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A STUDENT-DRIVEN INITIATIVE

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Welcome Note From the Editor-in-Chief

I am thrilled to introduce the first edition of the Journal of Medical Sciences (JMS) at NEOMED. The JMS is a peer-reviewed, and multidisciplinary journal run by medicine, graduate, and pharmacy students at Northeast Ohio Medical University. Fayez Safadi, Ph.D., and I created this student-led medical journal with the goal to foster the research and ideas of University students, faculty members, consortium hospital trainees, and affiliates, as well as to provide them with the tools and platform to publish their findings. We are excited by the outstanding opportunity the JMS provides for students in leadership (editorial board) and authors in publication. I am excited to share the work of our outstanding community in the first edition. The first edition of the JMS is published both online and in print.
To find more information regarding the JMS at NEOMED visit our website at **neomed.edu/journal-of-medical-sciences/**.

This project could not have been as successful without the unwavering support I received from my mentor, Dr. Safadi. Thank you, Dr. Safadi, for the immense amount of time you've dedicated to this endeavor helping to bring the idea of a student-led medical journal to fruition. I cannot wait to see what the future holds for the JMS, a future I am certain will be bright.

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A Histological and Qualitative Analysis of Muscle Spindle Density in the Distal Head of M. Extensor Longus Digiti Majoris

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ABSTRACT

Inconspicuous muscles in avian taxa have been previously discussed as vestigial remnants, however, evidence has shown that such muscles may hold a function in flight. Further investigations into inconspicuous muscles, such as *M. coracotriceps*, have demonstrated a muscle spindle density much greater than surrounding muscles. A higher density of muscle spindles suggests a proprioceptive function during flight. We investigated another diminutive muscle that may bear a similar function, the distal head of *M. extensor longus digiti majoris* (ED). Studies included a qualitative histological analysis comparing the density of muscle spindles in the ED to the adjacent proximal head of the *M. extensor longus digiti majoris* (EP) in 15 total samples excised from *Columba livia* (rock pigeon) and *Gallus gallus* (jungle fowl). EP is a functional muscle that serves as an osteo-pulley for the major digit, which we analyzed the ED against. Based on our qualitative histological analysis of ED, this muscle does not demonstrate a greater muscle spindle density compared to the EP. Although further research of this muscle in other Avian species may be necessary to discern its function, our research demonstrates no evidence of a proprioceptive function.

Keywords: Avian Species, Histology, Muscle Spindles, Flight

INTRODUCTION

Muscle spindles are intrafusal fibers that function to provide proprioceptive cues to the central nervous system for coordination via stretch receptors and provide reflex activity for motor neurons (*1*). Higher densities of muscle spindles are reported in avian muscles presumably to serve as kinesiological monitors during flight (*2*). Muscles with higher spindle density generally function in fine movements, postural control, and provide important mechano-sensory feedback to the central nervous system, indicating a proprioceptive function (*3*). Muscle spindles have also been seen in higher densities within avian skeletal muscles with slow-twitch fibers as opposed to their fast-twitch counterparts (*4*). This demonstrates that muscles with a higher density of muscle spindles are likely involved in sustained flight as opposed to the fast twitch muscles involved in takeoff and landing (*4*). These kinesiological monitors are often smaller, shorter muscles that act across a joint in parallel to a larger, longer muscle (*5*).

An example of a muscle with a proprioceptive function is the inconspicuous *M. coracotriceps* (*6*). This is a minute muscle that extends between the tendons of *M. expansor secundarium* and tendon of *M. humerotriceps*, and because of its size, it was previously regarded as vestigial. Eventually, research and analysis of this muscle discovered that *M. coracotriceps* was a slow tonic muscle with a muscle spindle density significantly greater than the adjacent, parallel, and functional *M. humerotriceps* (*7*). This discovery demonstrated that small and undervalued muscles can play an important role during flight.

Another example of a similar anatomical system in Aves is the distal head of *M. extensor longus digiti majoris* (ED). The ED has a tendinous insertion onto the tendon of the proximal head of the *M. extensor longus digiti majoris* (EP), which is located along the proximal end of

the major metacarpal *(8)*. This orients the smaller muscle belly, ED, in parallel with the larger muscle belly, EP (Fig. 1). The EP functions as an osteo-pulley to guide muscle tendons and change the direction of pull of the major digit (*8*). However, there are limited details available on the function of the ED and ideas on its function have been varied among sources with some researchers regarding it as nonfunctional or rudimentary (*6*). Alternatively, the use of ED as a kinesiological monitor with a dense concentration of muscle spindles is an additional possibility. There is limited evidence to support either argument, as there are few details available describing the function of the muscle.

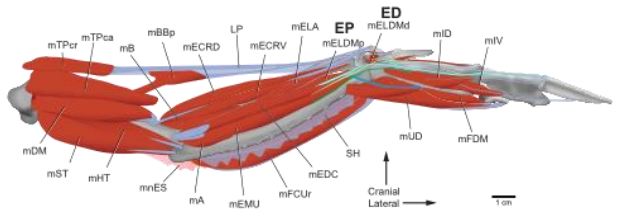

Figure 1. Shown is a figure of muscle architecture of the forelimb in Columbia Livia. The elongate proximal head of the M. extensor longus digiti majoris (EP), labeled above mELDMp , can be visualized here with its tendon course into the major digit. The ED, labeled above mELDMd, is a tiny muscle belly located adjacent to the EP with a tendinous insertion into the tendon of EP. Copyright 2016. Adapted with permission *(15).*

Additionally, the ED is present in only certain avian taxa. Distal limb reduction is an evolutionary pattern used by certain birds to eliminate unnecessary weight that is costly to takeoff, inertia, and landing during flight (*9, 10*). The evolutionary pattern depicts that birds that had distal limb reduction have lost the ED, while those without distal limb reduction have retained it. Species such as swifts and members of the "ground bird" assemblage, Cavitaves, have eliminated this muscle belly (*11*). These birds also have a flight style of greater wingbeat frequency. However, this muscle is preserved in rock pigeons, which do not exhibit distal limb reduction nor have a pattern of high wingbeat frequency (*11*). This evolutionary pattern raises additional unanswered questions about the function of ED. To investigate the function of the ED, we examined the quality of muscle spindle density to determine if it is a feasible kinesiological monitor during flight.

METHODS

The ED and EP were excised from five-frozen *Columba livia* (rock pigeon) and four *Gallus gallus* (jungle fowl). Four samples of ED and 4 EP were excised from *Columba livia* while 3 ED and 4 EP were excised from *Gallus gallus.* In total, we excised 7 ED and 8 EP (15 total samples). Each muscle belly was isolated and left overnight in 10% formalin, then washed two times in PBS solution, and finally dehydrated and stored in 70% ethanol. Next, the muscle bellies were processed in the Leica ASP300 Enclosed Tissue Processor (Leica Biosystems, Buffalo Grove, IL) for 24 hours. The following day, the muscle tissue was embedded in paraffin blocks and sectioned at 5-7µm thickness using a microtome and left overnight to dry on microscope slides. The sections were next stained using Hematoxylin and Eosin (H&E). The muscle tissues were examined under a light microscope. Fifteen sections were qualitatively examined for muscle spindles, 8 ED and 7 EP. The muscles were qualitatively inspected to examine the muscles under a light microscope and record if there were any obvious differences in muscle spindle density between the EP and the ED in both species. Based on the results of muscle spindle density in the *M. coracotriceps*, 6.33 muscle spindles per gram of muscle, we kept our threshold at six muscle spindles per gram of muscle to qualify it as a kinesiological monitor. We estimated muscle mass based on linear measurements. Samples were approximately 1 cm in length and diameter. Based on published estimates of muscle density at 1.06g/cm^3 we estimated mass of ED to be 1.06g (*12*).

RESULTS

Examination of the 8 samples of ED showed no qualitative difference in muscle spindle density in comparison to the 7 samples of EP. We did not find muscle spindles in the density expected of a kinesiological monitor. Out of the 15 samples examined, we did not notice a higher density of muscle spindles in the ED in comparison to the EP. Each muscle belly demonstrated approximately 0-2 total muscle spindles (Fig. 2), with consistent results across the ED and EP. The lack of a large quantitative count of muscle spindles allowed for quick inspection for each section. This finding was consistent across both species and there were no qualitative differences between them.

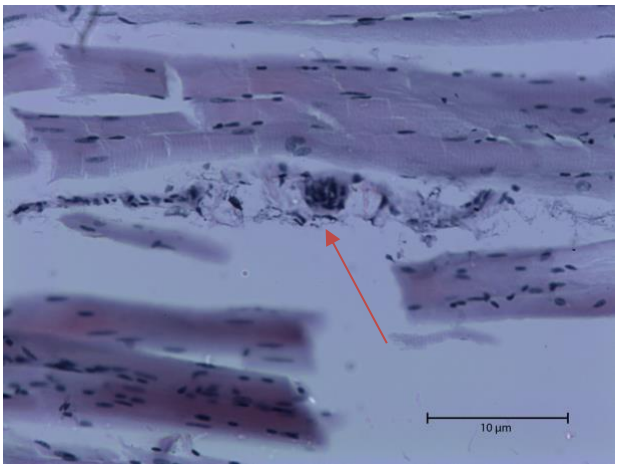

Figure 2. Pictured is a light microscopic photograph of a muscle spindle (red arrow) in the proximal head of the M. extensor longus digiti majoris (EP) in *Columba livia* (rock pigeon). Stained with hematoxylin and eosin. 20X objective. Image courtesy of Dr. Tobin Hieronymus.

DISCUSSION

Given the relative muscle spindle density in ED not exceeding that of EP, this muscle is unlikely to be a kinesiological monitor. This contrasts with the *M. coracotriceps* which showed a total muscle spindle density of over 14000 spindles per 2300 grams of muscle (15 times greater than any other muscles in the avian species) (*7*). This is a much higher density than the total 0-2 spindles examined in each of 15 samples of ED and EP, which were in the same order of magnitude in size as 1 gram of *M. coracotriceps*.

The evolutionary pattern of ED shows both preservation and loss in different bird species. The presence of this muscle belly is preserved in species that do not have distal limb reduction, such as jungle fowl and rock pigeons (*11*). This muscle is not retained in species such as perching birds (Passeriformes), swifts, members of the ground bird assemblage (Cavitaves), and members of the "metavian" assemblage (cuckoos, cranes, and allies) some of which show a pattern of distal limb reduction (Fig. 3) (*11,13*). Species that have undergone distal limb reduction have a flight style which demonstrates high beat wing frequency (*13*). There is reasoning that extra weight with vestigial structures in avian hands may be costly to inertia during flight (*10*). It has been previously demonstrated that higher intensity action of distal wing musculature is present during takeoff and landing for Aves during flight (*10*). During active flight, birds are efficient in minimizing muscle contractions and saving metabolic energy (*10*). A vestigial structure present in many clades would go against the efficiency of birds in flight. Therefore, this evolutionary pattern suggests that the ED is not of use in Aves with distal limb reduction, however, it may still serve a function in Aves that have retained it.

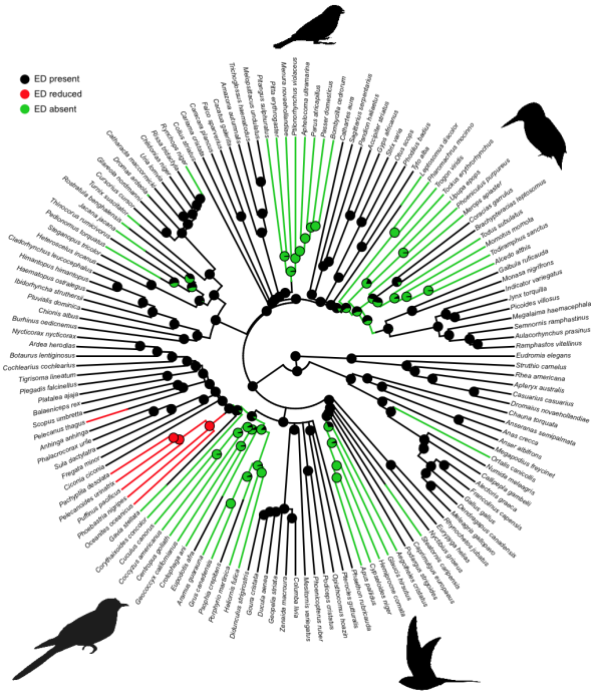

Figure 3. Phylogenetic Tree of the ED retention. Character states drawn from Livezey and Zusi (2007). Silhouettes from PhyloPic.org : *Hemiprocne mystacea* by Jerry Oldenettel (vectorized by T. Michael Keesey). *Passer domesticus* by Andrew Butko (modified). All silhouettes CC BY-NC-SA 3.0. creativecommons.org/licenses/by-nc-sa/3.0/. All other silhouettes public domain *(11).*

Another possible function of ED is based on its anatomical characteristics and relationship with EP. The tract of the muscle tendon of the EP is from the forearm to the major metacarpal in the hand and serves as the insertion point for the distal head (Fig. 1). The distal head inserts into the tendon at the proximal head of the major metacarpal. The EP has a dual function of digit extension and wrist flexion (*8*). ED inserts directly in the middle of the tract of the tendon for EP, therefore, for EP to produce the action of wrist flexion, ED may be serving a function to decouple digit extension from EP to wrist extension.

A similar example is the *quadratus plantae*, which corrects the tendon tract of the *flexor digitorum longus* in the feet of humans (Fig. 4). This also is a smaller muscle which has a tendinous insertion onto a larger muscle's tendon in a similar structure (avian hand vs human foot). *Quadratus plantae* realigns the tendon of *flexor digitorum longus* in human feet and allows it to properly flex the second through fifth digits in the foot. The architectural resemblance between ED and EP in Aves and *Quadratus plantae* and *flexor digitorum longus*

in humans supports the idea that ED may be performing a similar role as *Quadratus plantae*.

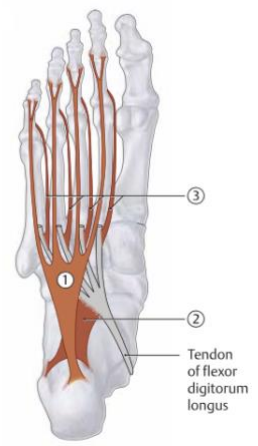

Figure 4. *Quadratus Plantae* (labeled as 2) inserting on the tendon of the *flexor digitorum longus*, allowing for proper flexion of digits 2-5. This file is licensed under the Creative Commons Attribution-Share Alike 4.0 International License. Image courtesy of Powellle 2020. https://commons.wikimedia.org/wiki/File:2_-_quadratus_plantae.png *(16)*

There are several limitations to our study. Firstly, we did not examine the muscle tendons under a light microscope, as we narrowed our focus on the muscle belly during the study. Although muscle spindles are the primary organ involved in proprioception, muscle tendons may contain Golgi Tendon Organs (GTO) which can also serve as proprioceptive monitors (*14*). Additionally, our sample size was only 15 total samples, and statistical analysis was not performed (due to the qualitative approach); additional samples and access to additional species would have made this study more effective. A quantitative analysis rather than a qualitative analysis would have allowed for a more thorough analysis and the inclusion of a statistical evaluation to definitively prove our findings; however, a qualitative analysis was performed due to time constraints and limited access to samples. Despite this, qualitative research on topics not previously explored, such as the ED and EP, can still provide meaningful insight for future studies. Therefore, future steps of this study include to expand it to multiple species with different flight patterns, such as perching birds and swifts, and additionally gathering a larger number of samples. In addition, testing the function of the muscle based on the anatomic characteristics mentioned above with techniques such as *in-vitro* contracture testing could help identify the function of the ED.

