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Viewpoint

Protection of Health Care Professionals During an Epidemic: Medical, Ethical, and Legal Ramifications

Achuta Guddati[1], MD, PhD

Augusta University, Augusta, NY, United States

Corresponding Author:
Achuta Guddati, MD, PhD
Augusta University
1411 Laney Walker Blvd
Unit 3
Augusta, NY, 30912
United States
Phone: 1 3124048928
Email: drgakumar@yahoo.com

Abstract

The welfare of health care professionals working in hazardous environments is a concerning issue. Personal protective equipment such as face masks, disposable gowns, hair covers, gloves, and shoe covers is often used to prevent contamination from patient contact and droplets. This is especially relevant during an epidemic, when health care professionals are at elevated risk of infection. Failure to provide adequate protection to health care workers during epidemics has medical, ethical, and legal ramifications.

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KEYWORDS

medical ethics; harm; protection; COVID-19

Introduction

Coronavirus disease (COVID-19) is caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); the disease manifests as severe acute respiratory illness in some patients and has been spreading globally since December 2019 [1]. Recently, a trainee physician pursuing a fellowship in sleep medicine decided to volunteer at a local hospital on the weekend to help address a physician shortage. Upon reaching the hospital, the physician was asked by the hospital administrators to help with coverage on a COVID-19 rule-out floor. He learned that the hospital system had dedicated one of its hospitals exclusively to the treatment of patients who tested positive for COVID-19, while the other hospitals in the system had each dedicated a ward to ruling out patients with COVID-19. The request to work on the COVID-19 rule-out floor was unexpected; however, recognizing the acute shortage of physicians, the physician agreed to work on this floor, where patients who were symptomatic but had uncertain history of exposure were being managed while their viral test results were pending. Upon entering the floor, the physician donned a surgical mask and proceeded to see his first patient. Before entering the room, he was stopped by the "manager" of the floor and was ordered to remove the mask. When the physician asked for the reasoning behind the order, he was told that the mask was not necessary while seeing patients who were not confirmed to be positive for COVID-19 and that the hospital needed to conserve masks. The physician disagreed with the manager and proceeded to examine the patient while wearing the mask. He explained to the patient that there was no cause for alarm and that he was wearing the mask only as a precautionary measure. The patient agreed and mentioned that it was important that the doctor did not contract the disease as well. When the physician left the room, the manager was waiting outside and insisted that the physician remove his mask because the other patients would panic if they saw all the medical staff on the floor wearing face masks. The physician disagreed and proceeded to see other patients while wearing the face mask; a few hours later, some of the other physicians on the floor started to use face masks. After completing his shift, the physician informed the medical staff that he felt that his life was endangered by the hospital policy and that would not be able to volunteer for any more shifts unless the policy was changed to allow use of face masks by physicians on the COVID-19 rule-out floor. This scenario depicts a real encounter which recently occurred and is typical of the many friction points that have been arising between health care professionals and the administrative staff of hospitals during the pandemic.

Medical Aspects

A COVID-19 rule-out floor has a higher probability of having infected patients, and exposure to these patients without adequate protection indeed poses a grave risk for health care professionals and their families. The morbidity and mortality of health care workers due to COVID-19 infection is suspected to be higher due to their exposure to higher viral loads. Allowing health care professionals to work unprotected in such environments will also increase the likelihood of contagion of their family members. The most critical consideration that must be taken into account is that the spread of COVID-19 infection to health care professionals will likely exacerbate the shortage of available personnel. The benefits of physicians wearing face masks to shield themselves from potential carrier patients outweigh the risk that the mask will act as a medium of contamination between patients. Furthermore, wearing one mask throughout a shift is different from donning a new mask when entering a different patient's room. However, the use of other protective wear such as gowns could lead to a rapid depletion of their supply. Hence, allowing health care workers to use face masks is a reasonable approach to prevent the spread of infection from patients to health care workers. This measure strikes a balance between using resources judiciously (one face mask vs several face masks and gowns) and protecting health care workers from infection. There is growing evidence that wearing face masks and maintaining social distance are the two most important factors in preventing the spread of COVID-19.

Ethical Aspects

Health care workers who continue to work in medical wards and intensive care units treating patients with COVID-19 are aware that they are at higher risk of contracting the infection. Continuing to work in such situations requires a moral commitment toward patient care that goes beyond the worker's job description. Many health care workers, especially physicians, may have sufficient financial reserves to stay away from work and go without pay until the epidemic subsides. In the absence of additional financial incentives for physicians to work in a hazardous environment, one can only rely on their consciences to motivate them to continue to contribute to patient care. Most people would agree that a physician who abstained from work due to a hazardous infectious environment would be within their legal rights; however, such an act would be considered unethical. Denying basic protective wear such as face masks to health care professionals in the current situation shows that hospital administrations are not only disregarding the altruistic nature of medical care but are themselves committing an unethical act of deliberately increasing the likelihood that health care professionals will be infected. Hospital administrations are expected to follow an ethical code of conduct while balancing the provision of patient care with the safety of the people who are providing it. It would be unimaginable to send firefighters with minimal protective gear to control raging fires, and such an act by the government would expose these personnel to grave risk of injury. This parallel is drawn between firefighters and health care professionals due to the similarity of the risks involved and the threats to human life that both professions experience.

Legal Aspects

All employees, regardless of their profession, are entitled to a safe work environment per US Occupational Safety and Health Administration (OSHA) guidelines [2]. Lack of data about the transmissibility of COVID-19 does not constitute reasonable grounds to deny minimal protection to a health care worker, especially when they are working in a high-risk environment such as a COVID-19 rule-out floor. There have been several recent reports of health care workers who raised concerns about safety being threatened by their employers with termination of employment [3]. It is possible that in the current emergent situation of a rapidly spreading viral infection, there is little time to debate the pros and cons of occupational health hazards. However, it is clear beyond reasonable doubt that denying basic protective wear such as face masks to health care professionals who are working on medical floors with patients highly suspected of being infected with COVID-19 constitutes criminal conduct. Even if no viral infection is contracted during such patient encounters, the mental stress to which these health care professionals are subjected may form grounds for legal recourse.

Conclusion

Health care professionals are cognizant of the acute shortage of personal protective wear in the current scenario of an epidemic. The Hippocratic Oath binds physicians to uphold ethical standards; however, a moral code of conduct is also expected from hospital administrations while balancing the provision of patient care with the safety of the people who are providing it. There will undoubtedly be much debate about this issue after this epidemic subsides, especially because there is currently a consensus that everyone should wear a face mask to decrease the possibility of infection with COVID-19. Adversity tests character—both of individuals and of organizations.

Conflicts of Interest

None declared.

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Abbreviations

COVID-19: coronavirus disease
OSHA: Occupational Safety and Health Administration

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Review

Venous Thromboembolism in Hospitalized COVID-19 Patients: Systematic Review

Kade Birkeland[1], PharmD; Raymond Zimmer[2], MD; Asher Kimchi[2], MD; Ilan Kedan[2], MD, MPH

[1]Cedars-Sinai Medical Center, Los Angeles, CA, United States

[2]Smidt Cedars-Sinai Heart Institute, Beverly Hills, CA, United States

Corresponding Author:
Ilan Kedan, MD, MPH
Smidt Cedars-Sinai Heart Institute
8501 Wilshire Blvd Suite 200
Beverly Hills, CA, 90211
United States
Phone: 1 3103853496
Email: kedani@cshs.org

Abstract

Background: Coagulopathy associated with COVID-19 infection and venous thromboembolism (VTE) have emerged as significant contributors to morbidity among patients infected with SARS-CoV-2.

Objective: We performed a systematic review to estimate VTE incidence in hospitalized patients and to analyze characteristic factors in the VTE cohort.

Methods: We searched PubMed and Google Scholar using specified title search terms “SARS-CoV-2” or “COVID-19” and “venous thromboembolism” and “anticoagulation” among others to identify peer-reviewed journal articles published between June 22, 2019, and June 22, 2020. Data were systematically extracted and synthesized using Microsoft Excel for analysis. The main outcome was VTE incidence, and measures included patient characteristics, anticoagulation, and clinical outcomes with assessment for associations.

