



The Impact of the COVID-19 Pandemic on Urology Residents: a Narrative Review

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Abstract

Purpose of Review The COVID-19 pandemic brought unprecedented challenges for urology resident education. In this review, we discuss the pandemic's impact on urology trainees and their education.

Recent Findings Urology trainees were often redeployed to frontline services in unfamiliar clinical settings. Residents often experienced increased levels of stress, anxiety, and depression. Many programs instituted virtual “check-ins” and formed liaisons with mental health services to foster cohesiveness. Urology trainees experienced the integration of telehealth into the clinical realm. Virtual surgery lectures and simulations were utilized to augment surgical education. Academic governing bodies upheld resident protections and provided dynamic guidance for training requirement throughout the pandemic. Medical students were unable to participate in traditional in-person away rotations and interviews, complicating the residency application process.

Summary The COVID-19 pandemic shook the healthcare system and ushered in seismic changes for urology trainees worldwide. Though the longstanding effects of the pandemic remain to be seen, urology residents have demonstrated tremendous resilience and bravery throughout this challenging period, and those qualities will undeniably withstand the test of time.

Keywords Urology · COVID-19 · Pandemic · Education · Internship and residency · Graduate Medical Education

Introduction

The Coronavirus-2019 (COVID-19) pandemic has had wide-ranging effects on the healthcare system. The “first wave” of COVID-19 cases rapidly overwhelmed the

resources of most nations and prompted unprecedented changes in healthcare delivery. Elective surgeries were cancelled, routine medical units were converted into intensive care units (ICUs), and healthcare workers were re-deployed to provide frontline care for COVID-19 patients. Medical education is typically a structured and regimented process, yet in light of a public health crisis of this scale, adjustments have been inevitable.

Urology is a multifaceted branch of medicine that combines surgical treatments with medical management in both the inpatient and outpatient settings. Accordingly, urology residency programs must combine surgical training with fostering the development of clinical skills and medical knowledge for the treatment of urologic patients. The COVID-19 pandemic has brought unprecedented challenges for urology resident education. With operating rooms shuttered, in-person clinics limited, and wide-spread healthcare worker redeployments, almost every aspect of urologic training has been disrupted including day-to-day training, credentialing exams, and the residency application process [1].

The impact of the COVID-19 pandemic on urology trainees has been an area of great research interest as training changes will likely have short- and long-term consequences

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for urology as a field. To this end, here, we seek to review the existing literature on the impact of the COVID-19 pandemic on urology residents and the training process.

Methods

On January 19, 2021, we searched PubMed, EMBASE (OVID), and Web of Science for publications using the Boolean operator search term "COVID-19" AND "Urology" AND ("Internship" OR "Residency" OR "training"). No limits were set on publication date given the novelty of COVID-19. All duplicate papers and all non-English language publications were excluded. All study designs and publication types were considered. Each paper was then read by a single reviewer and assigned a score of zero-, one-, or two-based relevance to the topic of resident education. All papers with a score of zero were removed from the analysis, any paper with a score of two was included in the analysis, and any paper with a score of one was submitted to another reviewer to determine eligibility. Our search methodology is summarized in Fig. 1. We identified 64 unique publications related to COVID-19 and urologic training. Papers were then analyzed by reviewers, and findings were organized into the following seven sections: redeployment, physical and mental well-being, operative experience and surgical training, telehealth training and integration, didactic learning, medical student education and residency

applications, and academic leadership responses. Given the novelty and dynamic nature of the COVID-19 pandemic and associated literature, this review is presented in a narrative format.