CONCLUSIONS

Our findings do not demonstrate increased muscle spindle density in the ED, in comparison to the EP, of *Gallus gallus* and *Columba livia*. Since muscles with proprioceptive functions typically demonstrate a high amount of muscle spindles, the ED is not likely to function as a kinesiological monitor. While we believe that further quantitative research on the ED among a wider variety of species may show different results, our research does not demonstrate any evidence of a proprioceptive function. Phylogenetic distribution suggests this muscle is not of use in Aves with distal limb reduction, however, it may still hold a function in the Aves that have retained it. A plausible function of ED is that it decouples digit extension of the EP to wrist extension, further supported by a similar anatomical architecture in the *Quadratus plantae* in the foot of humans. Future directions include gathering more evidence on the characteristics of the ED by expanding the study across more species of Aves with different flight patterns, and include testing the anatomical function of the ED.

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CONFLICTS OF INTEREST

All authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: AP, TH

Methodology: AP, TH

Investigation: AP, TH

Supervision: TH

Writing – original draft: AP, TH

Writing – review & editing: AP, TH

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Telehealth Access of Geriatric Patients During COVID-19: A Provider Team Survey

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ABSTRACT

The COVID-19 pandemic has prompted the rise in the use of virtual healthcare through Telehealth. The importance of Telehealth is multi-fold, from communicating with patients virtually to providing care when in-person services are unavailable. Although this virtual platform has significant benefits, the geriatric population is underutilizing this resource. Our initial objective was to understand the perceptions of healthcare providers and their assessment of the comfort level and the utility of telehealth software for geriatric patients. We surveyed Geriatric specialists, Social Workers, Registered Nurses, and healthcare management team members regarding their perceptions of the rise and utility of telehealth before and after the pandemic. The survey was conducted in Northeast Ohio, specifically from Summa Health Akron City Hospital and the Direction Home Akron Canton Area Agency on Aging and Disabilities. 72.7% of those invited completed the survey, specifically five (33.3%) were physicians. Additionally, we surveyed participants regarding patient capability and understanding of telehealth software. A large subset of participants using telehealth (69.2%) stated that their patients fell between "somewhat uncomfortable" to "completely uncomfortable" in utilizing telehealth. Regarding their use of blood pressure and glucose monitors, 76.9% felt their patients had a "medium comfort" level. Finally, 92.3% would find a volunteer service to help train patients and caregivers in the use of telehealth software and medical devices "extremely helpful." These data demonstrate a perception among geriatric providers that patients have difficulties using telehealth. Our goal is to develop a student-led virtual program to better assist patients and providers in the use of telehealth modalities.

Keywords: Telehealth, COVID-19, Geriatrics, Telemedicine

INTRODUCTION

From house calls to the increased use of larger institution-based practice, the delivery of healthcare is ever-changing. A new and rising mode of delivery— especially since the onset of COVID-19— is Telehealth, which allows the doctor to gain virtual connection with patients while maintaining physical distance. Video conferences, custom applications, web-based services, and remote monitoring are all encompassed within the broad approach. Advantages of incorporating these techniques include ease of use, improved communication, low cost, decreased travel time, increased access to care, and empowerment of patients to manage chronic conditions *(1)*.

Despite the clear benefits of using this system, there are difficulties that plague broader use of telehealth, such as availability, cost, technology dysfunction, trust, and impersonality *(2)*. A 2012 Health Information National Trends Survey demonstrated that older male adults with low socioeconomic status (SES) had decreased interactions with telehealth. While 30% of patients below 64 years use telehealth, less than 10% of patients above 65 use it *(3)*. In a qualitative interview study conducted in Manchester, geriatric patients described barriers to

telehealth, including lack of technical competence. Patients expressed that they find it difficult to remember and manage technical machinery, such as keyboards and keypads. Patients also have uncertainty when using the internet and lack adequate training to use blood pressure monitors and medical devices on themselves *(4,5)*.

Although practices can incorporate various forms of telehealth, there are concerns regarding whether the geriatric patient population has the capability to use the software. In this prospective observational survey, we surveyed geriatricians and healthcare providers working at Summa Health Akron City Hospital and the Direction Home Akron Canton Area Agency on Aging and Disabilities about their current use of telehealth in the delivery of healthcare before and after the spread of COVID-19. Further, we want to explore whether practitioners believe that patients can and have knowledge of how to use telehealth and medical devices at home or in independent living facilities. We plan to use data from this survey to develop a medical student-led virtual program to aid patients in using medical devices and telehealth modalities.

METHODS

A 23-item survey was developed with questions regarding provider background, patient population, telehealth utility among providers, and perceived level of comfort using telehealth and medical devices among patients for providers. The study was sent to healthcare providers to understand their perception of patient comfort with telehealth to better understand providers' need for software coaching. The questions were in Yes/No, multiple-choice, and single best-answer type formats, with space for a final comment at the end of the survey. The study protocol was approved by the Northeast Ohio Medical University Institutional Review Board in Rootstown, Ohio. Informed consent was implied by the subject's willingness to complete the survey. All the responses were anonymously collected to eliminate any potential bias. The 45-item, English-language, web-based survey tool (Qualtrics Survey Software, Provo, UT) was administered online from November 2020 to December 2020.

Twenty-two potential participants were identified as geriatricians from Summa Health Akron City Hospital and healthcare providers from the Direction Home Akron Canton Area Agency on Aging and Disabilities, an entity of the Ohio Department of Health. An e-mail invitation with an explanation of study protocol and consent was sent to study participants, with a subsequent e-mail invitation sent weekly to non-responders for a total of four weeks. All responses were entered into a Qualtrics Survey Software database and imported into Microsoft Excel to compute the appropriate descriptive statistics. Data were reported as mean (standard deviation), median (interquartile ratio), and proportions *(6)*.

RESULTS

General Participant Information (Table 1)

Of 22 potential participants, 16 (72.7%) completed the survey. Percentages are reported per number of participants that answered the question. Five (33.3%) participants were practicing geriatricians at Summa Health Akron City Hospital. Eleven (21.4%) were social workers, registered nurses, and healthcare management team members at the Direction Home Akron Canton Area Agency on Aging and Disabilities. Eleven (73.3%) of the participants reported that less than 25% of their patients resided in nursing homes. Ten (71.4%) of the participants reported that less than 25% of their patients resided in independent living facilities. Three participants (20.0%) reported that less than 25% of their patients resided at home. Most of the patients resided at home or in independent living facilities.

Telehealth Utility (Table 2)

Nine (60%) of the participants utilized telehealth to communicate with their patients, of whom five (55.6%) had utilized telehealth for less than six months. Of the nine participants, all saw less than 25% of their patients using telehealth prior to February 2020. After February 2020, three (33.3%) saw less than 25% of their patients using telehealth and two (22.2%) saw greater than 75% of their patients using telehealth. Among all participants, multiple modalities of telehealth were employed. Four people utilized FaceTime, two utilized Zoom, seven utilized Doxy, seven utilized telephone, one utilized Webex, and one utilized Skype.

Four (30.7%) participants reported that less than 25% of their patients had access to mobile devices at home. Nine (69.2%) of the participants reported that less than 25% of their patients had access to tablets at home. Thirteen participants reported that their patients used blood pressure monitors, twelve reported that their patients used blood glucose monitors, and five reported that their patients also used pulse oximetry machines, weighing scales, and INR machines at home.

	Respondents	Response
Participant role in practice:	15 (93.8)	
Social Worker		4 (26.7)
Nurse Practitioner		0
Physician		5 (33.3)
Health facility management		6 (40)
Description of administration of the practice:	15 (93.8)	
Community-based hospital		
Healthcare aging facility		5 (33.3)
		10 (67.7)
Length in practice:	14 (87.5)	
<5 years		3 (21.4)
5-15 years		5 (35.7)
>15 years		6 (42.9)
Perceived percentage of patients residing in a nursing home:	14 (87.5)	
<25%		
25-50%		11 (73.3)
50-75%		2 (13.3)
>75%		2 (13.3)
		0
Perceived percentage of patients residing in an independent living facility:	14 (87.5)	
<25%		10 (71.4)
25-50%		2 (14.3)
50-75%		2 (14.3)
>75%		0
Perceived percentage of patients residing at home:	15 (93.8)	
<25%		3 (20)
25-50%		3 (20)
50-75%		4 (26.7)
>75%		5 33.3)

Table 1: General participant information

	Respondents	Response
Participants who use TeleHealth:	15 (93.8)	
Length of TeleHealth utility:		9 (60)
<6 months		5 (55.6)
6-12 months		4 (44.4)
1-5 years		0
>5 years		0
Patients seen using TeleHealth prior to February 2020:		
<25%		9 (100)
Patients seen using TeleHealth after February 2020:		
<25%		3 (33.3)
25-50%		3 (33.3)
50-75%		1 (11.1)
>75%		2 (22.2)
Method of TeleHealth employed (check all):	14 (87.5)	
FaceTime		4
Zoom		2
Doxy.me		7
Telephone		7
Webex		1
Skype		1
Perceived percentage of patients with access to mobile devices at home:	13 (81.3)	
<25%		4 (30.8)
25-50%		4 (30.8)
50-75%		4 (30.8)
>75%		1 (7.7)
Perceived percentage of patients with access to tablets at home:	13 (81.3)	
<25%		
25-50%		9 (69.2)
50-75%		4 (30.8)
>75%		0
		0
Devices patients use to monitor health at home:	13 (81.3)	
Blood pressure monitors		13
Glucose monitors		12
Other: Pulse oximetry monitors**,** scales**,** INR machines		5

Table 2: TeleHealth Utility

Telehealth Comfort (Table 3)

Participants were also asked to assess their patients' comfort level with utilizing telehealth on a Likert scale of 1-5 (1= very uncomfortable, 5=very comfortable). Three (23.1%) perceived their patients to be at a 1 and zero perceived their patients to be at a 5. In asking how useful the participants thought a volunteer service would be in helping patients utilize telehealth on a Likert scale of 1 to 5 (1=very un-useful, 5=very useful), one (7.7%) perceived the service to be a 1 and 10 (76.9%) perceived the service to be a 5.

Participants were then asked to evaluate their patients' comfort level using devices to monitor health at home on a Likert scale of 1 to 5 (1=very uncomfortable, 5=very comfortable). Two (15.4%) perceived their patients as a 4 and zero perceived their patients as a 5. In asking how helpful a volunteer service would be to aid patients and/or caregivers in utilizing telehealth on a Likert scale of 1 to 5 (1=very unhelpful, 5= very helpful) nine (69.2%) believed their patients were at a 5.

Finally, we asked the participants which modes of telehealth they would find a student-led volunteer program useful for. Four (28.6%) reported they could use help in teaching patients how to use Zoom, eight for FaceTime, four for Facebook Messenger, seven for Doxy, eleven for telephone, six for e-mail, and four for other services such as Skype.

DISCUSSION

Our results emphasize the challenges faced by health care providers to reach geriatric patients, especially during a pandemic, when the need to maintain physical distance between the practitioner and patient is paramount. Table 2 demonstrates that healthcare practitioners are incorporating telehealth services to connect with their patients. In fact, most responding participants reported seeing less than 25% of their patients via telehealth prior to February 2020, then transitioning to over two-thirds of participants seeing more than 25% of their patients via telehealth after the beginning of the COVID-19 pandemic. The disparities in providing telehealth access may be demonstrated through the patient demographics of the geriatric providers: most patients live in private residences and have limited access to the support a nursing home or independent living facility may provide. This is underscored as most survey participants indicated that their patients' perceived comfort level using telehealth and telemonitoring devices was low. Consequently, many responders requested a student-led volunteer program, with 92% of participants estimating outcome of an intervention as beneficial to their practice. Respondents indicated highest utility for a program providing education for services such as Facetime, Zoom, Doxy, Telephone, Email, and Skype. We identified another possible intervention through provision of Telehealth-capable devices; 61% of providers reported 50% or less of their patient base had access to mobile devices at home and 100% of the providers indicated that less than half their patient base had access to tablets.

This work extends the findings of previous literature in identifying problematic areas for geriatric patients with respect to accessing telehealth treatment, particularly in the greater Akron area. In a review by Bashshur et al. in 2014., empirical evidence was identified supporting the use of telehealth in chronic disease management for reducing hospital admissions, length of hospital stays, emergency department visits, and even mortality *(7)*. This comes alongside acknowledgement of interventions showing that technology-based healthcare management can be implemented with notable results in older adults, especially as they often suffer from chronic disease *(8, 9)*.

Despite successful applications of telehealth in broader populations, geriatric patients face increased barriers to adoption, such as access to appropriate devices and low technological literacy. Sivakumar et al. note that successful deployment of interventions in India had to overcome low digital literacy, sensory issues, and cognitive impairment in administering geriatric telepsychiatry *(10)*. Parker et al. attributed low patient response via telehealth to a multitude of factors: lower intrinsic motivation, health literacy, and efforts to engage patients in newer forms of health technologies by the provider *(11)*. Due to the varied factors that contribute to the effectiveness of telehealth, it may be difficult for a geriatrician to transition employing newer technologies to reach patients.

Major strengths of our study include the fact that participants involved with the survey were all from the local community, focusing on the needs of the nearby geriatric population. Additionally, the high response rate (73%) of potential participants stresses the importance of the content of the survey to the participants. This is further supported by ardent request for student-led volunteer programs to target health literacy across a variety of disciplines, ranging from geriatric physicians at Summa Akron City Hospital to the staff at Direction Home Akron Canton Area Agency on Aging and Disabilities, including social workers, registered nurses, and healthcare providers.

Perceived patient comfort using TeleHealth (1=very uncomfortable, 5=very comfortable):	13 (81.3)	
1		3 (23.1)
2		6 (46.2)
3		3 (23.1)
4		1 (7.7)
5		0
Perceived patient aid in use of a mobile TeleHealth volunteer service (1=very un-useful, 5=very useful):	13 (81.3)	
1		1 (7.7)
2		0
3		0
4		2 (15.4)
5		10 (76.9)
Perceived patient comfort using devices to monitor health at home (1=very uncomfortable, 5=very comfortable):	13 (81.3)	
1		
2		0
3		1 (7.7)
4		10 (76.9)
5		2 (15.4)
		0
Perceived patient aid in use of a medical health device volunteer service (1=very un-useful, 5=very useful):	13 (81.3)	
1		0
2		0
3		1 (7.7)
4		3 (23.1)
5		9 (69.2)
Methods of TeleHealth participants suggest a volunteer service for:	13 (81.3)	
Zoom		
FaceTime		4
Facebook Messenger		8
Doxy.me		4
Telephone		7
E-mail		11
Other: Skype, Doximity		6
		4

Table 3: TeleHealth Comfort

There are also limitations to this study. Even though this survey was designed with the interests of pertinent stakeholders in mind, we identified potential participants from only two local institutions, resulting in a low sample size. In addition, the number of participants was limited to those interested in seeing the implementation of a program to aid their patients; this is indicative of self-selection bias. Finally, close-ended questioning can lead to loss of internal validity and objectivity. To address these limitations, we incorporated options to provide type-in-responses.

The results of the study were all estimates of patient comfort by providers. Further studies may incorporate patient feedback on utilizing telehealth at home. We are utilizing this data to develop a student-led virtual program to aid patients with using medical devices and assistance with Telehealth. Student volunteers will be trained to effectively communicate, educate, and formulate guides to aid the geriatric population in better understanding the technology necessary to use telehealth. Students will be able to answer questions related to using the software as well as home medical devices. This intervention aims to address the gaps noted by the geriatric providers. We hope to facilitate improved patient-provider communication and improve adherence to medical treatment and therapy. Further studies could determine the impact of this volunteer-led program in improving telehealth access and utilization.