Results: In total, 14 studies were included comprising 1677 patients. Most patients (n=1306, 82.4%) received anticoagulation (either VTE prophylaxis or treatment). VTE incidence was 26.9% (SE 3.1; 95% CI 20.8-33.1) and was correlated with systematic screening (r^2=0.34, *P*=.03) and study duration (r^2=–0.33, *P*=.03). D-dimer was higher for the VTE cohort (5.62 [SD 0.9] vs 1.43 [SD 0.6]; *P*<.001). Odds of VTE were higher at the intensive care unit (odds ratio [OR] 6.38, 95% CI 3.67-11.11; *P*<.001) but lower with anticoagulation (OR 0.58, 95% CI 0.36-0.92; *P*=.02).

Conclusions: Despite the utilization of background anticoagulation, VTE incidence was historically high. Future studies are needed to provide additional data to guide optimal VTE prophylaxis and diagnostic strategies.

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KEYWORDS

VTE; COVID-19; anticoagulation; SARS-CoV-2; review; heart; morbidity; hospital; incidence; treatment; incidence

Introduction

Coagulopathy is an impairment in the blood’s ability to form clots. Coagulopathy associated with COVID-19 infection has emerged as a significant contributor to morbidity among those infected with the illness. Although the incidence of coagulopathy is unknown, COVID-19–related coagulopathy has been described as having a unique hemostatic signature [1-3]. Typically reported abnormalities include a mildly prolonged prothrombin time/international normalized ratio (PT/INR) as well as an activated partial thromboplastin time (aPTT), mild thrombocytopenia, and elevated D-dimer and fibrinogen [3,4]. Generally, COVID-19–associated coagulopathy results in a prothrombotic state and is nonconsumptive or progresses to hemorrhage [5]. As such, observational studies and autopsy reports have focused on characterizing thrombotic complications, including venous thromboembolism (VTE).

Potential approaches to treatment are continuing to develop with increasing experience with COVID-19 infection. Institutions have described updated VTE prophylaxis protocols aimed to more aggressively prevent clots [1,2,6]. For example, some describe utilization of standard dose VTE prophylaxis

with unfractionated heparin (eg, unfractionated heparin 5000 units by subcutaneous injection twice daily or three times daily) or low molecular weight heparin (eg, enoxaparin 40 mg by subcutaneous injection every 24 hours) for all patients hospitalized with COVID-19 infection rather than based on risk assessment. Others deploy anticoagulation regimens that are higher intensity compared to standard dose VTE prophylaxis. For example, high dose, low molecular weight heparin (eg, enoxaparin 40 mg by subcutaneous injection every 12 hours) or empiric treatment anticoagulation (eg, unfractionated heparin by intravenous infusion; enoxaparin 1 mg/kg by subcutaneous injection every 12 hours) for high-risk patients, which is variably defined (eg, intensive care unit [ICU] level of care, clinical deterioration, rising d-dimer) and based on historical data in other high-risk populations (eg, bariatric surgery, third trimester pregnancy) [1,2,6]. Also, utilization of specific anticoagulation products will vary by country depending on regulatory approval and availability. In fact, early experience indicates that high-risk patients (eg, sepsis-induced coagulopathy score ≥4 or D-dimer >3 times the upper limit of normal [ULN]) are most likely to benefit from VTE prophylaxis [7]. However, evidence-based treatment protocols are needed to further improve in COVID-19 patients with VTE [1,2].

The mechanism of COVID-19–associated coagulopathy is not fully understood. However, the intense and sustained cytokine-mediated inflammatory response to SARS-CoV-2 infection is likely etiologic. As an example, elevated fibrinogen levels have been found to be associated with elevated interleukin-6 (IL-6) levels, while D-dimer also rises in parallel with C-reactive protein (CRP) [8]. Furthermore, inflammatory markers directly activate the clotting system as does tissue hypoxia, both on top of direct endothelial cell injury and subsequent dysfunction by SARS-CoV-2 cellular entry [7,9].

Serologic markers may be associated with severity of infection and may also be predictors of increased morbidity and coagulopathy. For example, D-dimer is a biomarker that increases as a result of thrombosis (eg, microvascular thrombosis, deep vein thrombosis [DVT], or pulmonary embolism [PE]) or systemic activation of hemostasis (eg, disseminated intravascular coagulation) and is associated with severe COVID-19 and mortality [10]. Tang et al [4] demonstrated that D-dimer elevation on admission and rising to at least 3-4 times ULN over the course of the hospital stay was associated with increased mortality. Other hemostatic markers such as PT and aPTT prolongation, elevated fibrinogen degradation product, and low platelets have also been associated with severe COVID-19 and mortality [4,11]. Governing bodies have recommended that D-dimer, PT, platelets, and fibrinogen be measured in patients with COVID-19 infection for risk stratification and prognosis [1,2].

We performed a systematic review of VTE in the setting of patients hospitalized with COVID-19 infection and summarized the potential treatment effects in VTE management in these patients. Our aim was to estimate the observed incidence of hospitalized VTE patients and analyze patient characteristics in the VTE cohort.

Methods

We performed a systematic literature search in PubMed with the title search terms “COVID-19” or “SARS-CoV-2” or “Novel Coronavirus 2019” and “venous thromboembolism” or “deep vein thrombosis” or “pulmonary embolism” or “thrombosis” or “thromboembolic” or “anticoagulation” or “heparin” or “thromboprophylaxis” to identify primary research studies that report the rate of VTE in patients hospitalized with COVID-19 infection who are treated with standard dose pharmacologic VTE prophylaxis, high dose pharmacologic VTE prophylaxis, treatment dose anticoagulation, no anticoagulation, or no documentation. A supplementary search was performed on Google Scholar using the same search terms and journal article references were reviewed to identify additional studies. Studies of adult populations that were published in a PubMed peer-reviewed journal from June 22, 2019, to June 22, 2020 were included for review. Data were collected for each included study design, population studied, VTE event rate, VTE diagnostic strategy, VTE prophylaxis or treatment strategy, hemostatic lab abnormalities, and clinical outcomes including ICU level of care and survival.

We excluded studies with arterial thrombosis, myocardial infarction or ischemic stroke, pediatric and fetal populations, and reviews, case reports, letters to the editor, or any study that had not yet undergone peer review. Clinical outcomes data for the included studies were pooled, and we conducted a systematic review and meta-analysis with a random effects model to measure a single group summary for VTE incidence as our primary outcome [12]. Confidence intervals were determined by the adjusted Wald method. Secondary outcomes included a single group summary for mortality with the same methodology as the primary outcome and patient demographics with clinical characteristics using descriptive statistics with weighted mean and weighted standard deviation. Assessment of variables associated with VTE incidence was conducted using univariate linear regression and multivariate linear regression. Assessment of binary variables associated with VTE occurrence was conducted using multiple logistic regression. Estimation of differences in continuous variables between patients with VTE and patients without VTE was conducted using the Z test (two samples for weighted means with weighted variance). Data were compiled using Google Sheets (Google LLC) and Microsoft Excel (Microsoft Corp).

The Cedars-Sinai Hospital Institutional Review Board requirement for approval was waived as this is a systematic literature review.

Results

The initial PubMed literature review returned 212 journal articles, of which 12 studies were included in our review. The supplementary Google Scholar and journal article references search identified an additional 2 studies. In total, 14 studies were included in our review [6,9,13-24] (Figure 1).

Studies included were observational (Table 1) and predominantly based on experience at a single center (single

center: n=10; multicenter: n=4). The total patient sample size was 1677 (range 26-388) and represented a multinational patient population (China: n=272; France: n=206; Italy: n=415; Netherlands: n=382; Spain: n=156; United States: n=44). The weighted median study duration was 37.2 (SD 17.4) days and 3 studies reported a median length of stay (LOS) (weighted mean LOS 9.5 [SD 1.8]days) with patients receiving both ICU and non-ICU levels of care (Table 2). Five studies (n=352) did not report the patient status (eg, discharged alive, expired, or admitted) at completion of the study period. For the other 9 studies, the designations and counts were as follows: nonsurvivors (n=244), discharged alive (n=717), admitted (n=369), and unknown (n=20).