Redeployment

In response to the global surge of COVID-19 patients, hospitals began diverting time, equipment, and personnel towards COVID-19 services. Many urology residents were redeployed and asked to work shifts in the emergency department (ED), ICUs, medical/surgical floors, and COVID-19 screening sites [1–6]. Residents in regions that had higher numbers of COVID-19 patients were more likely to be redeployed [7]. A urology program director (PD) survey from the United States (US) in March 2020 found that 75% of programs had at least one resident redeployed and 40% of programs had > 33% of the workforce redeployed [4]. Other studies from the US reported that > 80% of urology residents were involved in some capacity with COVID-19 patients [3, 7]. Ultimately, most programs discussed redeployment and planned to redeploy urology residents if required [3, 7]. Notably, those with high-risk comorbidities, pregnancy, or an immunocompromised state were often excluded from covering COVID-19 units [8]. One New York hospital system recruited urology residents and faculty to volunteer for redeployment on an

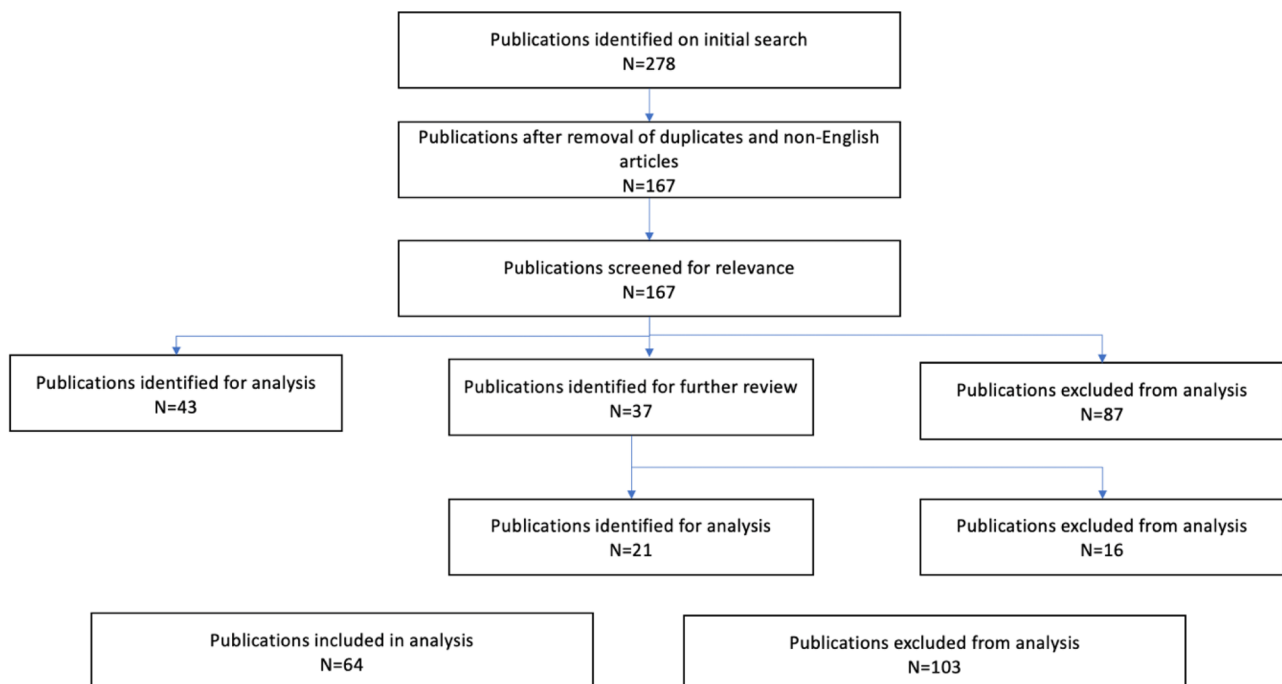


Fig. 1 Literature search methodology

“opt-in” basis, with all volunteers redeployed in pairs of 1:1 residents-to-attending [9]. A survey of residents in all Accreditation Council for Medical Education (ACGME) accredited urology programs in March 2020 found that urology residents who felt institutional support and shared responsibility with attendings were more likely to agree to voluntary redeployment [2].

In Europe, urology residents were also redeployed to other front-line services [10, 11]. In Italy, 8% of residents worked in non-urology units [12]. A British pediatric urology unit employed a “Consultant-of-the-Week” rotation, with a second consultant on standby for possible redeployment [13]. A survey of urology residents across Latin America and Spain found that 15% of respondents had their urology service closed, with all activity dedicated to COVID-19 patients [14]. In France, residents were tasked with caring for patients being actively transferred across the country and residents in PhD programs were also redeployed to COVID-19 units [15]. A survey of urology PDs in Canada revealed that 30% of programs redeployed their residents [16]. Similarly, in Singapore, urologists participated in COVID-19 screening and were redeployed based on hospital needs to frontline wards [17–19].