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CONFLICTS OF INTEREST

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Investigation: SM, SS

Visualization: SM, SS, SJ, AG, MM

Project administration: M, SS, SJ, AG, MM

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Burnout and Wellness in the College of Medicine at Northeast Ohio Medical University

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ABSTRACT

Burnout is a syndrome of professional distress defined by symptoms of emotional exhaustion, depersonalization, and a sense of reduced personal accomplishment. Previous surveys (Wellness Surveys) at Northeast Ohio Medical University (NEOMED) seemed to have demonstrated low scores in the wellness categories. As such, we sought to investigate further the frequency and factors of medical student burnout symptoms, the quality of medical student wellness, and contributing stressors at NEOMED. Over three weeks, an anonymous 8-question survey was sent out via e-mail to all NEOMED College of Medicine students. This survey included a novel scale created by the authors to measure burnout, wellness, and contributing stressors. The survey was done on Qualtrics SM Survey software and was statistically analyzed by class using Microsoft Excel. The survey was completed by 166 students (participation = 28%). Results demonstrated statistically significant differences in burnout and multiple components of wellness when stratified by class. Burnout and suboptimal wellness were most severe in preclinical (M1-M2) years. Groups rating higher frequencies of burnout also rated lower qualities of wellness. Nearly 50% of all respondents feel the challenge of medical school was more difficult than expected. At NEOMED, peak burnout frequencies and suboptimal wellness ratings are in the preclinical years. Groups that scored higher frequencies of burnout also scored poorer on wellness ratings. A systematic approach dedicated to promoting wellness at NEOMED may lead to lower frequencies of burnout.

Keywords: Burnout, Wellness, Education, Mental Health

INTRODUCTION

Burnout is a syndrome of professional distress defined by symptoms including emotional exhaustion, depersonalization, and a reduced sense of personal accomplishment (*1,2)*. This syndrome is highly prevalent in the medical field, affecting many physicians and physician trainees in the United States. Emerging research shows that nearly 50% of medical students, residents, and attending physicians in the US have experienced burnout; these rates are significantly higher than those observed in the general US population (*2*). Burnout has been linked to increased risk of anxiety, depression, and medical error (*3,4*). In a profession dedicated to caring for others, high rates of burnout may threaten to compromise compassionate and effective healthcare. Thus, burnout is an issue that requires close investigation to reveal where and how safeguards may be implemented at all levels. For medical providers, burnout may begin during the first years of medical training (*5*). As such, it is important to consider intervention at this stage.

Medical student wellness is a topic of increasing discussion nationwide. Wellness encompasses mental, physical, and emotional health (*6*). It has been shown to be a quality indicator that may inversely correlate to levels of burnout (*6*). The Liaison Committee for Medical Education (LCME) aids in the oversight of allopathic

medical student education. The LCME Standard 12.3 requires that "A medical school has in place an effective system of personal counseling for its medical students that includes programs to promote their well-being and to facilitate their adjustment to the physical and emotional demands of medical education" (*7*). Specialty training following medical school is largely governed by the Accreditation Council for Graduate Medical Education (ACGME). ACGME has a growing recognition that "Psychological, emotional, and physical well-being are critical in the development of the competent, caring, and resilient physician and require proactive attention to life inside and outside of medicine. Well-being requires that physicians retain the joy in medicine while managing their real-life stresses" (*8*). Every residency seeking ACGME accreditation must have "policies and programs that encourage optimal resident and faculty member well-being" (*8*).

The individual components of wellness (mental health, physical health, and emotional health) can significantly contribute to medical students' quality of life, academic performance, and clinical performance (*9*). For example, inadequate sleep, one of the physical health subcomponents of wellness, can contribute to medical error, depreciating test results, and cognitive decline (*9*). Within the wellness subcomponent - emotional health, a strong sense of purpose has been linked to longer, happier, and more fulfilled lives (*10*). During postgraduate medical training concerns over the worsening of provider mental health led the ACGME to mandate screening for anxiety, depression, and substance abuse disorders. Assessing components of burnout and wellness as a means of developing strategies to reduce burnout and promote wellness should be a standard part of modern medical training.

Based in Rootstown, Ohio, NEOMED has a mission to train patient care-centered physicians while aiming to be a national leader in community-centered medicine. Over the last two years, NEOMED has begun a series of dramatic changes in its curriculum. Student feedback had led to a complete overhaul of the NEOMED curriculum deemphasizing lectures and markedly increasing interactive teaching modalities, especially Peer Instruction. NEOMED has also begun devoting more time and resources to wellness-related topics and has created several initiatives to improve student wellness such as opening a Center for Student Wellness and Counseling Services, offering wellness days for first-year students, and integrating wellness exercises and discussions in the curriculum. Despite these initiatives, concerns exist about the rates of burnout and wellness among the NEOMED medical student population.

The global pandemic of 2020 undoubtedly added considerable burdens to already stressed medical providers (*11*). Individuals throughout the world faced issues of fear, grief, and loss during a time of decreased social support. Medical professionals were not spared these personal struggles while caring for suffering individuals. All of these challenged individual providers' senses of wellness and pushed toward ever higher and earlier rates of burnout (*11*). For medical students at NEOMED, there were unprecedented changes in training, evaluations, and applications for post-graduate training.

With increasing literature throughout the medical field regarding burnout and wellness, we sought to explore if burnout and suboptimal wellness are issues at NEOMED. To train high-quality patient care-centered physicians, we felt it would be advantageous to examine our environment and determine points of quality improvement. We believe that identifying of these possible issues can lead to targeted improvement projects and additional resource acquisition within NEOMED that can help improve student experience and wellness and ultimately prepare better physicians. We hypothesize that preclinical students will have the highest rates of burnout and that there will be a statistically significant difference between burnout symptom frequency and wellness quality depending on students' class year.

METHODS

An anonymous 8-question survey was sent out via e-mail to all NEOMED College of Medicine students over a 3-week span. This survey included a novel scale created by the authors to measure burnout, wellness, and contributing stressors. The survey was done on Qualtrics SM Survey software and was statistically analyzed using Microsoft Excel. Data were analyzed by class. The eight questions administered through the survey are discussed below.

Our first objective is to identify burnout and related stressors at NEOMED by determining: 1. the frequency of burnout symptoms among NEOMED College of Medicine students, stratified by class (M1, M2, M3, M4) 2. The rating of wellness among NEOMED College of Medicine students, stratified by class (M1, M2, M3, M4). 3. Major stressors among NEOMED College of Medicine students 4. Expected challenges of medical school at NEOMED versus experienced challenges in medical school at NEOMED and, 5. Targeted improvement strategies based on identified areas within wellness and burnout subcomponents and at which specific stage of medical training they are occurring in. Our second objective is to measure the degree of burnout symptoms and the quality of wellness stratified by demographic

information to determine if any specific group of people is not achieving wellness and how we may help them.

*M1 denotes first-year medical student; M2 denotes second-year medical student etc. It is of note that M1-M2 spend most of their time doing preclinical work (classwork and lectures), and M3-M4 spend most of their time in the clinical setting with patients.

Data Collection

In order to conduct our primary and secondary aims, we created an online survey. To investigate burnout, we proposed measuring three categories of our own conception that we believe represent the dimensions of burnout: *detached, drained, and defeated.* We elected to use the novel terms detached, drained and defeated, as we felt these more sufficiently captured the feelings medical students at NEOMED would potentially experience in response to a year in medical school during the COVID-19 pandemic. These terms were defined within the survey (Fig. 1A). To investigate wellness, we separated it into three categories proposed by Wallace et al.: *mental*, *physical*, and *emotional* health *(6)*. Likewise, as for burnout, we proposed to measure three subcategories of our conception (emotional, mental, physical health) for each larger category proposed by Wallace (9 subcategories total).

The questionnaire included eight questions and was administered in January 2021. Question 1 asked participants to provide separate ratings of the frequency they experienced the three components of burnout over the past two weeks (Fig. 1A). The two-week time frame was selected to provide insight into symptoms at that specific time range during the beginning of a medical school semester**.** Of the questions asked, Questions 2 through 4 asked participants to rate their satisfaction with each of the nine subcategories of wellness (Fig. 1B). The fifth question asked participants to compare the level of challenge they have experienced in medical school to what they expected before beginning (Fig. 1C). These first five survey questions were rated on scales of one to five, though the scales were distinct for each question (see Fig. 1). Herein, we refer to answers pertaining to burnout as *frequency ratings*, answers pertaining to wellness as *satisfaction ratings*, and answers pertaining to experienced versus expected challenge of medical school as *disparity ratings*. For this manuscript, students who reported frequency ratings of 4 or 5 for burnout metrics were considered at risk of burnout or experiencing burnout. Students who reported satisfaction ratings of 1 or 2 for wellness metrics were considered to have suboptimal wellness.

The sixth question sought to explore additional factors that may contribute to burnout. To accomplish this, we composed a list of nine potential stressors: finances, COVID-19, political climate, family issues, academic performance, relationships, health concerns, geographic environment, and discrimination. Participants were asked to select the three that were most contributory stressors at the time of participation. The final two questions were extended responses to allow further comments on the survey and potential areas of improvement for NEOMED. The estimated completion time was approximately 10 minutes.

After the survey, participants were asked to share limited demographic information, including race, gender, and class year. Completing this section was optional and did not affect prior responses in the overall analyses. Lastly, this project meets the criteria for a Quality Improvement project and did not require IRB approval.

Participation

The survey was distributed to all 599 students in the NEOMED College of Medicine. Participation was optional and anonymous (n =166; participation = 28%). The study was single blinded as the participants were aware of researchers, study goals, and the survey group they were in, and researchers were not aware of individual subject identities. The survey was open for three weeks from, January 18, 2021 to February 8, 2021, and was administered via Qualtrics SM Survey software. The timeframe of three weeks was selected to give participants ample time to take the survey and for the researchers to have the ability to address results promptly. The survey was emailed to all actively enrolled NEOMED College of Medicine students, with a weekly reminder email each of the following two weeks. The email also contained an information sheet that detailed the purpose of the survey, participation as being anonymous and optional, researcher contact information, the definitions of terms, and instructions for participation. No compensation was provided for survey completion.

Data analysis

The ordinal data collected for the first five survey questions was treated as numeric for the sake of comparative statistical analysis. We believe that this assumption is justified as the perceived difference between answer choices in the survey should be equal (e.g., the difference between very rarely and rarely should be equal to the difference between rarely and occasionally). Comparative statistical analyses were conducted within Microsoft Excel using a two-tailed, unpaired, two-sample t-test that assumed equal variances

and single factor analysis of variance tests as appropriate. A threshold of $p \leq 0.05$ was used to determine statistical significance. When single factor ANOVA testing revealed statistical significance, post-hoc two-tailed t-testing was conducted to determine which classes specifically differed from one another.

A

Q1

NEOMED Student Wellness Survey

AY 2020-21

You should have received an email from Arjun Pandya on Monday, January 18, where he explains the background and purpose of this wellness survey.

If you have any questions about it, please read that message. You can also contact apandya@neomed.edu, adadlani@neomed.edu, or rwelton@neomed.edu.

Please note that any feedback you provide is completely anonymous. **Be assured that you can speak freely.**

The first set of questions is about burnout (emotional, physical or mental exhaustion). It focuses on three aspects of it, which are listed and defined here:

- *Detached* – feeling down, cynical, pessimistic, treating people as objects
- *Drained* – feeling tired, experiencing somatic symptoms, feeling drained
- *Defeated* - feeling incompetent, inefficient, inadequate

Q2

During the past two weeks, I have felt:

	Very rarely	Rarely	Occasionally	Frequently	Very frequently
Detached	○	○	○	○	○
Drained	○	○	○	○	○
Defeated	○	○	○	○	○

B

How would you rate your **mental health** in the following areas?

	Poor	Fair	Neutral	Good	Excellent
Overall mood	○	○	○	○	○
Satisfaction with work/ life balance	○	○	○	○	○
Ability to make and meet life goals	○	○	○	○	○

How would you rate your **emotional health** in the following areas?

	Poor	Fair	Neutral	Good	Excellent
Quality of relationships	○	○	○	○	○
Ability to take time for yourself	○	○	○	○	○
Sense of purpose	○	○	○	○	○

How would you rate your **physical health** in the following areas?

	Poor	Fair	Neutral	Good	Excellent
Sleep	○	○	○	○	○
Diet	○	○	○	○	○
Exercise	○	○	○	○	○

C

How does the challenge of medical school (including lectures, exams, patient care and remote learning) you have experienced so far compare to what you expected medical school to be like?

- ○ Much worse than expected
- ○ Somewhat worse than expected
- ○ About what I expected
- ○ Somewhat easier than expected
- ○ Much easier than expected

Figure 1. Sample survey scales and verbiage used in assessing numerical ratings. A) Novel scale created by authors to rate burnout based on frequency of feeling *Detached, Drained,* or *Defeated* over the past 2 weeks. B) Novel scale created by authors to rate overall quality of wellness determined by the 3 categories, *Mental Health, Emotional Health, and Physical Health*, and 9 subcategories of wellness. C) Question used to determine experienced versus expected challenge in medical school.

RESULTS

Respondents included 51 M1s, 36 M2s, 46 M3s, and 32 M4s. There were no significant findings between groups when stratified by race and gender.

Burnout

Survey respondent data about our three categories of burnout is summarized in Table 1. The feeling of being *drained* was most frequently experienced among M2 participants, with a mean frequency rating of 3.83 (Table 1A). Being *drained* was least frequently experienced among M4 participants, with a mean frequency rating of 3.00. The percentages of students experiencing/at risk of feeling *drained* in each class were 56.9% of M1s, 63.9% of M2s, 44.7% of M3s, and 38.7% of M4s. Feelings of *detachment* were most frequently experienced among M1 and M2 participants, with mean frequency ratings of 3.14 for both classes (Table 1B). Feelings of *detachment* were least frequently experienced among M4 participants, with a mean frequency rating of 2.31. The percentages of students experiencing/at risk of *detachment* in each class were 37.2% of M1s, 41.7% of M2s, 17.1% of M3s, and 18.8% of M4s. The feeling of *defeated* was most frequently experienced among M2 participants, with a mean frequency rating of 3.25 (Table 1C). The feeling of being *defeated* was least frequently experienced among M4 participants, with a mean frequency rating of 2.39. The percentages of students experiencing/at risk of feeling *defeated* in each class were 35.2% of M1s, 55.6% of M2s, 21.3% of M3s, and 16.2% of M4s.

ANOVA testing revealed statistically significant differences between mean group frequency ratings for all three categories of burnout: *drained* (p=0.004), *detached* (p=0.006), and *defeated* (p=0.03). Two-tailed t testing revealed the following pairs of individual classes to differ significantly for feelings of *detachment*: M1 and M3, M1 and M4, M2 and M3, M2 and M4; feeling *drained*: M1 and M3, M1 and M4, M2 and M4; feeling *defeated*: M2 and M3, M2 and M4.

Components of Wellness: Mental Health

Survey respondent data pertaining to our mental health categories are summarized in Table 2. The *overall mood* was highest among M4 participants, with a mean satisfaction rating of 3.72 (Table 2A). The *overall mood* was lowest among M2 participants, with a mean satisfaction rating of 2.86. The percentages of students reporting a suboptimal *overall mood* in each class were 33.3% of M1s, 41.7% of M2s, 31.9% of M3s, and 15.7% of M4s. *Satisfaction with work/life balance* was highest among M4 participants, with a mean satisfaction rating of 3.68 (Table 2B). *Satisfaction with work/life balance* was lowest among M2 participants, with a mean satisfaction rating of 2.47. The percentages of students reporting a suboptimal *work/life balance* in each class were 43.2% of M1s, 58.3% of M2s, 36.1% of M3s, and 16.2% of M4s. The *ability to make and meet life goals* was highest among M4 participants, with a mean satisfaction rating of 3.69 (Table 2C). The *ability to make and meet life goals* was lowest among M2 participants, with a mean satisfaction rating of 2.82. The percentages of students reporting a suboptimal *ability to make and meet life goals* in each class were 41.2% of M1s, 44.4% of M2s, 34.0% of M3s, and 15.7% of M4s.