Figure 1. Study selection flowchart showing inclusion and exclusion criteria.

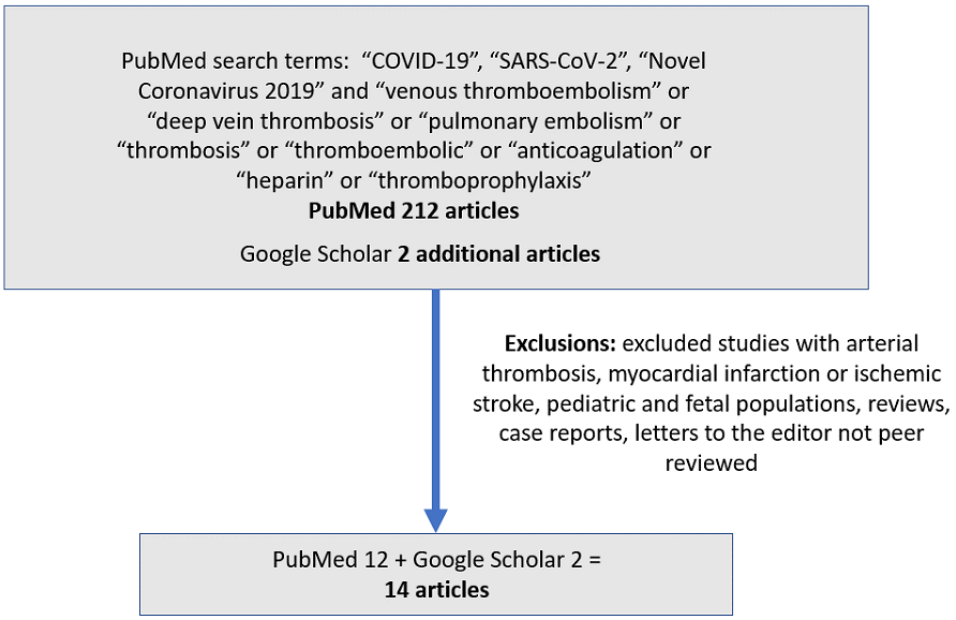


Table 1. Summary of included studies.

Study	Study design	Oxford level of evidence	Sample size, N	Study duration (days)
Lodigiani et al [13]	Prospective cohort	3	388	57
Llitjos et al [14]	Retrospective historical cohort	4	26	23
Wright et al [15]	Retrospective historical cohort	4	44	29
Artifoni et al [16]	Retrospective historical cohort	4	71	16
Poissy et al [17]	Case series	4	107	33
Faggiano et al [18]	Retrospective historical cohort	4	25	14
Demelo-Rodríguez et al [19]	Prospective cohort	4	156	14
Zhang et al [20]	Cross-sectional cohort	4	143	31
Helms et al [21]	Prospective cohort with historical controls	3	150	28
Voicu et al [22]	Prospective cohort	4	56	21
Ren et al [23]	Cross-sectional cohort	4	48	2
Middeldorp et al [6]	Prospective cohort	4	198	59
Cui et al [24]	Retrospective historical cohort	4	81	52
Klok et al [9]	Retrospective historical cohort	4	184	29

Table 2. Summary of patient clinical characteristics and factors.

Variable	Studies reporting variable	Sample size, N	Weighted mean (SD)
Age (years)	12	1514	64.2 (3.2)
Male	13	1570	66.8 (9.4)[a]
Female	13	1570	31.2 (10.0)[a]
BMI (kg/m^2)	4	339	27.7 (1.2)
BMI (>30 kg/m^2)	1	362	24.1 (0)
D-dimer (ug/mL)	11	998	2.1 (0.9)
Fibrinogen (mg/dL)	6	395	628.4 (118.3)
Prothrombin time (sec)	3	268	14.4 (0.9)
Platelets (x10^9/L)	8	869	232 (21.3)
SOFA[b] score	4	291	5.9 (3.1)
History of VTE[c]	6	1061	8.0 (4.5)[a]
Pre-existing anticoagulation	4	796	25.0 (8.1)[a]
ICU[d] level of care	14	1677	75.8 (53.4)[a]
Invasive mechanical ventilation	5	446	76.5 (55.8)[a]

[a]Expressed as weighted percentages.

[b]SOFA: sequential organ failure assessment.

[c]VTE: venous thromboembolism.

[d]ICU: intensive care unit.

In total, 13 studies reported utilization of VTE chemoprophylaxis or treatment anticoagulation. Most patients (n=1306, 82.4%) received anticoagulation; 17.6% (n=279) did not. Of the patients who received anticoagulation, standard dose VTE prophylaxis was most common (n=691, 52.9%). Patients were also prescribed high dose VTE prophylaxis (n=84, 6.4%) or treatment anticoagulation (n=197, 15.1%). In 25.6% (n=334) of patients prescribed anticoagulation, the dosage or intensity was not specified. VTE diagnosis was determined by systematic screening in 7 studies, 1 of which also implemented systematic screening for PE. For 7 other studies, VTE was diagnosed by usual practice. Three studies exclusively screened for DVT and did not report PE.

The combined estimate of VTE incidence was 26.9% (SE 3.1; 95% CI 20.8-33.1) (Figure 2). Occurrence of VTE (n=377) was more often attributed to DVT (n=262) and less often to PE (n=116). The combined estimate of mortality incidence was 24.4% (SE 7.1; 95% CI 10.5-38.2). Absolute values were 244 for nonsurvivors, 717 for discharged alive, 369 for admitted, and 20 for unknown.

Systematic screening for VTE (r^2=.34, *P*=.03) and study duration (r^2=–.33, *P*=.03) were both correlated with VTE incidence. There were no associations with VTE and mortality, percentage of patients prescribed anticoagulation, gender, age, or D-dimer level. Multivariate linear regression for the intensity of VTE prophylaxis and VTE incidence was not significant (r^2=.64; F=.25) nor was a model that included the percentage of patients prescribed VTE prophylaxis or anticoagulation, the percentage of patients in the ICU, gender, age, D-dimer level, study duration, and implementation of systematic screening for VTE (r^2=.67; F=.58).

Five studies compared clinical characteristics and outcomes for patients with VTE (n=157) to patients without VTE (n=296). D-dimer was significantly increased in patients with VTE compared to patients without VTE (5.62 [SD 0.9] vs 1.43 [SD 0.6]; *P*≤.001). VTE was decreased in patients receiving anticoagulation (either VTE prophylaxis or treatment anticoagulation) (OR .58, 95% CI .36-.92; *P*=.02) and was increased in patients receiving an ICU level of care during their admission (OR 6.38, 95% CI 3.67-1.11; *P*≤.001). There was no difference in VTE rates for nonsurvivors compared to survivors (OR 2.02, 95% CI .98-4.19; *P*=.06) (Figure 3).

Figure 2. Forest plot of the summary estimate of venous thromboembolism (VTE) incidence.