Urology programs and hospitals were put in the difficult position of creating and coordinating schedules for both COVID-19 services and routine urologic care [3, 7]. At Cleveland Clinic, approximately two-thirds of urology residents served as reserves with front-line residents cycling every week [20]. Similarly, other programs split residents into rotating “clean” and “COVID-19” teams [3, 7, 20–23]. A March 2020 survey of US urology PDs distributed by the Society of Academic Urologists (SAU) found that residents in > 90% of programs had a reduced hospital presence and > 80% of programs reported a decrease in overall work hours [7]. Concerns from PDs also included having adequate staffing when residents are quarantined due to a COVID-19 exposure or diagnosis [7].

Many urology residents were redeployed to hospital areas outside their usual scope of practice [23]. In the US, some urology residents were provided with airway courses to prepare for redeployment [7]. In Europe, urology residents underwent refresher courses on basic and advanced life support, and respiratory support and treatment in anticipation of redeployment [15]. One New York hospital urology department coordinated with medical colleagues to develop a novel “Emergency Department-Intensive Care Unit” to care for ED patients that required ICU-level care [9]. In anticipation of future pandemics, institutions should provide urology residents with training on assessment/management algorithms, airway and ventilator management, palliative care resources, personal protective equipment (PPE) conservation, and clinical trials [23].

Physical and Mental Well-Being

Many urologists were placed in highly stressful, unfamiliar clinical settings whilst caring for COVID-19 patients, particularly given the sudden increase in patient load and risk for workplace infection [24]. For urologists in training, the pandemic was a major stressor, potentially contributing to worsened caregiver mental health [25]. In a survey of French urology trainees 2 weeks after lockdown started, 92% reported being stressed and > 60% felt their quality of work was impacted [25]. Respondents were more stressed if they lived in high-risk regions, had COVID-19 patients in their care, or had personal history of respiratory disease [25]. In another survey from France, > 33% of urology residents reported new-onset anxiety, depression, and insomnia, with female gender and alcohol and tobacco use being independent risk factors [26]. A survey of US residents found that anxiety and depression were associated with perception of access to PPE, local COVID-19 severity, personal history of COVID-19 infection, and perception of susceptible household members [27]. Oftentimes, residents were separated from family and loved ones to prevent COVID-19 transmission, resulting in further isolation [28].

In a survey of Polish attending and resident urologists, almost 80% of respondents noticed that the pandemic had negative psychological effects on their colleagues, with 57.6% reported feeling increased sadness, anxiety, or increased stress levels and > 75% indicating a negative impact on family relations [29]. Respondents were mostly distressed due to the uncertainty regarding the duration of the pandemic (68.56%), implemented restrictions (51.97%), and the possibility of exposing relatives to COVID-19 (51.53%) [29]. Almost all (96.5%) respondents believe the pandemic had a moderate to high impact on their everyday clinical practice, and a majority of residents (62%) felt that the pandemic would harm their training [29]. A systematic review from August 2020 analyzing mental health issues among healthcare workers during the COVID-19 pandemic revealed a pooled prevalence rate of anxiety of 22.8% across 12 different studies [30]. Furthermore, in a survey of urology program leaders and urology trainees in the US, < 25% of respondents stated they had improved morale and < 30% felt more pride in their work [3]. Furthermore, 54% of respondents felt their home-lives were disrupted and 39% felt increased financial concerns [3].

Another key concern was physical safety of trainees. In New York, 99.2% of residents reported re-using or extending the use of their masks and approximately half of PDs reported that residents worked with suboptimal PPE [4]. The SAU PD survey from March 2020 found that there was concern with COVID-19 workplace exposure and concern for appropriate PPE availability in 89% and 78% of programs,

respectively [7]. Moreover, residents were exposed to COVID-19 positive patients in 52% of programs [7]. Residents with high-risk comorbidities were restricted from all patient care in 38% of programs, while 47% of programs restricted these residents from in-person interactions with COVID-19 positive patients [7].