ANOVA testing revealed statistically significant differences between mean group satisfaction ratings for all three categories of mental health: *overall mood* (p=0.01), *satisfaction with work/life balance* (p<0.001), and *the ability to make and meet life goals* (p=0.01). Post-hoc two-tailed t testing revealed the following pairs of individual classes to differ significantly for *overall mood*: M1 and M4, M2 and M4, M3 and M4; *satisfaction with work/life balance*: M1 and M4, M2 and M3, M3 and M4; *ability to make and meet life goals*: M1 and M4, M2 and M4, M3 and M4.

Components of Wellness: Emotional Health

Survey respondent data pertaining to our three categories of emotional health are summarized in Table 3. *Quality of relationships* was highest among M4 participants, with a mean satisfaction rating of 3.75 (Table 3A). *Quality of relationships* was lowest among M1 participants, with a mean satisfaction rating of 3.08. The percentages of students reporting a suboptimal *quality of relationships* in each class were 41.2% of M1s, 33.3% of M2s, 25.6% of M3s, and 18.8% of M4s. The *ability to take time for oneself* was highest among M4 participants, with a mean satisfaction rating of 3.84 (Table 3B). The *ability to take time for oneself* was lowest among M2 participants, with a mean satisfaction rating of 2.67. The percentages of students reporting a suboptimal *ability to take time for oneself* in each class were 41.1% of M1s, 52.8% of M2s, 31.9% of M3s, and 9.40% of M4s. Satisfaction with a *sense of purpose* was highest among M4 participants, with a mean satisfaction rating of 3.78 (Table 3C). Satisfaction with a *sense of purpose* was lowest among M2 participants, with a mean satisfaction rating of 3.11. The percentages of students reporting a suboptimal *sense of purpose* in each class were 39.2% of M1s, 36.1% of M2s, 25.5% of M3s, and 15.7% of M4s.

ANOVA testing revealed a statistically significant difference between mean group satisfaction ratings for the *ability to take time for oneself* ($p<0.001$). The differences between mean group satisfaction ratings for *quality of relationships* ($p=0.13$) and *sense of purpose* ($p=0.057$) were not statistically significant. Post-hoc two-tailed t testing revealed the following pairs of individual classes to differ significantly for *ability to take time for oneself*: M1 and M4, M2 and M4, M3 and M4.

A

Class	Drained (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	0.0	9.8	33.3	21.6	35.3	3.82	51
M2	8.3	5.6	22.2	22.2	41.7	3.83	36
M3	2.1	17.0	36.2	29.8	14.9	3.38	47
M4	16.1	19.4	25.8	25.8	12.9	3.00	32

B

Class	Detached (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	9.8	23.5	29.4	17.6	19.6	3.14	51
M2	16.7	22.2	19.4	13.9	27.8	3.14	36
M3	19.1	27.7	36.2	12.8	4.3	2.55	47
M4	34.4	25.0	21.9	12.5	6.3	2.31	32

C

Class	Defeated (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	15.7	27.5	21.6	17.6	17.6	2.94	51
M2	22.2	16.7	5.6	25.0	30.6	3.25	36
M3	23.4	23.4	32.0	14.9	6.4	2.57	47
M4	25.8	32.3	25.8	9.7	6.5	2.39	32

Table 1: Percent of NEOMED Medical Student Response for Symptoms of Burnout. Scale Based on Frequency of Symptoms Over Previous 2 Weeks: 1- Very Rarely, 2- Rarely, 3- Occasionally, 4- Frequently, 5-Very Frequently. A) Percent Drained, B) Percent Detached, C) Percent Defeated

A

Class	Overall Mood (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	17.6	15.7	21.6	39.2	5.9	3.00	51
M2	13.9	27.8	22.2	30.6	5.6	2.86	36
M3	6.4	25.5	17.0	44.7	6.4	3.19	47
M4	6.3	9.4	6.3	62.5	15.6	3.72	32

B

Class	Satisfaction Work/Life Balance (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	15.7	27.5	33.3	23.5	0.0	2.65	51
M2	33.3	25.0	11.1	22.2	8.3	2.47	36
M3	19.1	17.0	27.7	25.5	10.6	2.91	47
M4	9.7	6.5	12.9	48.4	22.6	3.68	32

C

Class	Ability to Make and Meet Life Goals (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	13.7	27.5	25.5	29.4	3.9	2.82	51
M2	25.0	19.4	13.8	27.8	13.9	2.86	36
M3	10.6	23.4	19.1	38.3	8.5	3.11	47
M4	9.4	6.3	12.5	50.0	21.9	3.69	32

Table 2: Percent of NEOMED Medical Student Respondents Rating Quality of Mental Health based on Overall Mood, Satisfaction with Work/Life Balance, and Ability to Make/Meet Life Goals. Scale: 1- Poor, 2- Fair, 3- Neutral, 4- Good, 5- Excellent. A) Overall Mood Rating Percent B) Satisfaction with Work Life Balance Rating Percent, C) Ability to Make and Meet Life Goals Rating Percent

A

Class	Sense of Purpose (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	15.7	23.5	11.8	31.4	17.6	3.12	51
M2	11.1	25.0	19.4	30.6	13.9	3.11	36
M3	6.4	19.1	12.8	38.3	23.4	3.53	47
M4	6.3	9.4	9.4	50.0	25.0	3.78	32

B

Class	Ability to Take Time for Yourself (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	17.6	23.5	29.4	25.5	3.9	2.75	51
M2	25.0	27.8	13.9	22.2	11.1	2.67	36
M3	12.8	19.1	23.4	31.9	12.8	3.13	47
M4	9.4	0.0	12.5	53.1	25.0	3.84	32

C

Class	Quality of Relationships (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	11.8	29.4	13.7	29.4	15.7	3.08	51
M2	19.4	13.9	8.3	44.4	13.9	3.19	36
M3	12.8	12.8	6.4	57.4	10.6	3.40	47
M4	12.5	6.3	12.5	31.3	37.5	3.75	32

Table 3: Percent of NEOMED Medical Student Respondents Rating Quality of Emotional Health. Scale: 1-Poor, 2-Fair, 3-Neutral, 4-Good, 5-Excellent. A) Quality of Relationships percent, B) Ability to Take Time for Yourself percent, C) Sense of Purpose percent

Components of Wellness: Physical Health

Survey respondent data pertaining to our three categories of physical health are summarized in Table 4. Satisfaction with *diet* was highest among M3 participants, with a mean satisfaction rating of 3.11 (Table 4A). Satisfaction with *diet* was lowest among M2 participants, with a mean satisfaction rating of 2.83. The percentages of students reporting a suboptimal *diet* in each class were 41.2% of M1s, 41.6% of M2s, 36.1% of M3s, and 31.2% of M4s. Satisfaction with *sleep* was highest among M4 participants, with a mean satisfaction rating of 3.22 (Table 4B). Satisfaction with *sleep* was lowest among M1 participants, with a mean satisfaction rating of 2.65. The percentages of students reporting suboptimal *sleep* in each class were 45.1% of M1s, 41.7% of M2s, 40.4% of M3s, and 28.2% of M4s. Satisfaction with *exercise* was highest among M4 participants, with a mean satisfaction rating of 2.75 (Table 4C). Satisfaction with *exercise* was lowest among M1 participants, with a mean satisfaction rating of 2.41. The percentages of students reporting suboptimal *exercise* in each class were 53.0% of M1s, 41.7% of M2s, 49.0% of M3s, and 43.8% of M4s.

ANOVA testing revealed there to be no statistically significant differences between mean group satisfaction ratings for all three categories of physical health: sleep ($p=0.17$), diet ($p=0.70$), and exercise ($p=0.62$).

Experienced vs. Expected Challenge

Survey respondent data pertaining to *experienced versus expected challenges* in medical school is summarized in Table 5. The disparity between *experienced versus expected challenge* was least severe among M1 participants, with a mean disparity rating of 2.6. The disparity between *experienced versus expected challenge* was most severe among M4 participants, with a mean disparity rating of 2.34. ANOVA testing revealed there to be no statistically significant differences between mean group disparity ratings ($p=0.65$).

DISCUSSION

Burnout, Wellness, and Stressor Analysis

In this study of burnout and wellness in the NEOMED College of Medicine, we sought to investigate further the frequency and factors of medical student burnout symptoms, the quality of medical student wellness, and contributing stressors at NEOMED. We were able to discover several notable findings. First, all three symptoms of burnout are most frequently experienced in the first two (preclinical) years of medical school. Second, all three mental health components were significantly different when separated by class, being most commonly ranked as suboptimal by the M2 class. Third, the only emotional health factor that differed significantly between classes was the *ability to take time for oneself*. There were no statistically significant differences in physical health between classes, however, a high percentage of all three factors were ranked suboptimal. Finally, there were no statistically significant differences between experienced and expected challenges of medical school amongst the classes, however, a high percentage of respondents rated their experience as somewhat or much more challenging than expected. Thus, our findings suggest that the preclinical stage at NEOMED may contribute to a higher frequency of burnout symptoms and poorer mental health quality. M1s and M2s experience significantly greater burnout symptoms than M3/M4s. Additionally, rating their experience as much more challenging/somewhat more challenging than expected (49% of M1 respondents, 50% of M2 respondents, 52% of M3 respondents, and 57% of M4 respondents) is a concerning finding.

Respondents were asked for factors that might be worsening burnout and suggestions that might improve resilience. Preclinical students' suggestions regarding burnout include: isolation (secondary to pandemic), a newly redesigned and intense curriculum, and the USMLE Step 1 Exam. Although the new curriculum had been instituted because of previous students' desire for more active and interactive learning experiences, the current students had concerns about this approach. The M1 class disliked the frequent graded quizzes that accompanied the Peer Instruction methodology. The M2 class suggested that mandatory class and lecture work interfered with preparation for the USMLE Step 1 Exam. These comments likely correlate with "Academic Performance" being listed as the most significant stressor for these classes. Clinical students experiencing burnout at less frequent rates may be due to different demands based on their stage of training and/or improved coping strategies.

In the wellness categories, all three subcomponents of *mental health* - overall mood, satisfaction with work/life balance, and ability to make/meet life goals - showed a statistically significant difference between classes [*overall mood* ($p=0.01$), *satisfaction with work/life balance* ($p<0.001$), and *the ability to make and meet life goals* ($p=0.01$)], with lower scores in the preclinical years.

A

Class	Diet (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	21.6	19.6	17.6	35.3	5.9	2.84	51
M2	19.4	22.2	19.4	33.3	5.6	2.83	36
M3	10.6	25.5	19.1	31.9	12.8	3.11	47
M4	15.6	15.6	28.1	37.5	3.1	2.97	32

B

Class	Sleep (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	25.5	19.6	19.6	35.3	0.0	2.65	51
M2	25.0	16.7	16.7	41.7	0.0	2.75	36
M3	17.0	23.4	10.6	40.4	8.5	3.00	47
M4	9.4	18.8	15.6	53.1	3.1	3.22	32

C

Class	Exercise (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	41.2	11.8	17.6	23.5	5.9	2.41	51
M2	38.9	2.8	30.6	22.2	5.6	2.53	36
M3	27.7	21.3	14.9	23.4	12.8	2.72	47
M4	25.0	18.8	18.8	31.3	6.2	2.75	32

Table 4: Percent of NEOMED Medical Student Respondents Rating Quality of Physical Health. Scale: 1-Poor, 2-Fair, 3-Neutral, 4-Good, 5-Excellent. A) Quality of Sleep percent B) Quality of Diet percent C) Quality of Exercise

Class	Experienced vs. Expected Challenge (%)					Mean Rating	Number of Responses
	1	2	3	4	5		
M1	11.8	37.2	33.3	13.7	3.90	2.60	51
M2	22.2	27.8	30.6	13.9	5.50	2.53	36
M3	10.7	41.3	39.1	8.7	0.00	2.46	47
M4	12.5	43.8	40.6	3.1	0.00	2.34	32

Table 5: Percent of NEOMED Medical Student Respondents Rating Experienced vs Expected Challenge of Medical School (based on lectures, exams, patient care and remote learning). Scale: 1- Much Worse Than Expected 2-Somewhat Worse than Expected, 3-About What I Expected, 4-Somewhat Easier Than Expected, 5-Much Easier Than Expected

Once again, the students on clinical rotations may have been partially protected by increased resiliency with accumulated experience of high stress and work demands in medical school. Within *emotional health*, the only statistically significant difference between groups was the ability to take time for oneself, which may also be related to a fixed schedule and fewer exams in clinical years**.** *Physical health* factors displayed no statistically significant differences between classes. However, nearly 50% of respondents rated their sleep and exercise as suboptimal, and nearly 40% rated diet is suboptimal. These findings may be due to the rigorous academic demands taking up most of the students' time (*12*). Overall, classes that demonstrated higher scores on metrics of burnout tended also to demonstrate poorer scores pertaining to wellness metrics.

Finally, almost 50% of total respondents rated their experienced challenge of medical school at NEOMED as *much worse* or *somewhat worse* than expected. These results did not significantly vary by stage in medical school. This is an issue that may be due to perceived expectations of medical school, changes due to remote learning during the COVID-19 pandemic, and factors controlled by NEOMED (e.g., curricular structure).

How can NEOMED respond?

As previously stated, NEOMED has taken steps in student wellness. NEOMED opened the Center for Student Wellness and Counseling Services (CSWCS), which offers free care for students. The CSWCS began providing telehealth and evening appointments to expand accessibility to students. Many students praised the CSWCS. NEOMED students have access to the Sequoia Wellness Center on the NEOMED campus, which offers a full range of gym equipment and aerobics classes as part of enrollment. NEOMED students are permitted to take "wellness" days. Despite these initiatives, with the high rates of burnout and suboptimal wellness coupled with the medical school experience being more challenging than expected, there is room for further improvement. NEOMED should continue considering student feedback for iterative curricular implementation and improvement. Implementing a new curriculum will present a challenge to any university. During the pre-clinical years, the Peer Instruction emphasis is a valuable learning system; however, based on student feedback, improvements can still be made to this curriculum (*13*). Student feedback from this study requested fewer hours of Peer Instruction and no quizzes on the day following an exam. Members of the M2 class requested limiting lectures to run up to the USMLE Step 1 board exam. Continuing to meet with students and understanding their perspectives on the curriculum can help create and adjust a curriculum conducive to learning and student wellness.

NEOMED may benefit from a large project dedicated to promoting the components of wellness, mental health, physical health, and emotional health. As a specific example to improve mental health, NEOMED can provide free access to meditation apps such as Headspace, which has been demonstrated to have reduced stress by 14% (*14*). A larger-scale initiative on physical health and spreading awareness on the importance of its subcomponents: sleep, diet, and exercise may also be beneficial as many students are suboptimal in these categories. Examples include: virtual Zumba or yoga classes, meditation classes, or dietitian/chef-led cooking classes. Finally, emphasis on the components of emotional health by continuing to improve communication and consideration of students' lives outside of school can also be of benefit. A promising new initiative, which began in 2020, is the Exceptional Student Experience, a comprehensive initiative designed by NEOMED faculty to deliver a student-centered medical

school curriculum with a focus on patient care with humanistic values, clinical competence, board exam performance, residency competitiveness, and readiness, and personal wellness.

How can students respond?