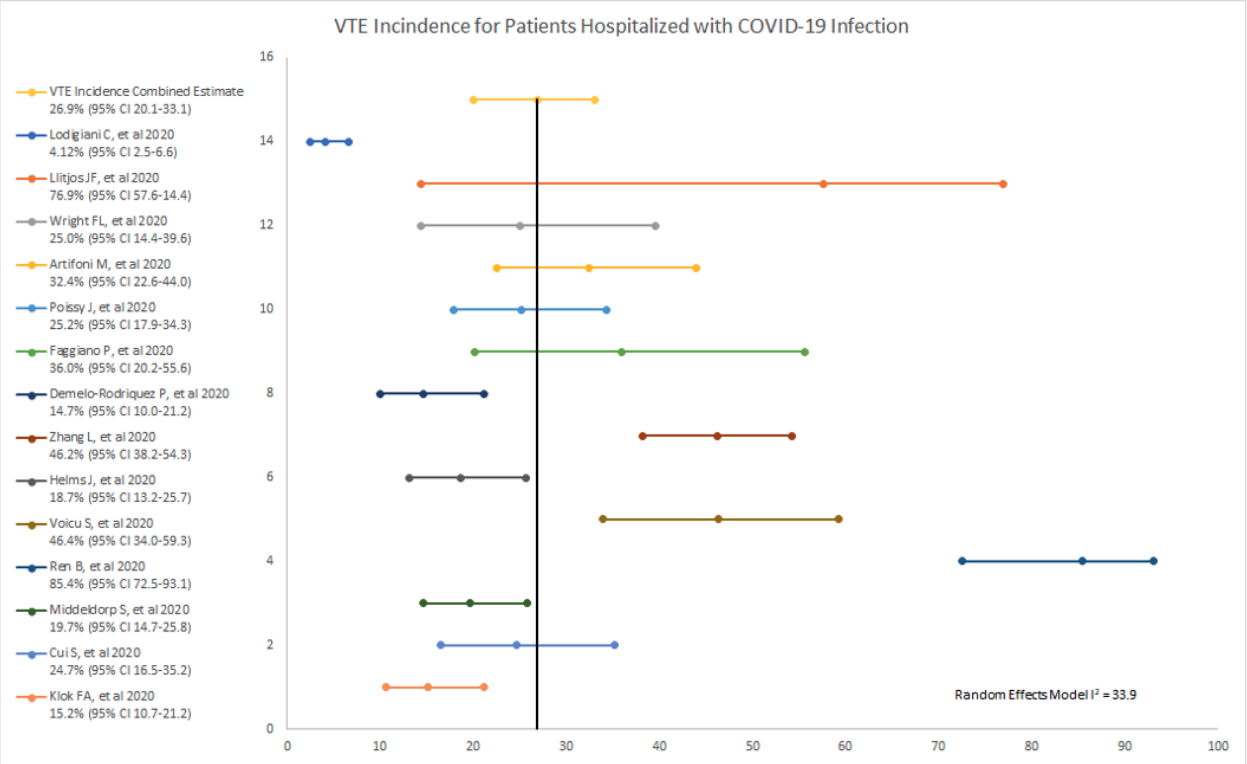
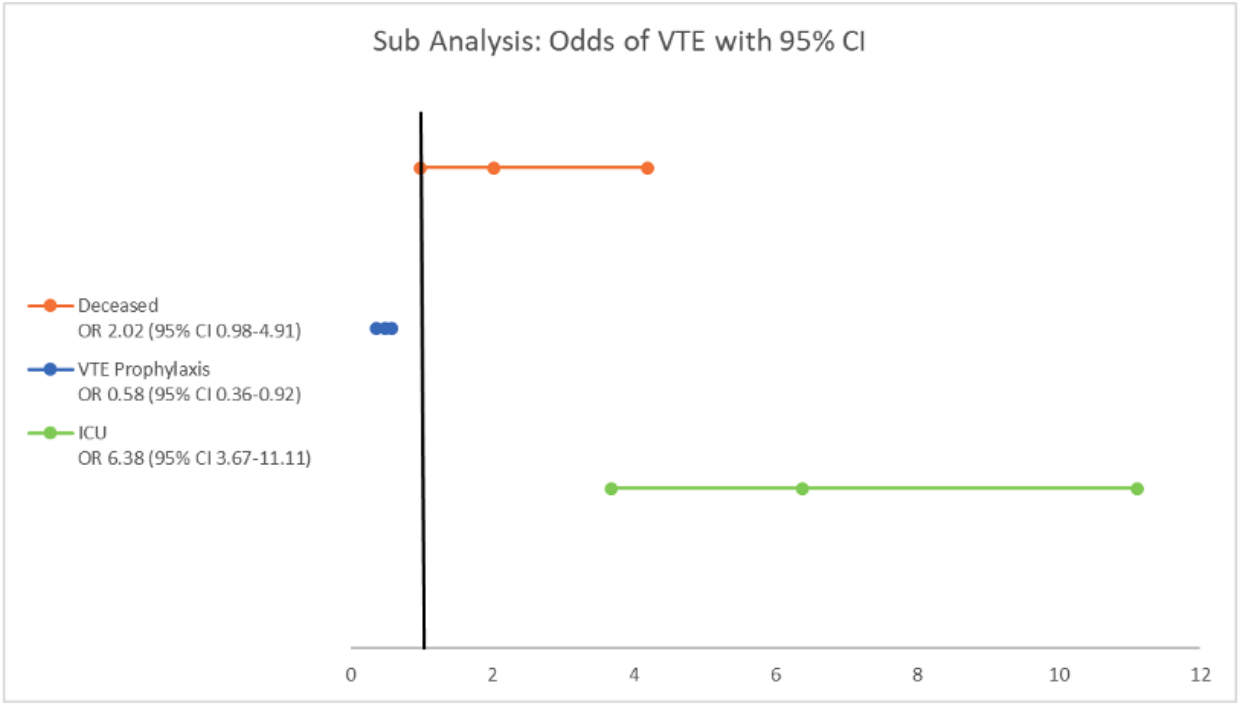


Figure 3. Forest plot of venous thromboembolism (VTE) with anticoagulation and intensive care unit (ICU) admission. OR: odds ratio.



Discussion

Principal Findings

In this review, we identified and evaluated 14 studies to assess the incidence of VTE in hospitalized patients with COVID-19 [10]. Our estimated VTE incidence of 26.9% is higher than what has been previously described in the placebo arms (VTE 5%-15%) of clinical trials that evaluated VTE prophylaxis in medically ill patients, as well as in French controls admitted to the ICU with acute respiratory distress syndrome (4.8%), influenza (7.5%) or any cause (6.1%) [2,21]. One explanation for this finding may be the consistently elevated coagulopathy associated with COVID-19 infection [1-3]. Although all 14 studies reported VTE incidence, there was variation in sample size, study duration, hospital LOS, level of care, and VTE prophylaxis and diagnostic strategies. Risk factors for VTE

were not reported. This may explain the degree of variation among individual studies around the summary estimate as well as the differences in degree of weighted impact. Further, more than a quarter of the patients included in our systematic review were still hospitalized at the time of study completion. Without including the entire duration of hospitalization for COVID-19 patients, the VTE incidence we report may be an underestimate.

Although the patient populations we evaluated encompassed Asia, Europe, and North America, demographics and clinical characteristics were similar and consistent with previous reports for patients with COVID-19 infection [10]. Accordingly, a high proportion of patients were candidates for anticoagulation and received anticoagulation during their hospitalization. Although the odds of VTE were lower in patients who received anticoagulation, there was no observed association between VTE incidence and anticoagulation intensity. Our review supports the increasingly standard practice of prescribing VTE prophylaxis for hospitalized COVID-19 patients [1,2]. However, future studies will be needed to guide recommendations for the optimal VTE prophylaxis strategy in this cohort of patients. Further research into the pathophysiology of hypercoagulability in these patients may also better inform the most optimal prophylaxis strategy.

In our review, systematic screening for VTE was correlated with VTE incidence. However, the clinical significance of positive studies is unknown (eg, asymptomatic venous clot or superficial venous clot). Study duration was negatively correlated with VTE incidence, which was not expected, likely reflecting heterogeneity in studied patient populations, including severity of illness, LOS, prevalence of VTE risk factors, and anticoagulation and diagnostic strategies.

Five studies reported data for patients with VTE compared to patients without VTE. The D-dimer level was significantly elevated in patients with VTE, which is consistent with previous studies and supports the prognostic value of D-dimer as a serum biomarker for assessing VTE risk in a hospitalized patient with COVID-19 [1,2]. Additionally, the odds of VTE were higher in patients in the ICU and lower in patients on anticoagulation. However, these studies did not specify the intensity of VTE prophylaxis or dosage. No other patient subgroups who may be at increased VTE risk (eg, comorbidities, pregnancy) were identified. There was no difference in mortality in these subgroups of patients, and therefore the impact of VTE on survival remains unknown and likely confounded by differences in patient populations.