A survey of urology programs in the US found that lower levels of anxiety and depression were associated with adequate access to PPE, while having a household member (including themselves) who was susceptible to severe COVID-19 reported higher levels of anxiety and depression [2]. In France during the height of the first-wave, 43% of residents felt they had insufficient PPE, and perceived access to adequate PPE and sufficient training about COVID-19 was inversely associated with anxiety and depression [26]. Similarly, many trainees in India reported inadequate PPE [2]. In Indonesia, PPE access varied by hospital type, as 60% of surveyed residents working at public hospitals had access to N95-masks, while 90% of residents at private hospitals had access to N95-masks [2]. Several urology residents and fellows ultimately contracted COVID-19 [8]. Given pandemic's stresses, trainees may develop post-traumatic stress syndrome (PTSD) and there is a disturbing notion that PTSD may become Persistent-Traumatic Stress Disorder [8].

Urology programs can undertake steps to help ameliorate pandemic-related trainee distress. Urology PDs and faculty can regularly interact with residents and allay trainee concerns by offering support, keeping lines of communication open, and demonstrating appreciation for residents' work. To monitor residents' mental health, recurring forums or town hall meetings can be held to allow for open discussion of the pandemic's challenges, evaluate mental well-being, and provide access to mental health resources [1, 9, 23]. This became a widely adopted practice, as programs in the US initiated regular video "check-ins" to evaluate resident well-being and discuss ever-changing hospital protocols [31]. Wellness initiatives were also implemented by some programs [7, 8]. Residents had increased free time and participated in physical exercise, attended virtual happy hours, and partook in professional help offered by their programs [7, 8]. Additionally, some programs provided childcare provisions and quarantine housing [7, 8].

Operative Experience and Surgical Training

In response to the COVID-19 pandemic, hospital departments worldwide limited procedures to urgent and non-deferrable cases [11]. Furthermore, to minimize exposure, unnecessary use of PPE, reduce operative times, and minimize the possibility of complications, senior surgeons and attendings have been encouraged to perform the majority of cases and often without the assistance of residents [15]. For

example, in Canada, trainee assistance in the operating room was severely restricted, with many programs allowing only attending urologists to perform the entirety of cases [28]. As PPE scarcity became less of a concern, residents were allowed to participate in surgery but in a limited capacity. This has manifested as decreased exposure to cases such as renal transplantation, robotic surgery, and reconstructive procedures [28].

Decreases in resident and trainee operative experience due to COVID-19 were rapid. In France, 2 weeks into lockdown, 83% of residents reported their surgical training had been negatively impacted [25]. In Italy, urology residents reported a 40–100% reduction in clinic visits, diagnostic procedures, endoscopic surgeries, and open and minimally invasive surgeries [32]. In India, residents reported an ~90% reduction in surgical volume and >80% of residents believed their training was negatively impacted [33]. One Brazilian residency program found that resident case volume dropped 50.8% overall compared to the previous year [34]. A survey by the Urology American Confederation (CAU) found that 82% of residents in Central and South America had decreased surgical volume [14]. Furthermore, 75% of respondents reported that their surgical training had been "completely affected," and 80% of respondents felt measures were required to make up for lost training [14].

In the US, urology residency PDs reported an 83–100% decrease in surgical volume, across urologic subspecialties [3]. Within the first 4 weeks of the COVID-19 pandemic in the US, 94% of residents reported that non-oncologic cases had been cancelled and 37% reported that oncologic cases had been cancelled [2]. This decrease in case volume has caused anxiety about future practice, and in a study of US training program faculty and residents, nearly 80% respondents felt their surgical training had been adversely affected, with >50% of trainees feeling increased anxiety about surgical competency following graduation [3]. These decreases in surgical volume have occurred against the backdrop of the ACGME having recently increased case minimums [35]. Indeed, 60% of PDs expressed concerns that residents will not meet case minimums, and 86% reported that double scrubbing cases had been reduced [7, 36].