In addition to NEOMED responding to factors outside a student's control, there are also several actions that students may take to improve symptoms of burnout. As demonstrated by our results, groups with higher scores on metrics of burnout also tended to demonstrate lower scores pertaining to wellness metrics. Therefore, these students may benefit by prioritizing components of wellness. For example, a sleep of an optimal duration (7-9 hours) is associated with higher test scores (*15*). Therefore, students may benefit by prioritizing this subcomponent of physical health, which can help improve a major stressor, academic performance *(15)*.

Additionally, it should be noted that there may be a reason to believe that experience at NEOMED may build resilience, demonstrated by improved metrics of burnout and some metrics of wellness in the later clinical years.

Lessons and limitations?

Our study has several limitations. The most significant potential factor is the low response rate. Our sample size of 166 out of 599 total students only captured 28% of the total student population. There may be a response bias based on the students who answered the survey. Responding students may be experiencing burnout and suboptimal wellness at more significantly different rates than nonparticipants of the survey. They may be seeking help to deal with these issues and view the survey as a platform for them to be heard. They were also given three weeks to respond, which may not have been a sufficient timeframe. Additionally, certain demographic factors including age and marital status were not collected to protect subject privacy. This limited our ability to determine how representative our respective samples were from each class. Finally, the timing of the survey in the middle of demanding preclinical semesters and the COVID-19 pandemic may have generated more unfavorable responses as it has shown to be a significant contributing factor to stress in the medical profession (*11*).

CONCLUSION

The medical school appears to be a stressful experience for NEOMED College of Medicine students, with peak burnout frequencies and suboptimal wellness ratings in the preclinical years. The effects of burnout can be detrimental to medical students, physicians, and to the entire healthcare system. Our findings demonstrated that the groups that scored higher frequencies of burnout also scored lower on wellness ratings, therefore, a systematic approach dedicated to promoting wellness at NEOMED may lead to lower frequencies of burnout.

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CONFLICTS OF INTEREST

All authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

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Using Ancient Spices to Treat Chronic Diseases: Turmeric's Potential to Modulate Disease Pathogenesis in Rheumatoid Arthritis and Inflammatory Bowel Disease

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ABSTRACT

This review aims to highlight two major health conditions that could benefit from regular supplementation of turmeric, as well as to discuss the importance of more widespread uses of this natural therapeutic in commonly used multivitamins and multi-drug regimens. There is a wide range of potential benefits patients could gain from this supplement, but we will be focusing only on the effects on inflammation in two of the most prevalent chronic inflammatory diseases, rheumatoid arthritis (RA) and inflammatory bowel disease (IBD). We propose that turmeric supplementation could be more commonly used in a healthcare setting as an adjuvant treatment in these inflammatory conditions. Future studies investigating turmeric's role for treatment in RA and IBD must aim to further evaluate the effects of curcumin on the human microbiota and how its bioavailability can be increased to provide therapeutic results.

Keywords: Turmeric, Anti-inflammatory, Irritable Bowel Disease, Rheumatoid Arthritis

INTRODUCTION

Turmeric is a rhizomatous herb that has been utilized in various capacities in both Chinese and Ayurvedic medicine for almost 4000 years (*1*). This spice has been utilized in the management of many anti-inflammatory disease processes throughout the world and has been documented in Ayurvedic medicine as a remedy for respiratory conditions, such as asthma, as well as for rheumatism, muscle aches, and wounds (*2*). The ancient Chinese documented similar usages, along with relief for abdominal pain (*2*). There is much evidence supporting the multiple health benefits of turmeric, suggesting the potential for it to serve as a more widespread option for inclusion in the treatment regimen for certain diseases, especially chronic inflammatory diseases (*3*). Modern medicine has slowly been catching on to the benefits of turmeric described by ancient civilizations. Today, many over-the-counter multivitamin supplements incorporate small doses of turmeric amongst their ingredients of fat-soluble vitamins, B vitamins, and other micronutrients (*1*).

Oxidative stress has been proven to be the pathological process behind many chronic diseases and cancers, making routine utilization of this natural anti-inflammatory herb something to consider in a healthcare setting (*3*). The mechanisms of turmeric's effects utilize antioxidant mechanisms similar to vitamins E and A, as it can neutralize free radicals that are damaging to normal body functions (*1*). The active component of turmeric is curcumin, and it is a compound that possesses many different actions *in vitro* and in experimental animal models (*4*). It has been shown to favorably affect lipid metabolism, antioxidant concentrations, multiple anti-inflammatory reactions, and numerous signaling pathways (*4*). Additionally, recent literature suggests that turmeric not only benefits those in inflammatory-mediated diseased states, but also healthy individuals, as well. A study by DiSilvestro et al. illustrated that low doses of lipidated curcumin promote a diverse range of health-promoting effects, such as lowering serum

triglycerides and proinflammatory cytokines, in healthy individuals without any underlying medical conditions (*4*). This has led investigators to believe that supplementation with low doses of curcumin could be of benefit in healthy individuals, as well. Additionally, curcumin has been shown to exert a multitude of effects on the human microbiome and intestinal system, which will be explored throughout this paper.

Despite these numerous potential benefits, the efficacy of turmeric as an anti-inflammatory agent has been questioned and seldom recommended clinically due to its poor bioavailability (*4*). For this reason, it is often combined with piperidine, a component found in black pepper, which increases its bioavailability by 2000% (*5*). The DiSilvestro study also managed to navigate its low bioavailability by utilizing a lipidated curcumin, which was able to enhance its anti-inflammatory effects (*4*). Therefore, it is clear that when bioavailability is increased, curcumin possesses its most potent and promising effects as an anti-inflammatory agent (*5*). Due to this, researchers have been investigating ways in which oral turmeric supplements can be chemically modified in order to increase the bioavailability of curcumin. Therefore, the low natural bioavailability should not dissuade its use, as there will likely be ways in which this can be adequately addressed in the near future.

This review aims to highlight two major health conditions that could benefit from regular supplementation of turmeric, as well as to discuss the importance of more widespread uses of this natural therapeutic in commonly used multivitamins and multi-drug regimens. There is a wide range of potential benefits from this supplement, but we will be focusing only on the effects on inflammation in two of the most prevalent chronic inflammatory diseases, rheumatoid arthritis (RA) and inflammatory bowel disease (IBD). We propose that turmeric supplementation should be more commonly used in a healthcare setting as an adjuvant treatment in these inflammatory conditions.

TURMERIC'S USE IN CHRONIC INFLAMMATORY DISEASES

Rheumatoid arthritis (RA) is the most common systemic inflammatory diagnosis. The prevalence of this chronic inflammatory disease is as high as 0.6% in North America (*6, 7*). Markers of this disease include anti-citrullinated protein, rheumatoid factor, elevated erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), all of which contribute to the destructive inflammatory component seen in this disease process (*8*). There are several proposed mechanisms of the inflammation seen in RA, and many that have not been explored yet. Most known mechanisms involve the machinery seen in the body's own defense mechanisms against foreign pathogens, including innate and adaptive immune systems (*9*). Turmeric may have the ability to tone down these widespread inflammatory effects, potentially relieving symptoms and slowing the destruction of tissue.

RA has multiple treatment options that come with various side effects. One option being methotrexate, which is often of clinical benefit but comes with many systemic side effects such as myelosuppression, mucositis, hepatotoxicity, and more (*10, 11*). Furthermore, exploring effective treatment options that have fewer side effects, such as turmeric, is very desirable considering the harsh effects drugs like methotrexate have on the body (*11*). Moreover, several studies on curcumin have shown effects in reducing proinflammatory biomarkers (*11*). A recent study revealed that curcumin, the active component of turmeric, has biochemical effects that can inhibit inflammation, synovial hyperplasia, and other aspects of CIA-induced rats via the mTOR pathway. (CIA-induced rats are collagen-induced arthritis specimens, a widely used animal model for rheumatoid arthritis) (*12*). Furthermore, curcumin inhibited the increased levels of proinflammatory cytokines and proteinases such as interleukin-1 beta (IL-1β), tumor necrosis factor alpha (TNF-α), matrix metalloproteinase-1 (MMP-1), and MMP-3 in CIA rats (*12*). A meta-analysis published in 2014 consisting of 342 subjects reveals a significant difference in CRP levels between curcumin and control groups. CRP directly correlates to bodily inflammation, further suggesting curcumin use can combat inflammation. This effect seemed to depend on the bioavailability and duration of supplementation (*13*). Additionally, a meta-analysis conducted in 2016 determined there is compelling evidence supporting the use of curcumin adjuvant to conventional RA therapy (*12*).

In addition to RA, inflammatory bowel disease has been increasing in prevalence over the last twenty years (*14*). According to the CDC, IBD, which includes Crohn's disease and ulcerative colitis, now affects approximately 3 million people or 1.3% of adults in the United States (*14*). While the pathogenesis of IBD remains largely unknown, it is thought to arise due to a dysfunctional or overly sensitive host immune response to bacterial and dietary antigens (*15*). The result is the breakdown of the microbiome and intestinal barrier, which is usually due to excess production of pro-inflammatory cytokines, such as TNF-α, IL-1 β, IL-6, and interferon-gamma (IFN-γ), all of which are triggered by the activation of nuclear factor kappa beta (NF-κB) (*15*). This ultimately results in unchecked intestinal inflammation and can lead to changes in the intestinal microbiome (*15*). If left

untreated, this inflammation can become chronic, result in systemic inflammation and even serve as a nidus for cancer (*15*).

The anti-inflammatory effects of curcumin have been viewed as a potential adjuvant treatment for those suffering from IBD since it has been shown to reduce the proposed inflammatory response implicated in IBD, help restore the integrity of the intestinal barrier and resist the degradation of intestinal epithelial tight junctions (*15*). Normally, the nitric oxide (NO) that is present at the physiological baseline serves to protect the gastrointestinal mucosa. However, the substantial amounts of NO that is released via inducible nitric oxide synthase (iNOS) during gastrointestinal inflammatory disease can result in tissue injury and subsequent necrosis (*15*). During inflammation, iNOS produces NO in pathogenic quantities. Therefore, it is likely that the chronic inflammation found in gastrointestinal inflammatory disease states may lead to the dissolution of the intestinal wall integrity due to the generation of reactive nitrogen species (RNS). Normally, curcumin reduces levels of reactive oxygen species (ROS), such as NO, in the intestinal mucosa (*6*). In a mouse model of ulcerative colitis, curcumin was able to inhibit the generation of iNOS by reducing the T-helper-1 (Th1) cytokine response, which ultimately led to reduced tissue damage (*6*).

Curcumin has been shown to exert a multitude of effects on the human microbiome and intestinal system. One study demonstrated that curcumin possessed bactericidal effects by eradicating *H. pylori* colonization *in vivo* through a proposed mechanism of inhibited bacterial cell division (*15*). In addition to these bactericidal effects, curcumin has been shown to promote and maintain a healthy gastrointestinal microbiome. One possible mechanism is curcumin's ability to promote the growth of short-chain fatty acid (SCFA)-producing bacteria. In a murine study conducted by Feng et al., curcumin supplementation promoted the diversity of SCFA-producing bacteria which have well-described protective effects on gastrointestinal mucosa by inhibiting inflammation *(15*, *16, 17*).

DISCUSSION

Before definite conclusions can be made, future studies must further evaluate the effects of curcumin on the human gastrointestinal microbiota, as most existing studies focus on its effects in animal models. One explanation for the lack of studies exploring this concept is the poor bioavailability of pure curcumin. For patients to be able to reap the anti-inflammatory rewards of turmeric, high doses (500 mg) of the active ingredient, curcumin, must be administered or it must be administered with compounds that help prevent its metabolism and increase its concentration in the body (*5*). As previously mentioned, curcumin is often combined with various organic compounds to drastically increase its bioavailability (*5*). Recent studies have shown that lapidated curcumin mixtures increase its availability, as do mixtures with piperidine, the active component of black pepper (*5*).

Endogenously, curcumin is rapidly metabolized by the *Blautia spp*, a bacterium native to the human microbiome (*5*). One could also glean that those future research directions focusing on downregulating the colonization of *Blautia spp* could also serve to inhibit the metabolism of curcumin, thus increasing its concentration in the body. However, further altering the microbiota possesses its own challenges and could allow for further dysregulation of the immune response in those suffering from inflammatory diseases like RA and IBD. Another route that could potentially increase curcumin's bioavailability is altering its structure or combining it with lipidated or piperidine compounds, as previous groups have done (*4,5*). Investigating ways in which oral turmeric supplements can be chemically modified to increase the bioavailability of curcumin is an active area of research. Therefore, the low natural bioavailability should not dissuade its use, as there will likely be ways in which this can be improved in the near future.

In general, natural and alternative medicine continues to be less explored than modern medicine, despite some evidence working in its favor (*4,5*). Turmeric, a natural supplement that has been used for thousands of years, works to decrease systemic inflammation and better disease trajectory. As discussed in this review, both RA and IBD could benefit from adjuvant turmeric supplementation. While the supplements may not often stand on their own as a sole treatment, the simple addition of one to a complex drug regimen can potentially improve disease trajectory. Furthermore, after validation through more clinical trials, this affordable addition could improve the disease trajectory of patients struggling with these inflammatory diseases (*18*). Due to a lack of human research trials on these supplements, they are often overlooked by healthcare providers, but there may certainly be a role for them in certain clinical situations. Since each person's immune system is unique, responses to turmeric supplementation may vary widely on a patient-to-patient basis. As such, physicians treating individuals with chronic inflammatory conditions such as RA or IBD might consider adding turmeric to their treatment plan.

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CONFLICTS OF INTEREST

All authors declare no conflicts of interest.

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Chemical and Histopathologic Effects of COVID-19 on Virchow's Triad

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ABSTRACT

Although COVID-19 is known primarily as a respiratory disease, infected patients have been known to experience COVID-19-associated coagulopathy from overactivation of immune response resulting in cytokine storm. As a fundamental principle of venous thromboembolism, Virchow's triad – consisting of stasis, hypercoagulability, and endothelial injury – remains the foundation for increased clotting risk which can often precipitate life-threatening complications, such as pulmonary embolism, if left untreated. We conducted a literature search using PubMed for evidence to explain the increased coagulopathy in COVID-19 positive patients in relation to the three pillars of Virchow's triad. Hypercoagulability in COVID-19 patients is increased due to cytokine-induced fibrin clot formation. Infected patients also have decreased ADAMTS13, which leads to endothelial injury. Lastly, the increased blood viscosity combined with patient immobility promotes vascular stasis. These factors put COVID-19 patients at an increased risk of acquiring blood clots. In conclusion, we have defined a plausible mechanism by which COVID-19 may induce venous thrombosis using the three components of Virchow's triad. Due to the fatal nature of vascular complications, it is important to consider prophylactically treating these patients with a low molecular weight heparin regimen in order to mitigate the effects of hypercoagulability.

Keywords: COVID-19, Virchow's triad, venous thromboembolism, hypercoagulability, endothelial injury, venous stasis, anticoagulation

INTRODUCTION

On March 11, 2020, the World Health Organization (WHO) declared novel coronavirus disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), herein labeled COVID-19, to be a global pandemic (*1*). Although bats are the primary vector for SARS-CoV-2, this is an RNA virus that is easily transmitted via respiratory droplets between humans (*2*). Although the clinical course of COVID-19 is most commonly associated with fever, viral pneumonia, and acute respiratory distress syndrome (ARDS), this disease has an additional relevance to the field of vascular surgery due to its adverse effects on coagulation (*3*). The prothrombotic state acquired due to COVID-19 demonstrates that its effects extend beyond the realm of pulmonology and must be understood by specialists in cardiovascular and hematologic fields, as well.