The strengths of our analysis are the inclusion of populations from across the globe, overall sample size, and consistency among studies in reporting data for VTE incidence, level of care, and strategies for VTE prophylaxis as well as diagnostic strategy.

There are several noteworthy limitations in our study. First, the studies included in our analysis are observational. Given that there are no randomized clinical trials at this time, it is difficult to eliminate confounding variables when assessing VTE and clinical associations. Furthermore, the included studies are heterogeneous with respect to reporting of patient demographics, clinical characteristics, method of VTE diagnosis, and strategy for anticoagulation. These studies suggest increased incidence of late or delayed VTE risk [6]. Further, the studies did not consistently report duration of illness, severity of illness, hospital LOS, risk factors for VTE, or presence of other non-VTE indications for anticoagulation. Most importantly, a significant proportion of patients included in our analysis were still hospitalized at the time the study was completed.

Future potential areas of research include arterial thrombosis, hypercoagulability risk factors, occurrence of late-term thrombosis post discharge, and the presence of long-term coagulopathy. As worldwide cases continue to surge, VTE risk in nonhospitalized patients with less acute and nonpneumonia COVID-19 infection also warrant further investigation. Wearable technology is actively being investigated to monitor COVID-19 infection in the community and at home. Examples include the DETECT Health Study, the COVIDENTIFY Study, and the TemPredict Study. A proposed framework exists to develop novel clinical indications for wearable technology, such as early detection of VTE in ambulatory patients based on potential physiologic or wearable markers that could signal increased VTE risk or association. However, feasibility studies would need to be conducted to validate novel use cases [25].

Conclusion

Coagulopathy associated with COVID-19 infection has emerged as a contributor to morbidity among patients infected with SARS-CoV-2. Early reports demonstrate a significantly increased incidence of VTE. We performed a systematic review to estimate the observed incidence of hospitalized VTE patients with COVID-19 infection. Despite utilization of background VTE prophylaxis and anticoagulation, VTE incidence is historically high. Future studies will provide additional data and generate insights to guide therapeutic decision making and optimize VTE prophylaxis and diagnostic strategies.

Authors' Contributions

KB contributed to project design, literature review, statistical analysis, manuscript writing, and manuscript preparation and editing. RZ participated in manuscript preparation, manuscript writing, and project design. AK participated in manuscript editing. IK contributed to project design and manuscript writing.

Conflicts of Interest

None declared.

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Abbreviations

aPTT: activated partial thromboplastin time
CRP: C-reactive protein
DVT: deep vein thrombosis
ICU: intensive care unit
IL-6: interleukin-6
INR: international normalized ratio
LOS: length of stay
OR: odds ratio
PE: pulmonary embolism
PT: prothrombin time
ULN: upper limit of normal
VTE: venous thromboembolism

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Original Paper

Effect of Health Care Provider Delays on Short-Term Outcomes in Patients With Colorectal Cancer: Multicenter Population-Based Observational Study

Ahmed Abdulaal[1], BSc, MBBS; Chanpreet Arhi[1], MRCS; Paul Ziprin[1], MB BCh, MD, FRCS

Imperial College London, London, United Kingdom

Corresponding Author:
Ahmed Abdulaal, BSc, MBBS
Imperial College London
Department of Surgery and Cancer, St Mary's Hospital Campus, Praed Street
London, W2 1NY
United Kingdom
Phone: 44 0754513315
Email: ahmed.abdulaal@nhs.net

Abstract

Background: The United Kingdom has lower survival figures for all types of cancers compared to many European countries despite similar national expenditures on health. This discrepancy may be linked to long diagnostic and treatment delays.

Objective: The aim of this study was to determine whether delays experienced by patients with colorectal cancer (CRC) affect their survival.

Methods: This observational study utilized the Somerset Cancer Register to identify patients with CRC who were diagnosed on the basis of positive histology findings. The effects of diagnostic and treatment delays and their subdivisions on outcomes were investigated using Cox proportional hazards regression. Kaplan-Meier plots were used to illustrate group differences.

Results: A total of 648 patients (375 males, 57.9% males) were included in this study. We found that neither diagnostic delay nor treatment delay had an effect on the overall survival in patients with CRC (χ^2_3=1.5, *P*=.68; χ23=0.6, *P*=.90, respectively). Similarly, treatment delays did not affect the outcomes in patients with CRC (χ^2_3=5.5, *P*=.14). The initial Cox regression analysis showed that patients with CRC who had short diagnostic delays were less likely to die than those experiencing long delays (hazard ratio 0.165, 95% CI 0.044-0.616; *P*=.007). However, this result was nonsignificant following sensitivity analysis.

Conclusions: Diagnostic and treatment delays had no effect on the survival of this cohort of patients with CRC. The utility of the 2-week wait referral system is therefore questioned. Timely screening with subsequent early referral and access to diagnostics may have a more beneficial effect.

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KEYWORDS

surgery; cancer; colorectal; delay

Introduction

Colorectal cancer (CRC) is the second most common cause of cancer-related deaths in the United Kingdom, and it accounted for 42,000 cases of cancer diagnoses in 2018 [1]. In fact, the United Kingdom has lower survival figures for all types of cancers than many European countries despite similar national expenditures on health [2]. The EUROCARE-4 study demonstrated that age-adjusted 5-year CRC mortality in the United Kingdom is significantly higher than that in the Nordic countries and Central Europe [2]. Abdel-Rahman et al [3] found that CRC accounted for the largest number of avoidable cancer-related deaths in the United Kingdom, with approximately 4090 avoidable cases.

Although surgery with curative intent is the preferred treatment modality for CRC [4], Gatta et al [5] found that only a small proportion of patients had undergone an elective procedure in the United Kingdom, usually owing to the advanced stage of cancer at diagnosis. A large proportion of patients with CRC are admitted as emergencies in the United Kingdom [6]. Emergency patients have a 1-year mortality that is ≥25% higher than patients who present through the screening and elective

pathways [7]. The variability in the CRC survival is the greatest in the first year following diagnosis [8]; therefore, emergency patients may account in part for the higher 1-year mortality risk in the United Kingdom.

Thomson and Forman [9] demonstrated that patients with breast cancer who survive up to 1 year are more likely to survive up to 5 years. However, CRC is more complicated, as the 5-year conditional survival remains significantly worse for this cancer type [9]. This suggests that systematic delays such as delays in the referral, diagnosis, and treatment could have a constitutive effect on the long-term outcomes in patients in the United Kingdom and Europe [9]. Therefore, identifying and reducing the delays may lead to the detection of CRC at an early stage and diminish the proportion of emergency presentations, thereby eradicating the survival gap.

Previous studies have shown mixed results, while some studies have found no association [10], negative association [11], or "U-shaped" association [12] between delay and survival in patients with CRC. Many studies focus solely on the diagnostic interval [13] or consider general delays [14]. The aim of this study was to investigate the effect of diagnostic and treatment delays and their subdivisions on the survival of patients with CRC. We aimed to identify whether health care provider delays seen in the Imperial College Healthcare National Health Service Trust are related to the survival of patients with CRC. The hypothesis was that delays were associated with an increased risk of death.

Methods

Data Sources

Data were obtained from the Somerset Cancer Register, which is a database that collects wait times and outcomes data in line with the national database requirements [15]. Dataset collection was performed from January 2013 to March 2016.