Telehealth Training and Integration

As the surge of COVID-19 patients continued to rise and overburden hospitals and staff, many hospitals began implementing telemedicine into clinics and offices [1, 7, 11, 23]. Telemedicine facilitated continuation of routine urologic care while promoting social distancing [1, 7, 16]. The use of telemedicine increased 700% compared to before COVID-19 [7, 37]. Additionally, the Centers for Medicare and Medicaid Services (CMS) allowed compensation for virtual patient visits

[23, 38, 39]. A survey of US urology PDs from March 2020 found that residents were using telehealth in 52% of programs, with remote clinical work in 77% [7]. To limit unnecessary exposure, many urology residents were asked to evaluate inpatient consults via telemedicine or to have patient's follow-up as outpatient for non-urgent urology issues [7, 23]. One group described a triage pathway for inpatient urology consults and found that many inpatient urology issues can be appropriately managed via telemedicine [39]. Similar approaches were seen in the UK and Singapore [13, 17]. A survey of US urologists found that up to 80% of office care was replaced with telemedicine [8]. A survey from the Poland found an increase in telemedicine use to 77.7% from 43.6% prior to COVID-19 [40, 41].

Training in telemedicine lagged behind its rapid adaptation. In Italy, <50% of urology residents surveyed had access to telehealth training [42]. In the US, 82% urology residents surveyed felt inadequately trained on telehealth visits [2]. As implementation of telemedicine continues, residency programs should consider revising curriculums to incorporate telehealth education [5, 31, 43, 44]. Telehealth is also novel for many patients as demonstrated by a 2019 survey which found that only 10% of Americans had used telemedicine as a means for care [45]. With the increased use of telemedicine during the pandemic, many patients have likely now become more comfortable with the technology [9].

Multiple modalities for telehealth communication have been described in the literature, including telephones, tablets, computers, or web-based software [8, 46]. Though triaging strategies have been described, there is no standard consensus on what urologic issues can be managed via telemedicine, and no testing to assess appropriate training and proficiency when using telemedicine for urologic care [47, 48]. In Indonesia and Poland, most urologists prefer a return to in-person care after the pandemic [40, 41, 49]. Surveys of urology residents and providers have also described worry of "suboptimal care" with continued use of telemedicine after the pandemic [8]. Additionally, in a recent study of oncology patients, the majority supported the use of telemedicine during the pandemic, but 60% reported a desire for in-person visits once the pandemic concludes [50]. Vaccine distribution and improvements in COVID-19 patient care will likely reduce the use of telemedicine, but elements of virtual patient care are likely to remain after the pandemic [50, 51].

Didactic Learning

Similar to clinical education, didactic education has been altered by the pandemic [23, 24, 52]. Limitations of in-person gatherings restricted urology residents from attending academic events such as grand rounds, educational conferences, and resident courses [1]. A survey of US

urology PDs in March of 2020 found that in half of programs didactic education had been negatively impacted by the pandemic and that all programs had transitioned to videoconferencing for didactics [1, 7, 20–22, 51–56]. Similar trends were observed internationally. In Italy, urology residents reported an increase in virtual "smart learning" [12, 21]. In a hospital in Singapore, all in-person teaching rounds were cancelled, and all academic meetings, perioperative patient discussions, and resident education were maintained via smart audio/video-based applications [17]. For residents in the CAU, 93% acquired urological information through online modalities such as "webinars," pre-video edited surgeries, journal clubs, and podcasts [14]. Notably, 65% of these residents felt that their academic training was partially or completely affected by the pandemic [14].