Around the world, multiple medical centers have noted that arterial and venous clotting may complicate the disease course of COVID-19. Helms, et al. noted that in a French hospital, 28 out of 29 dialysis patients with COVID-19 experienced thrombosis, which obstructed dialysis filter function thus compromising renal replacement therapy in critically ill patients (*4*). In the United States, a study of over 3,000 hospitalized COVID-19 patients revealed a rate of thrombotic complications over 10% for non-ICU patients and almost 30% for ICU patients (*5*). Since the venous thrombosis rate in COVID-19 patients is higher than that in uninfected individuals (21% vs. 0.5%), it is crucial to investigate the underlying

mechanisms of pathologic thrombosis due to COVID-19 (*6,7*). A deeper understanding of the vascular pathophysiology could potentially guide clinical solutions for affected patients.

Virchow's triad is a well-recognized axiom in venous thromboembolism (VTE). Rudolf Virchow was a 19th century German physician who defined clotting as the combination of three factors: hypercoagulability, endothelial injury, and stasis. Kushner et al. define hypercoagulability as a condition in which blood is at a greater propensity to clot often due to oral contraceptive use, chemotherapy drugs, or thrombophilia. Any insult to the wall of the blood vessel can produce an endothelial injury, promoting activation of the clotting cascade for vessel repair and disruption of laminar blood flow, which can initiate thrombosis. Lastly, stasis is a reduction of flow, which permits blood to pool and clot (*8*). As earlier studies have demonstrated increased thrombosis in COVID-19 patients, we sought to explain these findings as they relate to Virchow's triad. Hypercoagulability and endothelial injury are directly affected by the coronavirus due to its usage of spike (S) protein to infiltrate (*9*). We reason that stasis is a contributing factor to thrombosis in COVID-19 patients likely due to prolonged bed rest and immobility. In this paper, we will explore the pathology of COVID-19 at the cellular and biochemical level, with a focus on Virchow's triad and shed light on possible treatments for patients.

METHODS

A literature search was performed to investigate the effects of COVID-19 on Virchow's triad. Using PubMed, we conducted individual searches on the components of Virchow's Triad. The inclusion criteria used were as follows: 1) published within the last year to ensure relevance, 2) written in English, and 3) full-text must be available. The primary exclusion criterion was case report articles, as these were not considered to be adequate evidence for evaluating widespread effects on Virchow's Triad. The search terms "COVID-19" and "hypercoagulation" resulted in 411 articles. These were then screened by two of the investigators (JN, AM) based on their pertinence to elucidating biochemical mechanisms and/or histopathology. Articles without this focus were removed from our search. This yielded 9 studies describing the mechanism of action for hypercoagulability in COVID-19. We repeated this process with the other two components of Virchow's triad, yielding 132 articles involving "endothelial injury" and 5 articles each involving "cytokine injury" and "stasis". However, we chose to expand this search to "COVID-19" and "stasis" in order to yield greater results. We had a total of 16 results after expanding the search and included 7 of these stasis-related studies after applying the screening criteria. Altogether, we compiled a total of 21 articles regarding the components of Virchow's Triad.

RESULTS

Hypercoagulability

SARS-CoV-2 belongs to a family of coronaviruses that infect human host cells. However, these family members differ in virulence and have unique thrombotic activity. Based on initial investigations, Gabutti et al. postulate that the S protein for SARS-CoV-2 has a higher affinity for human angiotensin converting enzyme 2 transmembrane receptor (ACE-2R) than the previous SARS-CoV reported in 2002 (*10*). Although the specific differences between SARS-CoV-2 and SARS-CoV S proteins are still under investigation, it is known that the higher ACE-2R affinity for the current virus has allowed for lower viral loads to produce symptoms in the host (*10*). Despite the differences between the two strains, SARS-CoV-2 spike protein shares approximately 75 percent amino acid sequence homology with the SARS-CoV spike protein (*11*).

Similar to its predecessor, SARS-CoV-2 uses a transmembrane protease, serine 2 (TMPRSS2) enzyme as a primer for the surface unit of its S protein, which binds to the ACE-2R and achieves viral entry into host respiratory epithelium (*12*). Since SARS-CoV-2 shares a high degree of amino acid sequence homology with SARS-CoV, it is logical that there are similarities in biological pathogenesis (*13*). SARS-CoV-2 causes tissue damage and vascular leakage due to cytotoxic T cell and neutrophil activation, coupled with upregulation of pro-inflammatory cytokines interleukin 6 (IL-6), tumor necrosis factor alpha (TNFα), interleukin 1 beta (IL-1β), and C-C motif chemokine ligand 2 (CCL2) (*12*). Furthermore, COVID-19 increases activation of pro-fibrotic genes transforming growth factor beta 1 (TGFβ1), connective tissue growth factor (CTGF), and platelet derived growth factor subunit A (PDGFA). The combination of pro-inflammatory cytokines and pro-fibrotic genes leads to the coagulation cascade cleavage of prothrombin to thrombin and subsequent transformation of fibrinogen to fibrin (*12*). The cytokine-induced cascade of fibrin clot formation generates the abnormal hypercoagulation associated with COVID-19, which is similar to chronic (compensated) disseminated intravascular coagulation (DIC), with rapid consumption of endogenous coagulation factors promoting blood clots (*14*). It is important to note that COVID-19-associated coagulopathy (CAC) is a preliminary stage, which could further progress to DIC (15). The primary notable difference between CAC and sepsis-induced DIC is that initially, fibrinogen remains elevated in CAC as an acute phase response. Eventually, as CAC progresses,

fibrinogen decreases to low levels in DIC (*15*). The underlying mechanism of this difference is not yet well understood. Additionally, platelet aggregation and abnormal thrombus formation rapidly causes tissue hypoxia (*16*). Vascular events predominantly reported in COVID-19 patients with severe infection include VTE and pulmonary embolism (PE). Patients have developed rare complications such as venous gangrene of the extremities, which can lead to critical limb ischemia, but the more common and potentially worrisome event of VTE is a PE presenting with dyspnea, syncope and/or palpitations (*17*). Rapid deterioration has been noted and if left untreated, is fatal (*18*).

Endothelial Injury

Weibel-Palade bodies (WPB) stored in endothelial cells contain P-selectin and ultra-large Von Willebrand Factor (ULVWF) (*19*). Based on current knowledge of the mechanisms of COVID-19-induced cytokine storms, IL-8 and TNFα have particular importance due to their impact on endothelial cells. Specifically, their activation causes the release of P-selectin and ULVWF from WPBs, thereby accelerating clotting and contributing to the development of VTE (*20*). P-selectin plays a vital role in the leukocyte adhesion cascade by binding to P-selectin Glycoprotein Ligand-1 (PSGL-1) on neutrophils (*21*). With regards to coagulation, ULVWF is known to initiate clotting by promoting the glycoprotein Ib receptor to bind to glycoprotein IIa receptors on platelets (*22*). This step of clotting is known as platelet aggregation, in which platelets can connect to one another.

Homeostatic autoregulation of the clotting process is facilitated by the ADAMTS13 enzyme, which works by cleaving endothelial-bound ULVWF into smaller components such that thrombi do not form (*22*). Deficiencies in ADAMTS13 can present as thrombotic thrombocytopenic purpura, which produce microthrombi dispersed throughout the body (*22*). In COVID-19 infection, IL-6 generation downregulates ADAMTS13, thus increasing the propensity for ULVWF to aggregate and create thrombi (*22*). Similar to IL-6, activated neutrophils have adverse effects on ADAMTS13 activity. Activated neutrophils and neutrophil extracellular traps (NETs) produce reactive oxygen species (ROS) in the process of fighting viral infections such as COVID-19. Increases in ROS levels prevent ADAMTS13 from cleaving ULVWF along the endothelium (*23*). The subsequent cytokine storm propagates endothelial dysfunction and hypercoagulation, two of the three components of Virchow's triad, and serves as a plausible framework to understanding the presentation of VTEs in COVID-19 patients.

Stasis

The third element of Virchow's triad is venous stasis. Although current literature does not have a quantitative measure of the degree to which venous stasis is associated with COVID-19 infection, behavioral and physical explanations for a potential association exist. Fatigue is a common clinical presentation of COVID-19, and it is hypothesized that this symptom occurs due to an IL-6 cytokine surge, which is known to influence skeletal muscle fatigability in mice (*24*). In addition, most patients experience respiratory difficulties, such as dyspnea, pleurodynia, cough, and expectoration (*25*). The constellation of symptoms (common to most viral-induced respiratory infections) likely occur due to the viral destruction of lung parenchyma and interstitial inflammation (*25*). COVID-19 is known to cause mast cell degranulation (*26*). As a result, histamines are released, increasing vascular permeability of pulmonary endothelial cells. The subsequent leakage of transudative fluid in the pulmonary interstitium is associated with dyspnea from increased work of breathing and discomfort (*26*). Pulmonary edema reduces the lung's ability to oxygenate blood, resulting in an increased arterial-alveolar gradient. Combining this increased respiratory effort with IL-6-induced systemic fatigue, COVID-19-infected persons are less likely to be mobile. With immobility, venous blood begins to pool due to reduced velocity and decreased muscle activity, which can promote higher risks of venous thromboembolism (*27*). It has been shown in the past that those who are in a stationary position for a prolonged time are at a higher risk of developing blood clots (28). One study by Murugesan et al. mentions that post-operative deep venous thrombosis (DVT) in Caucasian populations occurs in 15-40% of hospitalized patients (*28*). While the exact cause of this is unknown, it can be hypothesized that post-surgical bed rest is a contributing factor, since immobility is a common cause of thrombosis in obese populations and video game users (*29*).

Stasis is also impacted by hyperviscosity, which is strongly associated with COVID-19. A study from Emory University involving a cohort of 15 COVID-19 patients identified blood viscosities exceeding 95% of the normal limit (*30*). One potential explanation for this phenomenon is the correlation between severity of COVID-19 disease course and increased plasma fibrinogen levels, fibrinogen-to-albumin ratio (FAR), and D-dimer levels. Specifically, one cohort study found that patients with severe disease were in a hypercoagulable state with shortened prothrombin time (PT) and activated partial thromboplastin time (aPTT), which stabilized as patients' condition improved (31). As a result, there may be a critical threshold of FAR that can serve as a predictor of the severity of disease (*31*).

Treatments

As of January 2021, the American Society of Hematology and American College of Chest Physicians have provided guidelines stating that all adult patients admitted to the hospital for COVID-19 infection should be placed on prophylactic low molecular weight heparin (LMWH) over unfractionated heparin (UFH) and direct oral anticoagulant, unless contraindicated (*32*,*33*). Studies in China have shown clinical benefits of this therapy. In a cohort of 449 COVID-19 patients in Tongji hospital, 99 patients were placed on a LMWH regimen. In patients who had a D-dimer score greater than six times the normal limit, a LMWH regimen for at least 7 days improved the 28-day mortality risk (*34*).

In a cohort study with over 2,500 patients at the Mount Sinai Health System, the benefits of systemic treatment-dose anticoagulation for hospitalized patients were evident. The in-hospital mortality rate for patients on mechanical ventilation was 62.7% for patients who did not receive anticoagulation when compared to 29.1% for patients that did (*35*). However, the potential benefits of anticoagulation need to be weighed against the potential risk of major bleeding on an individual patient basis prior to initiating systemic treatment-dose anticoagulation. For those who experience heparin-induced thrombocytopenia, it is beneficial to use non-heparin anticoagulants such as bivalirudin or argatroban as prophylactic treatment over fondaparinux or rivaroxaban (*36*). In more critically ill COVID-19 patients, the use of intermittent pneumatic compression (IPC) is recommended for prevention of VTE with the use of UFH in cases of severe renal impairment (*36*).

CONCLUSION

For each component of Virchow's triad, we have provided a plausible mechanism by which COVID-19 may induce venous and, rarely, arterial thrombosis. Similar to its predecessor, SARS-CoV, the infection caused by SARS-CoV-2 virus is thought to recruit pro-inflammatory cytokines and cause excess stimulation of the coagulation cascade resulting in hypercoagulability. As a result of the cytokine storm response to COVID-19 infection, the production of IL-6 and ROS downregulated ADAMTS13 enzyme allowing ULVWF to contribute to endothelial injury and *in situ* thrombosis. Finally, COVID-19 infection may promote venous stasis, the final component of Virchow's triad, as infected patients experience fatigue and immobilization during hospitalization, which further increases the risk of adverse thrombotic events due to reduced blood flow. Anticoagulation drugs should be considered a front-line therapy for patients requiring hospitalization and empiric therapeutic dosing for those needing ICU admission. In conclusion, COVID-19 patients are at a greater risk of blood clotting due to the mechanisms defined by Virchow's Triad.

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Efficacy of the Glasgow Coma Scale in Determining the Severity of Traumatic Brain Injury

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ABSTRACT

Mr. D, a 52-year-old male, was in an un-helmeted motorcycle collision with a concrete barrier resulting in polytrauma and traumatic brain injury. Mr. D was assessed by emergency services to be unresponsive with a Glasgow Coma Scale (GCS) of 13. He sustained an open skull injury, subdural hematoma, multiple facial fractures, and traumatic vitreous humor hemorrhage with unresponsive, dilated pupils. He received CT and X-ray imaging before undergoing multiple surgeries for repair and debridement of injuries. After being weaned off sedation, he entered a state of post-traumatic amnesia lasting two months. Fifteen days post-accident, he began a regimen of amantadine to stimulate interaction and participation in physical therapy. Mr. D remained for two months until he progressed with physical therapy and was independent with his mobility. He was admitted to an inpatient traumatic brain injury facility because he was mentally unable to care for himself.

Keywords: Traumatic Brain Injury, Glasgow Coma Scale, Physical Medicine & Rehabilitation

INTRODUCTION

Traumatic brain injury (TBI) is abnormal brain functioning resulting from an external injury (*1*). TBIs are characterized by three periods – impaired consciousness, post-traumatic amnesia (PTA), and functional recovery (*2*). PTA is defined as a period of time when a person is unable to retain new information following a TBI (*2*). It is an important indicator of long-term outcomes post-TBI (*2*). The duration of PTA is closely tied with functional outcomes with long durations of PTA correlating with decreased functionality (*2*). The initial severity of TBI is evaluated with the Glasgow Coma Scale (GCS) whereas PTA can be assessed with the Galveston Orientation and Amnesia Test (GOAT) and the Orientation Log (O-Log).

The GCS is composed of three parts – eye opening (scored 1 to 4), verbal response (scored 1 to 5), and motor response (scored 1 to 6). Lower scores on each part indicate decreased functioning and, therefore, a more severe injury. The sum of the three scores is used to further classify TBIs as severe (GCS 3-8), moderate (GCS 9-13), or mild (GCS 14-15). This is meant to be an objective measure to gauge clinical status and outcome at the time of injury as well as progression over time. Serial GCS can be used to follow patients and assess their improvement or deterioration following a TBI (*3*).

The GOAT is a 10-item questionnaire measuring the patient's orientation to time, place, and person in addition to assessing PTA and retrograde amnesia. PTA differs from retrograde amnesia in that PTA describes an inability to form new memories for a period of time following the TBI, while retrograde amnesia is the loss of memories just prior to the accident. The GOAT is scored out of 100 with scores of less than 75 indicating ongoing PTA. Emergence from PTA is indicated by two consecutive scores of greater than 75 on the GOAT (*2*).

The O-Log is also a 10-item questionnaire that measures orientation more specifically than the GOAT; the O-Log assesses orientation to city, kind of place, name of

hospital, month, date, year, day of week, clock time, traumatic event/accident, and injury/deficits resulting from the accident. Each of these measures are scored out of three for a total of 30 points. The goal of the O-Log is to follow orientation improvements over time (*4*). This case report seeks to highlight the limitations of GCS in predicting the duration of PTA and prognosis post-TBI and to consider how the initial GCS can be improved to better evaluate patients at the scene of trauma.