Study Population

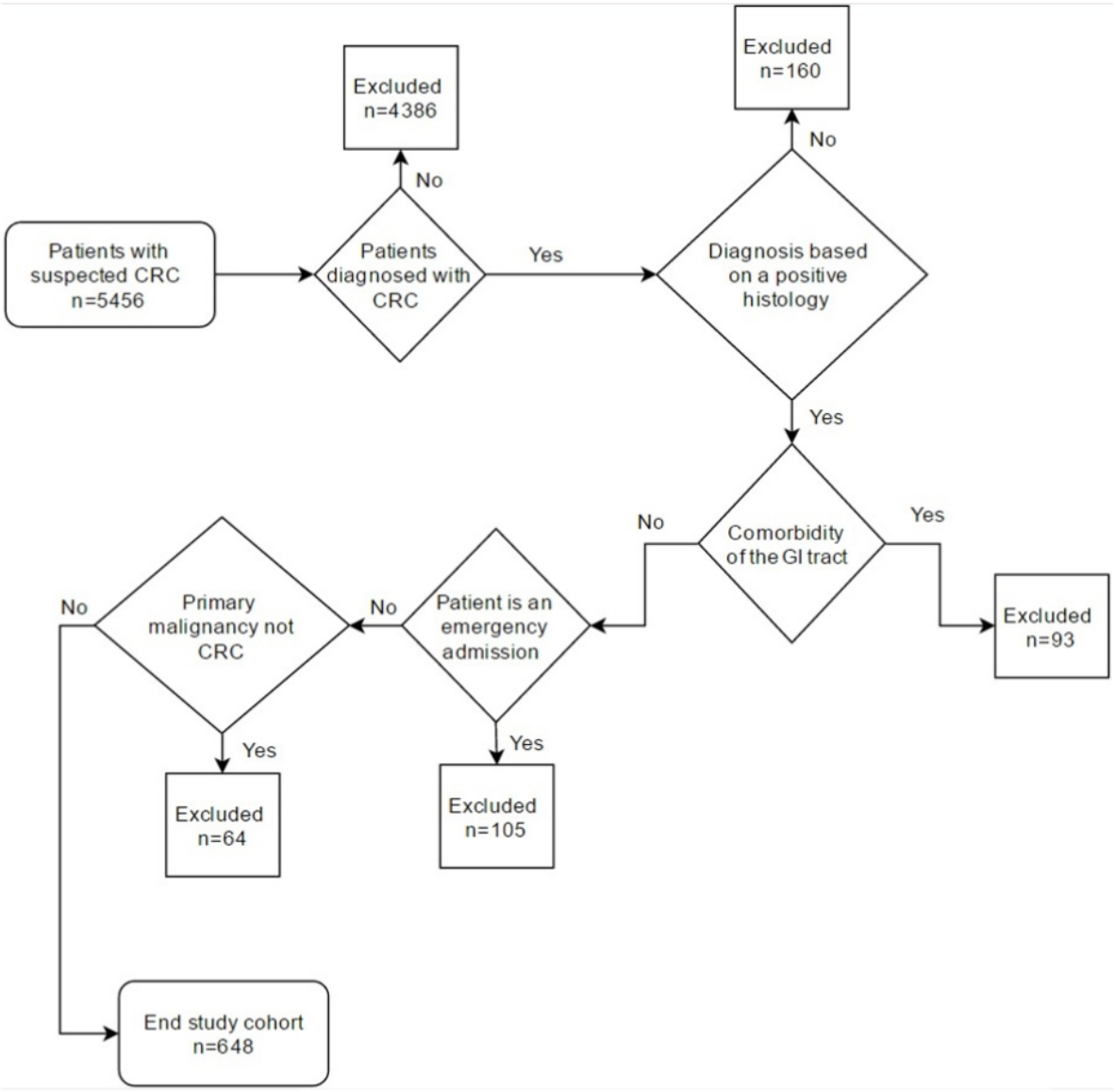
A total of 5456 patients were investigated for CRC. Patients not diagnosed with CRC were excluded (n=4386). To ensure database validity, the patients' sources of referral were examined. Of the excluded patients, 4118 (93.9%) patients within the first exclusion were referred through the 2-week wait pathway. In the United Kingdom, a 2-week wait referral is an urgent referral made by a patient's general practitioner, wherein the patient should be seen within a 14-day period by a secondary care specialist. Such a referral should be made when a patient presents with symptoms that may indicate cancer. Of the 4118 patients with CRC, 246 were diagnosed through the 2-week wait pathway, representing a 5.9% conversion rate. This is in line with the 5.4% conversion rate that was reported for bowel cancer observed at the national level [16]. Patients whose date of diagnosis did not reflect a positive histology finding were excluded (Table 1, n=160). These groups were excluded owing to uncertain diagnoses. Utilizing the date of positive histology results as the date of diagnosis has been employed by another study [12].

Patients with comorbid conditions of the gastrointestinal tract were excluded. This included patients with metastases from other primary cancers (n=11) or benign neoplasms (n=75). Patients with metastasis to the gastrointestinal tract may experience shorter diagnostic delays as a result of heightened physiological disturbance and yet exhibit worse outcomes [17], whereas those with benign neoplasms may exhibit a more insidious symptom development but a relatively favorable outcome [18,19]. Patients with inflammatory bowel disease were identified by searching multidisciplinary team reports for the following terms: colitis, proctitis, ulcerative, ulcerative colitis, Crohn(s), Crohn's, and inflammatory bowel disease. Those with inflammatory bowel disease were excluded (n=7). Patients with inflammatory bowel disease represented 1.1% (7/648) of the cohort, which is in line with the expected prevalence of 1%-2% observed in all patients with CRC [20]. Patients who were referred following an emergency admission (n=105) were excluded. Emergency presentations typically experience shorter delays and worse 1-year and 5-year outcomes [7,21], which may produce a misleading negative association between the delay and the survival [22]. Patients diagnosed with malignancies of the small intestine, anus, or anal canal were excluded (n=64). The algorithm for patient inclusion is illustrated in Figure 1.

Table 1. Patient groups that were not diagnosed with colorectal cancer following a positive histology finding of a primary colorectal tumor (n=160).

Category of patients excluded	Patients, n (%)
A clinical diagnosis alone (patient symptomatology + a radiological investigation)	138 (86.2)
Diagnosis made after a positive serological tumor marker result	1 (0.6)
Unknown basis of diagnosis	1 (0.6)
Patients with an unrecorded basis of diagnosis	20 (12.5)

Figure 1. The algorithm used for patient inclusion. CRC: colorectal cancer; GI, gastrointestinal.



Study Design

This was a multicenter population-based observational study. When assessing survival, other studies have demonstrated different trends based on the cancer type [23,24], and therefore, colon and rectal cancer cohorts were considered independently.

Lead Time Bias

Patients included from the national bowel cancer screening program (n=92) were particularly susceptible to lead time bias. This bias occurs when outcomes are measured following diagnoses that reflect different starting points along the natural history of a cancer [25,26]. This may lead to a statistical extension in survival length without an actual increase in the duration of life for the patients detected through screening programs [14,27]. In order to account for the lead time, a correction by Duffy et al [28] was used, which estimates the additional follow-up time owing to earlier cancer detection. It assumes an exponential distribution of the sojourn time (E[s]) [29]—the interval in which a cancer is asymptomatic but can be detected by screening and is defined as $E(s) = (1-e^{(-\lambda t)})/ \lambda$, where t is the time at which a patient is last known to be alive and λ is the transition rate from preclinical to clinical cancer [28]. The transition rate is calculated as 1/mean sojourn time. Brenner et al [30] described age-specific and sex-specific estimates of the sojourn time for CRC. A weighted arithmetic mean sojourn time was calculated as 4.86; thus, λ=0.21. E(s) was subtracted from the observed survival time or time to the last known follow-up of patients referred through screening.

Immortal Time Bias

Patients receiving treatment for their CRCs were necessarily alive between receiving a diagnosis and initiating treatment. This period is described as an immortal time, wherein the study outcome cannot occur [31]. Such patients may therefore have an artificial increase in their survival time if it is measured from the date of diagnosis, and this would introduce bias when analyzing the effect of the treatment delays on the study outcomes [31,32]. To obviate this bias, survival was measured from the date of the first treatment when considering the effect of the treatment delays. Survival was measured from the date

of diagnosis when considering the diagnostic delays and overall delays.