To supplement didactic education, individual urology programs, academic societies, and urologic educators from around the world began finding new and innovative ways to maintain residency education virtually [1, 7, 20–22, 51–56]. In the US, virtual lecture series were created including the Educational Multi-institutional Program for Instructing Residents lecture series by the New York section of the American Urological Association (AUA) [57] and the Collaborative Online Video Didactics lecture series by the University of California at San Francisco (UCSF) [27, 52, 58]. Similarly, new lecture series have been implemented at several Canadian programs [59]. Recorded videos of surgical procedures and massive online open courses allowed urology residents to study surgical steps, techniques, and technologies, through videos with expert commentary [5, 10, 52]. Live online courses were available via web-based platforms, allowing urology residents the chance to interact and ask questions in real time [52, 60]. A group from Turkey created an online residency training program for urology residents and reported a high resident satisfaction rate [61]. The European Association of Urology released virtual courses and surgical videos to supplement lack of in-person resident education [15]. In response to the cancellation of the AUA annual meeting in 2020, the AUA published surgical videos and the abstracts from the meeting [51]. To practice surgical techniques, individual programs also offered simulator trainings and surgical skills laboratories [1, 56].

The new virtual courses and lectures produced during the pandemic allowed urology residents to tailor courses to their interests [52]. These courses prompted discussion of a shift towards standardized virtual-based curriculums for programs [27, 61]. Though virtual didactics may facilitate ease of attendance, that does not always translate into increased participation. Several virtual sessions per day may lead to fatigue, and the ability to attend didactics remotely has created an expectation that residents attend all meetings, regardless of their location or scheduled

time-off. Lines between work, home, and relaxation have also been blurred. Furthermore, the loss of face-to-face interactions during didactic sessions may cause a loss of a cohesive team-based structure and fewer “in-the moment” teaching points [42]. The interpersonal connection that is lost with virtual didactics may weigh on resident morale [31].

Though virtual didactics have shortcomings, overall, in both the US and internationally, urology residency programs have reported positive outcomes [7, 62]. In the US, most programs are planning to continue to use of video conferencing after the pandemic [7]. A survey of urology residents from 58 countries revealed that residents favored videos related to surgical steps and updates on guidelines [15]. Though long-standing effects of COVID-19 on urology education are difficult to predict, video conferencing may become integrated into urology education, even after the pandemic concludes [10].

Medical Student Education and Residency Applications

The pandemic has changed how medical students apply to urology programs. On May 14, 2020, the Association of American Medical Colleges and ACGME issued a joint statement which strongly encouraged programs to conduct virtual interviews [63, 64]. The SAU strongly discouraged “away-rotations,” recommended all programs commit to online interviews, and delayed the match until February 1, 2021 [65]. Additionally, the SAU implemented a new format for interview offers, with all programs offering interviews on single date and requiring only two letters of recommendation [66]. Similarly, the Association of Faculties of Medicine of Canada suspended visiting elective applications [67]. Nearly every accredited Society for Urologic Oncology (SUO) fellowship program also switched to virtual interviews [1, 5].

A survey of “pre-urology” medical students revealed widespread concern regarding the absence of away rotations and in-person interactions [67, 68]. Most students reported decreased opportunities for exposure to urology, raising concerns about the average foundational knowledge and practical experience in urology [67, 68]. Furthermore, students were concerned about how programs would evaluate their candidacy, and their ability to make informed decisions about residency selection [68]. To better delineate candidates that are “good fits,” some programs instituted the use of personality testing situations and objective behavioral questions [69]. Given lack of in-person rotations, residency programs may be forced to rely more heavily on undergraduate performance, research, volunteer work, core-clerkship performance, and virtual interviews [67].

Students in the 2021 urology residency application cycle often used virtual open houses to learn about programs. Additionally, urology programs increased their social media presence, particularly on Twitter and Instagram [70]. A Twitter survey distributed via the medical student group “UroResidency” found that applicants felt virtual open houses were helpful, especially those that included resident participation, discussed a program’s strengths and weaknesses, had a resident question-and-answer session, and provided information about various training sites [71]. A survey of applicants from the 2019 and 2020 AUA matches similarly found resident-applicant interaction to be important but felt that could not be duplicated virtually [72]. However, respondents did feel that faculty interviews could be duplicated virtually, suggesting that frank discussions with residents can help applicants can develop an understanding of a program’s culture [72]. Furthermore, 86% of respondents felt that in-person visits had moderate, large, or very large impacts on applicants’ rank lists, with 87% noting it could not be duplicated virtually [72].