CASE DESCRIPTION

Mr. D, a 52-year-old male, was an un-helmeted motorcycle driver who presented to the Emergency Department following a high-speed collision with a concrete barrier. His initial GCS was 13, and he tested positive for alcohol, amphetamines, cocaine, and opiates. He had sustained a frontal open-skull injury, bilateral frontal subdural hematomas with small contusions, minor brain contusion, multiple facial fractures, proximal ulnar and humeral medial epicondylar fractures of the left elbow, and traumatic vitreous humor hemorrhage with dilated pupils unresponsive to light. He underwent several surgeries to clean wounds, beginning a lengthy treatment process. Surgeries included tracheostomy, facial fracture repair, maxillomandibular fixation to wire his jaw shut, washout of the left elbow fracture with external fixation, irrigation and debridement of left elbow open fracture, and partial extensor tendon repair to left middle finger.

An initial assessment by the Physical Medicine & Rehabilitation (PM&R) physician predicted a mild TBI with short-lived, if any, agitation. This proved to be an inaccurate prediction. The patient remained sedated for three days after his accident. After being weaned off sedation, he continued to be somnolent and difficult to arouse. During his hospital stay, the patient required non-violent restraints at several points. He was in a state of PTA and had difficulty paying attention and following commands. After being in the hospital for 15 days, the patient was given 100-mg Amantadine twice a day to help stimulate interaction and his participation in therapies. He remained in a PTA state for approximately two months. He was not qualified for admission into inpatient rehabilitation because adequate supervision after discharge is required at the time of admission, so he remained in the acute care surgery unit for the entirety of his hospital stay. He progressed with therapies during his hospitalization to the point where he became independent with his mobility and no longer had any physical therapy goals necessitating an inpatient rehabilitation admission. The PM&R physician recommended that Mr. D be transferred to an inpatient TBI facility for further care.

DISCUSSION

Mr. D is a 52-year-old male who sustained a TBI and polytrauma after an un-helmeted high-speed motorcycle collision with a concrete barrier. His TBI was initially judged to likely be mild at the time of presentation, though his GCS of 13 indicated a moderate TBI. His hospital course was prolonged with PTA and agitation lasting two months, an indication of severe TBI and a poor prognosis of decreased functional recovery.

There are several factors of TBI that make assessment of injury and treatment difficult. Patients are often assessed with the GCS soon after traumatic injuries, which also gives a rough estimate of the severity of TBI (*3*). The patient's initial GCS was scored at 13, indicating a moderate TBI. His recovery in the hospital was prolonged, and his orientation was assessed every few days with the O-Log and GOAT to determine the duration and severity of PTA. He remained in PTA for just over two months, suggesting that the TBI he incurred was severe. This can be assumed because patients with severe TBI often have PTA, the length of which can be used as a prognostic indicator of long-term outcomes post-TBI (*2*). The length of time the patient remained in PTA, just over two months, suggests that he will have less functional outcomes and goals and is unlikely to ever be able to return to work or recover fully from this accident.

The disconnect between the patient's GCS and resulting estimated prognosis was found to be highly inaccurate compared to the reality of his prolonged hospital stay and duration of PTA. The GCS is commonly used to assess TBI in emergent situations because it is easily administered. However, the inconsistency of the initial GCS and the patient's outcomes in this case has raised concerns about whether GCS is the best scale for initial assessment of TBI. A highly inaccurate prognosis given too early to patient families can cause distress when patients do not recover as quickly or as completely as estimated. The GCS will need modification to improve its accuracy in determining TBI severity. GCS needs to give a more accurate representation of severity of TBI and better estimation of functional recovery. O-Log and GOAT both include measures of orientation whereas GCS only assesses body functions – do the eyes open? are they responsive to light? – which fail to account for mental functioning and orientation. In the initial patient assessment with GCS, it would be helpful to include parts of the GOAT or O-Log to create a more accurate modified GCS and allow for a better assessment of patients following trauma.

CONCLUSIONS

The length and severity of PTA is a good indicator of long-term functional outcomes following a TBI. The GCS is quick and easily administered, though it is not always adequate in determining the severity of a TBI and is not always accurate in estimating prognosis. In the future, research should evaluate whether the GOAT or the O-Log are better measures for determining severity and length of PTA and which allows for better monitoring over time. More precise protocols are needed for the treatment of patients with severe TBI, and future controlled studies should work to improve the efficacy of the assessments as well as the treatments used.

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Robotic Assisted Laparoscopic Prostatectomy Post-Prostatic Urethral Lift Implants

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ABSTRACT

Prostate cancer is the second most commonly diagnosed form of cancer in men. While there are several treatment options for prostate cancer, robotic assisted laparoscopic prostatectomy is a customary option in the treatment of clinically localized disease. It entails prostate removal using the Intuitive da Vinci surgical system. Another very prominent urologic condition affecting older males is benign prostatic hyperplasia (BPH); BPH has an increased lifetime prevalence reaching 80% of men by the 9th decade of life. It is characterized by lower urinary tract symptoms due to prostatic enlargement. These conditions often develop concomitantly in males given the high prevalence of each. Surgical advancements such as the prostatic urethral lift (PUL) system are becoming more commonly utilized. However, patients with benign prostatic hyperplasia who independently develop clinically significant prostate cancer may necessitate definitive management, namely prostatectomy. In this case report, we discuss a 67-year-old male presenting with Gleason group 2 (3+4=7) prostate cancer with previous PUL implants, who then underwent robotic assisted laparoscopic radical prostatectomy. Prostatectomy following prior PUL implantation has never been fully discussed in the literature, and there are no intraoperative or postoperative complications from prostatectomy to report thus far.

Keywords: Prostatectomy, Prostate Cancer, Benign Prostatic Hyperplasia, Prostatic Urethral Lift

INTRODUCTION

Prostate cancer is one of the most pervasive oncologic and urologic conditions that males endure. It is the second most commonly diagnosed cancer in males, second only to lung cancer (*1*). Depending on patient presentation and prostate cancer grading, options such as prostatectomy or radiation therapy may be pursued. There are many factors for clinicians to consider in the course of prostate cancer workup, and grading methods such as the Gleason grade and score remain the gold standard. Gleason grading is comprised of two Gleason scores. The Gleason system is a scoring system from 1-5, where 1 most histologically represents normal prostate cells and 5 is most resemblant of high-grade cancerous cells *(2)*. The first number is the most predominant type of cell from the biopsy, and the second number is the second most predominant. Grade 1 is a scoring of 3+3=6, Grade 2 is 3+4=7, Grade 3 is 4+3=7, Grade 4 is 4+4=8, and Grade 5 is any score equating to 9 or 10 total. Gleason scoring, prostate-specific antigen, patient history, and physical exam are all essential for the diagnosis and treatment plan of prostate cancer.

BPH is another frequently diagnosed urologic condition. As the name suggests, BPH is a proliferation of smooth muscle and epithelial cells within the prostatic transition zone typically due to increased levels of androgens *(3)*. Due to this enlargement, outflow from the bladder to the proximal urethra can be greatly diminished. Men may experience more lower urinary tract symptoms (LUTS) as the prostate tissue grows. LUTS constitutes symptoms of urinary urgency, frequency, straining, nocturia, and intermittency of urinary stream (*4*). The prostatic urethral lift system is a novel therapy intended for the treatment of BPH.

The PUL system was first studied in 2011 and since then has obtained FDA approval in the United States and the United Kingdom as a minimally invasive therapy for BPH (*5*). The PUL procedure is unique in comparison to other endoscopic treatments for BPH in that the technology is mechanical rather than cavitating or ablative, such as transurethral resection of the prostate (TURP) (*6,7*). TURP has historically been the "gold standard" surgical procedure for relief of BPH. As mentioned, TURP is an ablative procedure that entails highly charged electroresection to remove prostate tissue (*8*). With PUL, non-absorbable implants are placed transurethrally to lift and hold enlarged prostate tissue in order to increase the urethra's lumen and decrease outflow obstruction (Fig. 1). This system has become increasingly more popular as an alternative to TURP and other surgical BPH treatment options, given the lower incidence of side effects coupled with favorable sexual, urinary, and functional outcomes *(9)*. Now, if patients have a large median prostatic lobe or if total prostate volume is greater than 80 grams, patients are not candidates for PUL. Regardless, PUL has become increasingly more utilized.

The TURP procedure, and now PUL, aim to relieve LUTS secondary to BPH. However, patients undergoing these procedures may still develop prostate cancer concomitantly that is unrelated to their BPH. Typical management options for prostate cancer, such as active surveillance, prostatectomy and radiation therapy, are logical to consider for these patients. Specifically, robotic assisted laparoscopic prostatectomy has become increasingly employed compared to open prostatectomy. Robotic prostatectomy offers many benefits such as improved surgical view, reduced blood loss, and lower incidence of urinary incontinence and erectile dysfunction when compared to open technique (*10*). While the L.I.F.T study briefly mentions two instances of prostatectomy after PUL at 2 and 5 year follow-ups, this is not discussed in depth (*11,12*). There are currently no case reports in the literature detailing the full course of prostatectomy after the placement of PUL devices.

CASE REPORT

This case report details a 67-year-old otherwise healthy male who was in active surveillance for low risk prostate cancer. He was diagnosed with low volume Gleason grade 3 prostate cancer in 2013, and elected to be managed with active surveillance. Surveillance magnetic resonance imaging (MRI) of the prostate seven years later revealed a 47-gram prostate with a new nodular mass measuring 11mm.

Additionally, four PUL implants were placed for BPH relief at an outside institution in 2019, aligning with standard recommendations of 4-6 implants. The patient continued to experience LUTS such as hesitancy, nocturia, and weak urinary stream. Three supplementary PUL implants were placed in 2020 in response to his persistent symptomology.

Given the concerning MRI findings, the patient was re-biopsied for evaluation of prostate cancer approximately three months after the additional implants. The repeat biopsy revealed Gleason grade 2 (3+4=7) prostate cancer. Furthermore, Decipher testing, which is a genomic test to help further stratify biopsied prostate cancer and guide treatment management, indicated the cancer was clinically significant high-risk disease (*13*). The results of this test further ascertained the need for definitive prostate cancer treatment.

We discussed with the patient how our literature search showed minimal information regarding prostatectomy following PUL implants. The patient was scheduled for robotic assisted laparoscopic radical prostatectomy at the end of 2020. Emphasis was made to identify the PUL implants when dissecting the prostate. In total, seven PUL implants were identified. There was little difficulty identifying the urethral end piece and the capsular tab of each prostatic urethral lift device. The urethral end piece is considered the inner portion of the device while the capsular tab is the outer metallic clip. Care was taken to minimize cautery usage around the clip as this resulted in arcing. There were no abnormal fibrotic tissue changes surrounding the implants; dissection and extraction of the implants were not problematic. The capsular tabs were disconnected from the suture and were individually removed. The urethral end pieces and sutures from the seven PUL implants were left with the prostate specimen. The remainder of the operation and dissection was uneventful for robotic prostatectomy. Vesicourethral anastomosis was achieved without any unexpected difficulties. There was no other evidence of inflammation or adherence surrounding the prostate in the surgical field of view. There was no additional challenge encountered to nerve-sparing technique.

DISCUSSION

Findings recorded in this case report are significant because there was an absence of difficulties, and radical prostatectomy performed as usual despite the prior placement of PUL implants. It was theorized that there may be increased adhesions surrounding the prostate given the presence of foreign bodies, making dissection more difficult. Moreover, we were unsure how the implants would affect our ability to use electrocautery for extraction. This patient also had three additional implants due to continual LUTS.

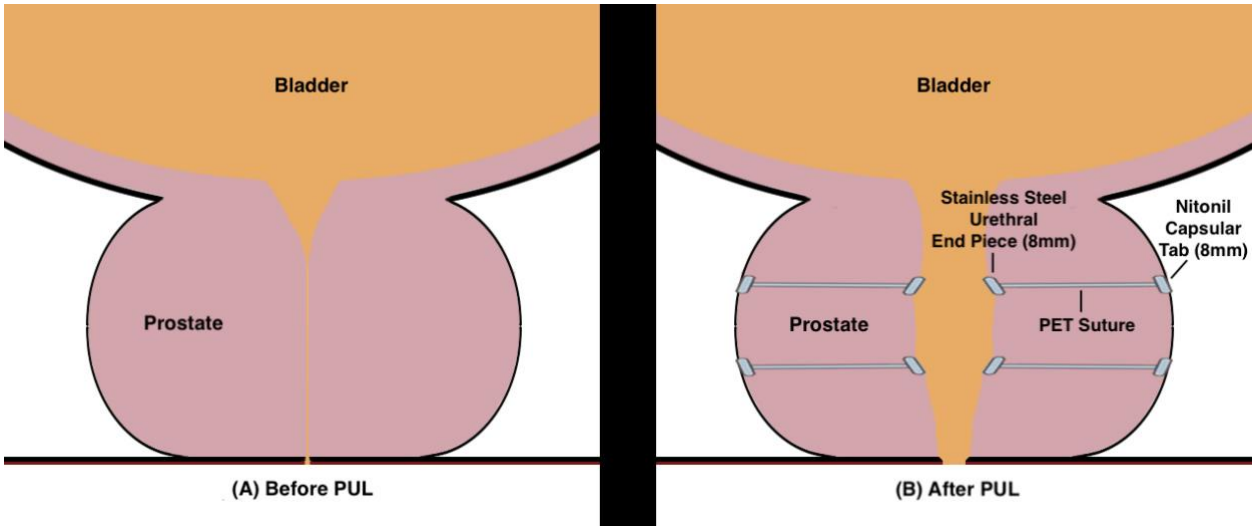

Figure 1. Benign prostatic hyperplasia before prostatic urethral lift implantation (a) and following four prostatic urethral lift implants (b). (A) Diagram showing an enlarged prostate that significantly obstructs urinary tract outflow from the bladder through the urethra. (B) Placement of four prostatic urethral lift implants to unobstruct urinary flow.

Usually patients do not require additional PUL implants, so this did add some consideration in regard to more adhesions. However, the number of implants did not greatly impact the decision to pursue prostatectomy as this was necessary to treat the patient's prostate cancer. Ultimately, the patient tolerated the procedure well and has been seen in the postoperative period. He is currently without clinical evidence of prostate cancer recurrence. The patient has had minimal LUTS and incontinence post-surgery. He has not reported significant worsening of sexual function following prostatectomy.

The absence of unexpected events is encouraging as the prostatectomy was performed safely and efficiently without compromising surgical technique. Prostate cancer and BPH are both highly prevalent urologic conditions. It is common for both pathologies to develop concomitantly. Therefore, as the PUL procedure becomes more widely adopted for BPH relief, it is reasonable for urologists to expect to encounter patients with PUL implants that have later developed prostate cancer.

It would be advantageous to see additional case reports of prostatectomy in patients with BPH who received PUL implants. Specifically, seeing how different Gleason grades affected the ability to extract the implants during prostatectomy, if at all, would be beneficial.

CONCLUSION

This is the first known case report of radical prostatectomy in a patient with PUL implants in place. Without other significant literature, it was uncertain what complications or challenges would be faced in the surgical setting. Prostatectomy was performed for this patient without deviation from standard operative technique. Furthermore, there are no intraoperative or postoperative complications to report following prostatectomy thus far. This case report will aid urologists in their decision-making when similar clinical scenarios arise. Our case shows that prostatectomy in the setting of prior PUL implantation is feasible and, in this case, added no additional challenge to robotic prostatectomy.

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Improving Community Health by Encouraging Remote Office Visits

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ABSTRACT

The COVID-19 pandemic has affected patient access to healthcare in the field of dermatology. Due to efforts to minimize in-person healthcare visits, wait times for dermatology visits have increased, negatively affecting patients' finances and furthering concerns about their skin conditions. This commentary highlights how the pandemic will potentially change the future of dermatology by promoting the use of telemedicine to reduce office wait times during the pandemic and beyond.