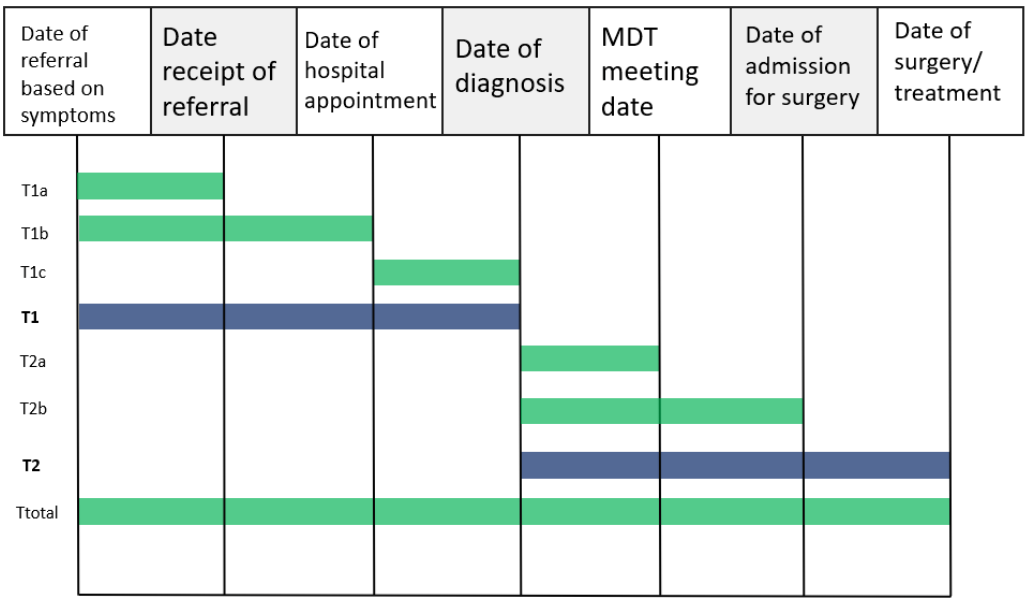
Study Variables

The effect of health care provider delay on survival was investigated. Survival was measured until death or censoring. Patients were censored at the last known live follow-up or at the end of the study period if no record of a follow-up is available; however, they were not recorded as deceased.

Delay

Delays were categorized into diagnostic and treatment delays. Delays and their subdivisions were analyzed separately as each delay type represents a discrete segment of the patient pathway [33]. Figure 2 illustrates all the delays considered in this analysis.

Figure 2. Representation of the delays and delay subdivisions considered for the analysis. T1: diagnostic delay; T1a: delay from referral based on symptoms to receipt of referral; T1b: referral delay; T1c: delay between hospital appointment and diagnosis; T2: treatment delay; T2a: delay between diagnosis and multidisciplinary team (MDT) meeting date; T2b: considered for those patients who received a surgical intervention; Ttotal: total delay from referral to surgery or treatment.



Covariates

The covariates considered in this study were related to the patient demographics, including age, gender, and ethnicity. The data of the location, histology, grade, and stage of the tumor were also included. Patient performance status, which reflects the functional status of the patients [34], was also considered. Covariates that succeed diagnosis but may confound treatment delay and survival included treatment modality, intent (as categorized by synchronous insertion into the Somerset Cancer Register database at the time of treatment), and setting. These covariates were therefore included in the treatment delay models.

Statistical Analysis

The median and IQR were calculated for diagnostic, referral, and treatment delays along with the delay quartiles. A survival analysis was conducted for all the delays and their subdivisions. Kaplan-Meier survival estimates were plotted for diagnostic and treatment delays by quartile. Group differences were analyzed using the log-rank test. The Cox proportional hazards regression analysis was used to investigate the effect of the covariates and to adjust for the confounding factors. To ensure the result validity, multiple sensitivity analyses were performed. Although deaths are regularly reported to the registry, diagnostic and treatment delay analyses were repeated for patients with a known live follow-up or death date. Next, all models were stratified by cancer stage, as stage may act as an intermediate factor between diagnostic delay and survival and it drives treatment regimens [14,23]. As suggested by previous researchers [13,35], analyses of diagnostic delays were repeated after excluding the covariates of tumor stage and grade to account for any confounding created by including them in the primary model. A P value of ≤.05 was considered statistically significant. SPSS statistics version 21 (IBM Corp) was used for the analysis.

Results

Study Sample

Of the 648 eligible patients, 375 were males (57.9%) and 272 were females (41.9%). Gender was not recorded for 1 patient (0.1%). The mean age was 69 years (range 29-96 years; 95% CI 67.8-70.2). There were 243 (37.5%) cases of rectal cancer and 405 (62.5%) cases of colon cancers. Of the 243 patients with rectal cancer, 30 (12.3%) died. Among the 405 patients with colon cancer, 38 (9.4%) died. The mean follow-up period for the patients with a known live follow-up was 383 days (95% CI 276.76-399.2). Patient characteristics are summarized in Table 2.

Table 2. Patient characteristics by cancer type (N=648).

Patient characteristics	Colon cancer cohort (N=405), n (%)	Rectal cancer cohort (N=243), n (%)
Age (years)		
≤60	92 (22.7)	53 (21.8)
61-65	52 (12.8)	32 (13.2)
66-70	52 (12.8)	48 (19.8)
71-75	57 (14.1)	46 (18.9)
76-80	65 (16.0)	30 (12.3)
81-84	51 (12.6)	12 (4.9)
≥85	36 (8.8)	22 (9.1)
Gender		
Male	229 (56.6)	146 (60.1)
Female	176 (43.4)	96 (39.5)
Unknown gender	0 (0)	1 (0.4)
Race/ethnicity		
Caucasian	173 (42.7)	104 (42.8)
Black	25 (6.2)	8 (3.3)
Asian	20 (4.9)	8 (3.3)
Mixed	2 (0.5)	2 (0.8)
Other	41 (10.1)	26 (10.7)
Unknown	144 (35.5)	95 (39.1)
Cancer site[a]		
Proximal colon	169 (41.7)	N/A[b]
Transverse colon	39 (9.6)	N/A
Distal colon	186 (45.9)	N/A
Unspecified colon	11 (2.7)	N/A
Rectosigmoid junction	N/A	31 (12.8)
Rectum	N/A	212 (87.2)
Cancer stage[c]		
I	60 (14.8)	44 (18.1)
II	65 (16.0)	43 (17.7)
III	159 (39.3)	94 (38.7)
IV	73 (18.0)	36 (14.8)
Unknown	48 (11.9)	26 (10.7)
Histology		
Adenocarcinoma	364 (89.9)	208 (85.6)
Mucinous adenocarcinoma	16 (4.0)	7 (2.9)
Signet ring cell carcinoma	2 (0.5)	0 (0)
Neuroendocrine tumor	4 (1.0)	3 (1.2)
Liposarcoma	1 (0.2)	0 (0)
Other carcinoma	11 (2.7)	14 (5.8)
Unknown histology	7 (1.7)	11 (4.5)
Tumor differentiation		

Patient characteristics	Colon cancer cohort (N=405), n (%)	Rectal cancer cohort (N=243), n (%)
Well differentiated (G1)	7 (1.7)	3 (1.2)
Moderately differentiated (G2)	264 (65.2)	162 (66.6)
Poorly differentiated (G3)	87 (21.5)	41 (16.9)
Anaplastic (G4)	1 (0.2)	1 (0.4)
Cannot be assessed (GX)	6 (1.5)	5 (2.1)
Unknown differentiation	40 (9.9)	31 (12.8)
Treatment type		
Active monitoring	4 (1.0)	10 (0.4)
Chemotherapy	71 (17.5)	56 (23.0)
Palliative care	15 (3.7)	7 (2.9)
Surgery	292 (72.1)	140 (57.6)
Radiotherapy	2 (0.5)	21 (8.6)
Unknown treatment	21 (5.2)	18 (7.4)
Treatment intent		
Adjuvant	21 (5.2)	7 (2.9)
Curative	268 (66.2)	128 (52.6)
Diagnostic	6 (1.5)	5 (2.1)
Monitoring	4 (1.0)	1 (0.4)
Neoadjuvant	6 (1.5)	7 (2.9)
Palliative	30 (7.4)	25 (10.3)
Radical/curative	3 (0.7)	17 (7.0)
Unknown	67 (16.5)	53 (21.8)

[a]Proximal colorectal cancers are defined as cancers arising from the caecum up to and including the splenic flexure [36]. Cancers of the transverse colon are identified with the International Classification of Diseases for Oncology-10 code C184, which reflects "malignant neoplasms of the transverse colon." Distal cancers are those arising in the descending (C186) or sigmoid (C187) colon.