Some programs utilized virtual grand rounds as a means for applicants and programs to interact. In one study, urology applicants presented a virtual grand rounds and then students and faculty/residents were surveyed [70]. Among students, 82.4% felt that virtual grand rounds were useful to learn about programs [70]. Among faculty, 70.3% felt they confidently gained knowledge of the applicant, and 47.6% felt confident in their ability to evaluate applicants [70]. Furthermore, 64.7% of applicants felt confident in establishing rapport with the program, while only 36.9% of faculty felt confident establishing rapport with applicants [70]. Moving forward, virtual grand rounds may serve as a helpful tool in selecting urology applicants [70].

Medical student education also shifted during the pandemic, with a greater reliance on virtual didactics and self-directed learning. In Singapore, students continued to be educated in urologic fundamentals through live remote teaching, videoconferencing, and pre-recorded lectures [19]. Similarly, medical students were able to make use of educational virtual lecture series initiated by the New York Section AUA, UCSF, and others [5]. Another major change brought on by the pandemic was the potential for students to graduate early and join the workforce. Senior medical students in Europe were able to graduate early to increase the COVID-19 response taskforce [15]. In the US, though senior students in some programs were offered a similar opportunity, few partook, possibly due to external pressure from students’ families who feared COVID-19 exposure [8]. Overall, though there have been significant short-term changes, the long-term effects of the pandemic on “pre-urology” medical student education and residency applications are yet to be determined.

Academic Leadership Responses

The pandemic has prompted a myriad of responses and strategies by academic leadership and medical education governing bodies. At the onset of the pandemic, the majority of US urology PDs reported concerns that residents will not meet the case minimums required for graduation [7]. This is not exclusive to urology as index case numbers have decreased in many training programs across disciplines [73]. There is concern that institutions pressure programs to graduate residents regardless of clinical competency, as currently there does not exist a congressional legislation or CMS precedent to fund extended training for those with case log deficiencies or inadequate clinical experiences [73].

The American Board of Urology (ABU) has stated that “the ABU will make every effort not to punish a candidate who misses training in a circumstance that is out of their control” [74]. However, the ABU also requires that residents must work > 46 weeks/year during residency training [75]. It has yet to be seen how the ABU will respond to candidates who have worked < 46 weeks/year due to a COVID-19 related absence. In the UK, the Joint Committee on Surgical Training created a “no fault” outcome to the Annual Review of Competency Progression, whereby trainees who have not been able to meet training level requirements can have their training extended or be permitted to progress despite not all competencies being achieved in time [76].

The American Medical Association stated that trainees should not be required to use vacation time when ill with COVID-19 or for exposure quarantine, and salary or benefits should not be compromised [77]. In light of hazards associated with the pandemic, some hospitals have even provided salary increases [73]. The ACGME sought to limit potential harm to trainees and required adequate PPE for residents to prevent COVID-19 exposure, emphasized its position on work hour limitations, and warned against involuntary furloughing of residents [17]. However, the ACGME approved redeployment of residents from subspecialty training, put a halt on program oversight visits, and relaxed previously held minimum procedural and clinical standards [78, 79].

Conclusions

Throughout the ongoing COVID-19 pandemic, urology resident physicians were often redeployed and many had to contend with constant contact with sick patients and shortages in PPE, leading to increased stress levels. Teleconferencing technology was widely and rapidly adapted and was used to facilitate didactic education, residency interviews, and patient visits. Urology program leaders and academic governing bodies have and should continue to

evaluate training modifications in response to disruptions brought on by the pandemic. As the pandemic subsides, there should be continued efforts aimed at protecting the health and wellbeing of trainees to reduce medical errors and workforce attrition. Though it is unclear how long the effects of the pandemic will last, urology residents have demonstrated tremendous resilience and bravery throughout this difficult life-changing worldwide event, and those qualities will undeniably withstand the test of time.

Compliance with Ethical Standards

Conflict of Interest Dr. Khusid has nothing to disclose. Dr. Kashani has nothing to disclose. Dr. Fink has nothing to disclose. Dr. Weinstein has nothing to disclose. Dr. Gupta has nothing to disclose.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors were performed in accordance with all applicable ethical standards including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines.

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