When you read this article, the figures would have changed to more threatening numbers, which indicates that there are numerous male patients. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 [1], ACE2 is expressed in multiple organ systems including type II alveolar cells of the lungs, intestine, heart, kidney, and the testis [2]. SARS-CoV-2 has been detected in multiple organs. However, whether the virus exists in the testis remains controversial. Li et al [3] reported the presence of SARS-CoV-2 in the semen samples while [4] and [5] detected otherwise. In this report, we performed systematic review to evaluate the presence of the SARS-CoV-2 in the testis and the possibility of the impact of SARS-CoV-2 infection on male fertility.

3. Review

3.1. No SARS-CoV-2 Was Detected

Kate E. Stanley et al. [6] obtain an in-depth understanding of the possible biologic consequences of SARS-CoV-2 infection on reproduction by observing the expression patterns of known viral host entry proteins. Their results from scRNAseq data suggest that sperm cells may not be exposed to the increased risk of viral entry mediated by ACE2 and TMPRSS2, although there is no co expression in any testicular cell type, and they were unable to interrogate Sertoli cells [6]. They [6] found moderate ACE2 expression in tes-

ticular tissue, whereas expression of TMPRSS2 was found to be low or undetectable by bulk RNAseq and protein platforms. And [4] also found ACE2 and TMPRSS2 are rarely expressed in the human testes, with almost no overlapping gene expression in the scRNA-seq dataset of human testicular cells at the University of Utah, being consistent with.

Kate E. Stanley et al's study. Furthermore, [4] single-cell transcriptome data suggested ACE2 RNA expression occurs at low levels and they did not detect SARS-CoV-2 within semen of COVID-2019 patients, which indicates that SARS-CoV-2 would not be able to gain entry to testicular cells through an ACE2/TMPRSS2-mediated mechanism. All semen samples of COVID-2019 patients were negative for SARS-CoV-2 RNA and testicular samples from one deceased COVID-2019 patient were negative in Song et al's study [7]. In other studies, semen and urine samples from an Italian man were negative for SARS-CoV-2 RNA [8], and [5] did not detect SARS-CoV-2 in semen samples of 23 COVID-2019 patients using RT-qPCR.

3.2. SARS-CoV-2 Was Detected

Contrary to the above findings, SARS-CoV-2 was detected in semen samples of 6 COVID-2019 patients, while the remaining 32 semen samples were negative for SARS-CoV-2 RNA in Li et al's study [3]. However, we found that Li et al's study did not describe the semen collection or analysis in detail, nor excluded the possibility of viral contamination from non-semen sources, such as urine of these patients. Through postmortem examination of the testes from 12 COVID-19 patients, Yang et al. [9] found that one case was positive for the virus in the testis, nine cases were negative for the virus in testicular tissue. They also performed electron microscopy for three cases, and viral particles were not identified in any case [9]. For the positive case, they considered that the testicular tissue sampled contained predominantly fibrovascular tissue and very few seminiferous tubules. It is likely that RT-PCR detected the virus present in blood rather than in testicular tissue [9].

3.3. SARS-CoV-2 Damage to Testis

A study on testicular samples shows that severe acute respiratory syndrome corona virus (SARS-CoV) has a significant impact on the reproductive system [10]. Xu et al [10] observed the pathological changes of the testis in 6 patients who died from SARS and compared them with the control group. They [10] found that SARS caused orchitis. The testes are extensively destroyed and there are few sperms in the seminiferous tubules. They also found that the basement membrane of seminiferous tubules was thickened, with obvious leukocyte infiltration and macrophage staining, which suggests the influence of immune response on testis. However, SARS-CoV was not detected in the affected testis. Yang et al. [9] found that SARS-CoV-2 caused significant injury to Sertoli cells and seminiferous tubules, and there was reduction of Leydig cells and mild inflammatory infiltrates in the interstitium. The above

shows that SARS-CoV-2 cause orchitis and may lead to infertility.

4. Conclusion

As mentioned above, no strong evidence of SARS-CoV-2 in semen of males COVID-19 patients, while COVID-19 can cause damage to testis, suggesting that early intervention and treatment are needed to avoid irreversible damage to the male reproductive system.

5. Acknowledgements

Financial disclosure: This work was supported by grant from the National Natural Science Foundation of China (grant number 81671216, 81371379)

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