Keywords: Telemedicine, Teledermatology, COVID-19, Dermatology, Remote, Wait Times

INTRODUCTION

The COVID-19 pandemic has affected all aspects of the healthcare field, particularly in dermatology. Conditions presented in the field of dermatology may generally be considered non-emergent during a pandemic. Furthermore, patients with non-acute conditions such as alopecia and acne have had their visits and procedures postponed to maintain social distancing (*1*). The long wait times for appointments are problematic due to financial burdens for patients to self-maintain their skin conditions while waiting for appointments. There is also added fear and anxiety when waiting and concerns that skin conditions will worsen. The pandemic has proven that dermatology visits can proceed via telemedicine, and patients can have their skin conditions resolved with expedience through approved online platforms (*2*). The ability for telemedicine to present socially distanced skin findings in real time can be a way to resolve the long-wait times even after the pandemic (Fig. 1).

DISCUSSION

In dermatology, there is a continued need to screen, monitor, and treat skin conditions that may affect the future health of a patient. Skin cancers (melanoma and non-melanoma types) and other progressive skin diseases like atopic dermatitis, psoriasis, and impetigo can lead to morbidity and mortality if not detected in a timely fashion (*2*). Long wait times for in-person dermatology appointments were problematic even before COVID-19 and have further worsened for patients whose conditions are deemed 'non-emergent' amid office-visit restrictions brought upon by the pandemic (*1*). The extended wait times have led to quality-of-life issues and financial burdens such as paying for over-the-counter medications to maintain the conditions (*2*). However, the pandemic has shown that telemedicine is an effective resource to relieve the burdens experienced by patients and follow-up with them over time to see treatment progress (*2*).

Temporary policy changes in the United States have been implemented to allow physicians and patients to remain connected via telemedicine during the pandemic (*3*). These changes allow communication without violating HIPAA, provided that the encounters adhere to certain regulations. For example, dermatologists may communicate with patients over "non-public facing" applications such as FaceTime, Zoom, and iMessage (*4*). It is suggested for patients to establish telemedicine visits with in-state medical practices to allow for easier access to appointments after the pandemic (*5*).

Within the private media platforms that allow for telemedicine, there are several ways for the patient to present their skin condition to the dermatologist. One is through the exchange of pictures that target the lesion, and another is through video visits. This depends on the request of the dermatologist (*6*). Although dermatologists cannot physically examine skin lesions through a screen, being able to visualize the patient's general appearance and extent of disease is helpful in monitoring disease progression and guiding treatment.

Before the pandemic, there were barriers to telemedicine that prevented its widespread adoption. For example, physicians invested in costly HIPAA-compliant platforms to complete the telemedicine visits. Furthermore, the physician and patient were required to have previously established care before the telemedicine visit (*7*). The temporary cessation of regulations for telemedicine have shown that visits can still be effective for patient health and resolve the long wait-time issues for dermatology visits.

There are efforts to make long-lasting changes to regulations with telemedicine, which can change the future of dermatology visits and their long wait times (*8*). These efforts include expanding broadband networks, allowing insurers to provide reimbursement for remote visits, and increasing digital literacy (*8*). Insurance programs and healthcare providers have also supported the transition to telemedicine during the pandemic. They offer waivers, flexibility, and reimbursements state-by-state. It is imperative to view state guidelines for telehealth before beginning telemedicine visits. Also, it is important to be cognizant of patients' levels of comfort with technology. Low income and less educated populations may need resources to understand and utilize telemedicine. Hospitals can partner with public libraries and colleges to design educational programs and technology classes. These programs should be in multiple languages and offer 24/7 online help for those who may not know how to use these resources (*9*).

CONCLUSION

Although the COVID-19 pandemic has brought along many uncertainties, it has addressed a long-standing issue with dermatology visits: a solution to the long wait times that patients experience when getting their skin conditions checked. This pandemic has shown that telemedicine is a valuable resource that should be adopted throughout the rest of the pandemic and beyond. With the ability to conduct virtual physical exams, observe skin lesions through video, and send pictures of skin conditions through online modalities, these visits can be effective and address patient concerns. Future legislative action to allow a broader range of telemedicine services and provide appropriate physician compensation is currently being discussed to address these issues and allow for a more effective dermatological practice.

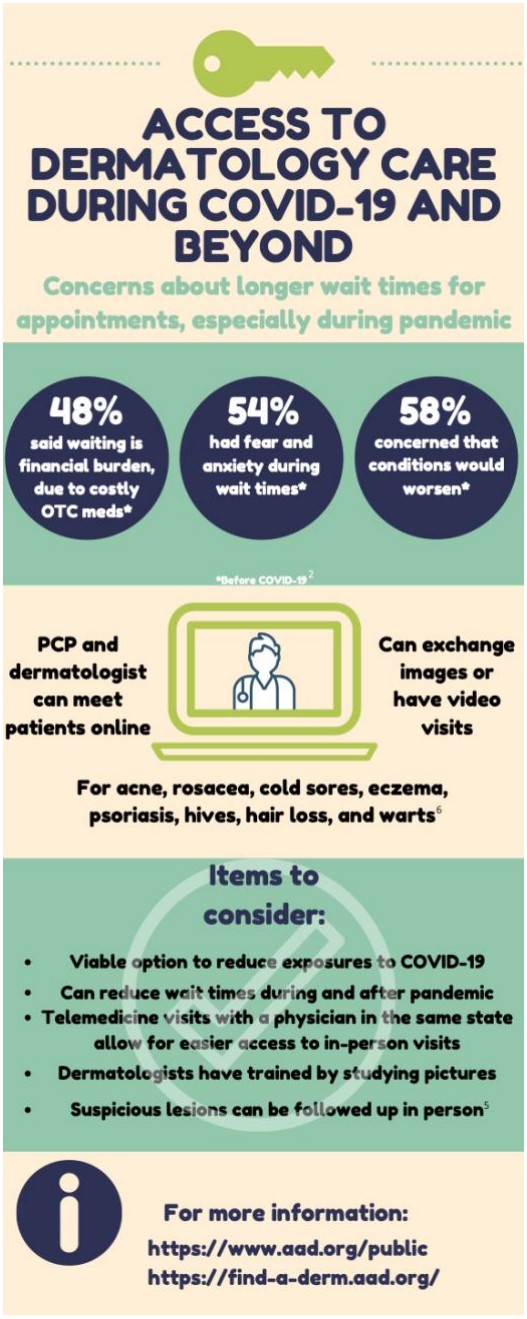

Figure 1. Access to dermatology care during COVID-19

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Investigation: RK

Methodology: EM

Project administration: RK, EM

Resources: RK

Validation: EM

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Enhancing Diversity in Medical Education Representation of Cutaneous Disease: VisualDx Skin-of-Color Atlas

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DISCUSSION

Cutaneous presentations of dermatologic and systemic disease may vary widely based on a patient's skin tone (*1*). Recent studies have demonstrated that medical education resources display a significant underrepresentation of pathology in individuals with skin of color (SoC). For example, only 24% of dermatologic images in common medical school board materials (Pathoma, Uworld, First Aid) represent pathology in SoC (*2*). Another study showed that medical students are more likely to misdiagnose conditions on images with SoC, including squamous cell carcinoma, urticaria, and atopic dermatitis (*3*). The differences in presentation based on skin tone can be seen in **Figures 1 and 2**: two potentially life-threatening infectious diseases with diagnosis necessary in a timely manner. Accurately diagnosing these conditions without proper exposure during medical training can pose a major challenge. With an expanding population of approximately 40% of United States citizens being of SoC, it is crucial that medical students receive proper training in identifying conditions on patients of all skin tones (*4*).

The COVID-19 pandemic has recently brought to light the gross underrepresentation of cutaneous pathology in SoC. In early 2020, dermatologists created an international registry to compile cases of dermatological manifestaions of COVID-19, to gather clues to the disease and aid diagnosis. Out of the 700 submissions to the registry, there were only 34 Hispanic patients and 13 black patients represented (*5*). Despite the pandemic starting in March, it took until July of 2020 for the first pictures of "Covid toes" in nonwhite patients to be published in the Journal of the American Academy of Dermatology. This prompted Adelekun et al. to launch an investigation on how severely underrepresented SoC truly is. According to their study published in April 2020, only 4.5% of images in general medicine textbooks illustrate dermatologic diseases in dark skin (*6*). It is clear that the underrepresentation of SoC in medicine is not a new issue, and physicians worldwide are starting to notice the injustice.

VisualDx is an award-winning diagnostic clinical decision support system that has taken steps to combat this healthcare inequality. It is an innovative tool that has nearly 29% of its leading medical image library representing presentations in SoC (*1*). This virtual platform has a leading SoC atlas with a user-friendly interface that allows for rapid diagnosis in real-time. By listing the chief complaint, location of the finding, symptoms/signs, or other notable findings, VisualDx can identify differential diagnoses and visual depictions that match the listings. The SoC atlas allows skin conditions to be identifiable across several races. The company has also launched Project IMPACT, a global effort to address implicit bias in medicine. Project IMPACT hosts monthly webinars that educate healthcare professionals and students on cultural awareness in medical practice, identifying diseases on SoC and new advancements for treating skin conditions.

At Northeast Ohio Medical University (NEOMED), we also seek to use innovation to foster diversity and fight racial disparities in medicine. With the help of a generous donation and support from the Dermatology Interest Group (DIG), NEOMED was able to purchase a one-year subscription to VisualDx for all students in the College of Medicine. We believe this software can be helpful to

students in all stages of medical training. Preclinical students can benefit by supplementing course material with VisualDx and applying it toward relevant clinical content. Meanwhile, students in their clinical years can use the tool on rotations in an effort to reduce diagnostic errors by augmenting a clinician's point of view. We plan to incorporate VisualDx into both preclinical and clinical lectures to highlight the variance of skin pathology presentation in SoC. We will aim to do this by incorporating images of dermatopathological conditions in SoC from VisualDx into the M1 and M2 NEOMED lectures covering infectious disease and dermatology topics. Currently, only several lectures explicitly highlight disease presentations on SoC. We hope that by bringing awareness to VisualDx as a resource of diversity and inclusion, lecturers will have an easy way to locate and incorporate images of SoC reflecting any cutaneous disease they discuss in their lectures. Additionally, many medical schools across the country have started incorporating diversity, equity, and inclusion (DEI) statements into their lectures and grand round presentations to foster a more inclusive learning environment. With the promotion of VisualDx, we hope all NEOEMD associated faculty will gradually begin to incorporate these DEIs into their curriculum and utilize the images from VisualDx to practice inclusivity in medicine. Ultimately, we hope to expand further VisualDx access to the College of Pharmacy and NEOMED postgraduate students to continue our goal of enhancing diversity and improving healthcare outcomes.

Our research into the present substantial issue of inequality in medicine has motivated us to make a difference in the NEOMED community. In a year with a global pandemic, our system has further shown its cracks with the COVID-19 morbidity and mortality rate disproportionately affecting black Americans (*7*). However, maybe this enormous flaw in the healthcare system is what it takes to start the conversation, to create a movement. This step in improving the gap in medical education is our small step, a step in the direction of positive change, a step in the direction of **equality** in healthcare.

Figure 1. Acute Meningococcemia in a patient with skin-of-color (SoC) (left) and in white skin (right). Note difference in the optics of color- presentation of red rash on a dark background (presents as dark brown) versus a white background. Image reproduced with permission from VisualDx *(8)*.

Figure 2. Rocky Mountain Spotted Fever on patient with SoC (left) and white skin (right). Once again, note subtle differences again with optics of color- presentation of a red rash on a dark background versus a white background. Image reproduced with permission from VisualDx *(9)*.

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Human Connection Through Wi-Fi: Is it possible?

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LETTER TO THE EDITOR

Due to the COVID-19 pandemic, all medical student assessments at Northeast Ohio Medical University (NEOMED) were redesigned to be performed virtually. This included my final standardized patient encounter. As nerve-wracking as it may feel to perform any aspect of the physical examination, it serves as a rite of passage for medical students transitioning into clinical rotations all around the country. My biggest concern was that my practice sessions and other standardized patient encounters had always occurred in person over the course of my first two years of medical school. Would I be able to successfully examine a patient virtually? Would I be able to connect with my patient to gather the sometimes personal, yet pertinent, details of medical history through a virtual platform? Knowing specific questions to review each organ system was not enough, and I knew I needed to identify more strategies to connect with patients.

Empathizing and connecting with my patient through a virtual platform proved to be much harder than I expected. I no longer had the privilege or security of directly facing my patients. Human connection and empathy were the original foundation of my history-taking and physical examination skills. Staring at my laptop screen, I practiced. I practiced using my eyes to gaze with compassion. I practiced keeping my lips sealed to motivate my patient to overcome their hesitations. I practiced using my hands to encourage my patient to open up and trust me with their problems. I practiced nodding my head to affirm my patient's feelings. Every part of my physical nature served to complement my purpose. This was not so that my encounter would feel scripted. Rather, I did not want my screen to numb my non-verbal communication skills just because I could hide behind it. On test day, I was able to virtually empathize with my patients by making eye contact, listening to their problems, and trying to absorb each part of the conversation and guide it in the direction the patient wanted. In the words of my standardized patient, "I felt you were truly listening and concerned about me as your patient. When you consistently looked at the screen [maintaining eye contact] … I felt very important and that I had your 100% attention throughout the encounter."

During these unprecedented times, this feedback is promising. Although this encounter was different, I am grateful for the unexpected exposure to telemedicine—a service that most medical students are not typically exposed to. This experience has prepared me, as a future physician, to engage with patients via telemedicine as human connection is very much possible with an online platform. For patients who are unable to travel, the elderly, or those whose needs can be met via telemedicine, this is a great opportunity to receive the undivided attention and care of a physician. To start honing my skills during my medical school education has been invaluable as the use of telemedicine will only continue to grow in the field of medicine.

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Cardiac Metabolism in the Disease of Acute Myocardial Infarction

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ABSTRACT

Overproduced reactive oxygen species (ROS) with decreased oxidative phosphorylation is a hallmark of the post-ischemic heart, which results in reperfusion-induced oxidative injury of the citric acid cycle (CAC). During ischemia, hypoxic conditions slow down the CAC resulting in succinate accumulation. Succinate is then rapidly oxidized during reperfusion, fueling ROS overproduction and contributing to ischemia-reperfusion (I/R) injury. We test the hypotheses that 1) reperfusion re-accelerates the CAC to correct succinate accumulation and 2) a vicious cycle caused by excess ROS can impair and downregulate the CAC plus other metabolic pathways in the post-ischemic heart. Nine–ten-week-old Sprague-Dawley rats (n=15) were subject to coronary ligation for 30-min followed by 24-h reperfusion. This process allowed us to closely mimic acute myocardial infarction (MI) and I/R injury. The non-ischemic and risk-regions of myocardium were excised, and the mitochondria were isolated. Dimethyl labeling was used to illuminate key metabolic pathways. Previous studies showed data that I/R impairs ADP-dependent O_2 consumption rate and ATP generation via downregulating CAC and fatty acid β-oxidation. However, a major finding in our study was that I/R dramatically upregulated the Phosphocreatine (PCr)/Creatine (Cr) shuttle ($p<0.05$) via upregulation of mitochondrial S-type creatine kinase (Ckmt2). The increased PCr formed in the mitochondria is transferred to the cytosol for ATP regeneration in-situ, which therefore increases the bioenergetic support of the post-ischemic myocardium. Therefore, we conclude that upregulating the PCr/Cr shuttle via increased Ckmt2 serves as feedback regulation of I/R, which can be useful for therapeutic intervention by increasing oxygenation and bioenergetics of the ischemic heart.