[b]Not applicable.

[c]Dukes' staging was reconciled with the TNM staging system as follows [37]: Dukes' A or TNM stage T1-T2, N0, M0 = Stage I; Dukes' B or TNM stage T3-T4, N0, M0 = Stage II; Dukes' C or TNM stage T any size, N1, M0 = Stage III; Any metastasis = Stage IV.

Diagnostic Delays

Diagnostic delays were calculated for 361 (89.1%) of the 405 patients with colon cancer and 216 (88.8%) of the 243 patients with rectal cancer. The median diagnostic delay was 34 days for both cancers (IQR 19-59 and 22-63 days, respectively). An analysis of the relationship between the cancer stage and diagnostic delay was performed. Diagnostic delays were right skewed and not normally distributed following the Kolmogorov-Smirnov test (P=.04); therefore, a Kruskal-Wallis H test was utilized. There was no correlation between diagnostic delay and cancer stage in the patients with colon cancer (χ^2_4=6.9, P=.14) or rectal cancer (χ^2_4=4.7, P=.32).

Referral Delay

Referral delay was calculated for 390 (96.3%) of the 405 patients with colon cancer and 238 (97.9%) of the 243 patients with rectal cancer. The median referral delay was 10 days (IQR 4-15 days) for patients with colon cancer and 11 days (IQR 6-16 days) for patients with rectal cancer. The majority of the patients with colon cancer (285/390, 73.1%) and rectal cancer (172/238, 72.3%) experienced a referral delay of less than 2 weeks. However, 13.1% (51/390) of the patients with colon cancer and 13.4% (32/238) of the patients with rectal cancer experienced a referral delay of at least one month.

Treatment Delays

Treatment delays were calculated for 327 (80.1%) of the 405 patients with colon cancer and 208 (85.6%) of the 243 patients with rectal cancer. The median treatment delay was 31 days (IQR 19-55 days) for patients with colon cancer and 42 days (IQR 27-106 days) for patients with rectal cancer. In all, 16.5% (54/327) of the patients with colon cancer and 11.5% (24/208) of the patients with rectal cancer experienced a treatment delay of <2 weeks. The majority of the patients with colon and rectal cancer experienced a treatment delay of ≥4 weeks (168/327, 51.4% and 142/208, 68.3%, respectively). Treatment delays displayed a similar skewness to diagnostic delays and were not significantly associated with cancer stage in either patients with colon or patients with rectal cancer (χ^2_4=8.6, P=.07 and χ^2_4=9.4, P=.054, respectively).

Colon Cancer Delay and Survival

The log-rank test indicated no difference between long-term survival and diagnostic delay quartile (Figure 3, χ^2_3=1.5, *P*=.68). Diagnostic delay was a nonsignificant predictor of survival in the multivariate Cox regression model (*P*=.23). Additionally, there was no significant relationship between treatment delay quartile and survival in the log-rank test (Figure 4, χ^2_3=0.6, *P*=.90) or Cox regression model (*P*=.33). Tumor grade was an independent predictor of survival in both diagnostic and treatment delay models (*P*=.005 and *P*=.02, respectively), as was the tumor stage (*P*<.001 for both models).

Figure 3. Kaplan-Meier plot illustrating the survival function by diagnostic delay quartile with time.

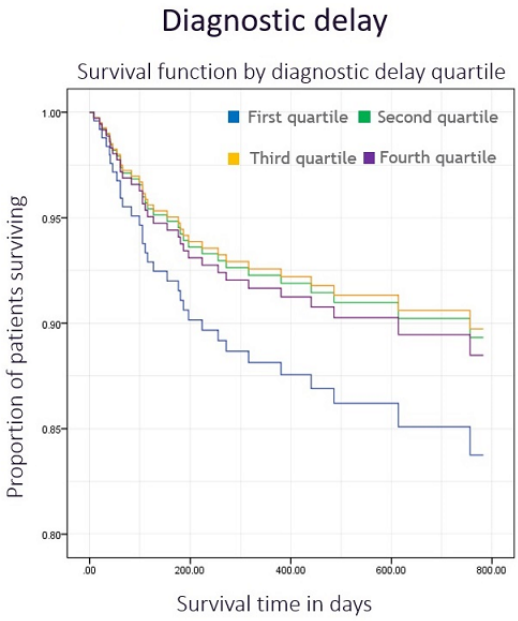
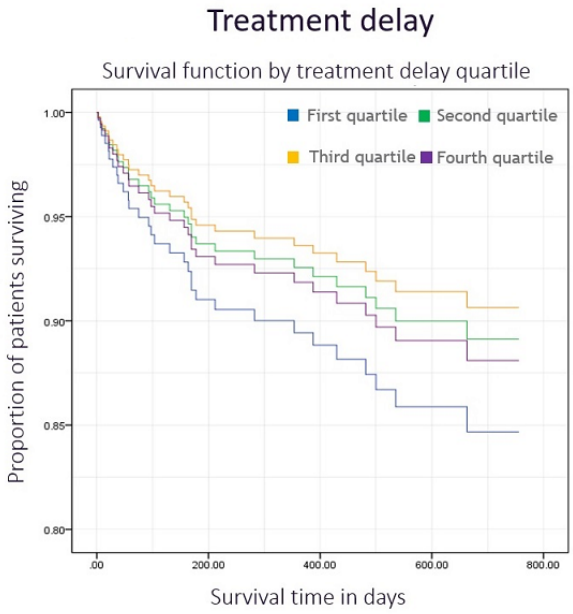


Figure 4. Kaplan-Meier plot illustrating the survival function by treatment delay quartile with time.



Rectal Cancer Delays and Survival

The relationship between diagnostic delay and survival in rectal cancer appears nonsignificant in the log-rank test (χ^2_3=5.5, *P*=.14). However, adjusting for covariates in the Cox regression model reveals a significant relationship between delay quartile and survival (*P*=.03). Patients with the shortest delays were significantly less likely to die than those with the longest delays (hazard ratio 0.165, 95% CI 0.044-0.616; *P*=.007). Figure 5 illustrates these results. Tumor stage remained significant (*P*=.04); however, tumor grade did not (*P*=.06). Treatment delays did not affect survival in either the log-rank test (χ^2_3=0.1, *P*=.99) or the Cox regression model (*P*=.98). Figure 6 illustrates the survival function by treatment delay quartile. None of the covariates analyzed were significant in this model, except for tumor stage, which achieved a borderline result (*P*=.053).

Figure 5. Kaplan-Meier plot illustrating the survival function by diagnostic delay quartile with time.

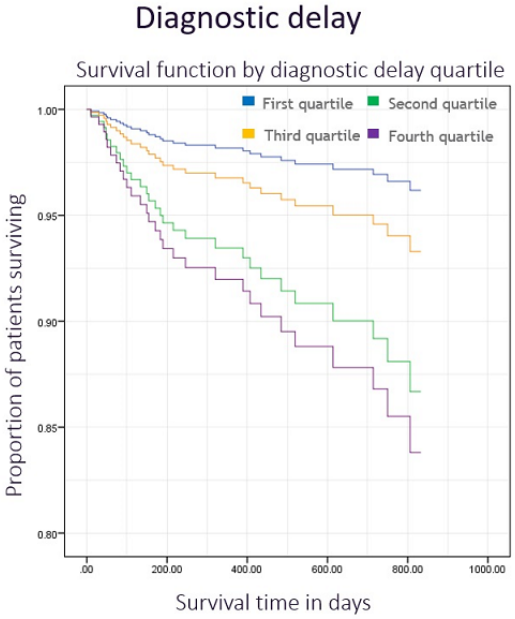
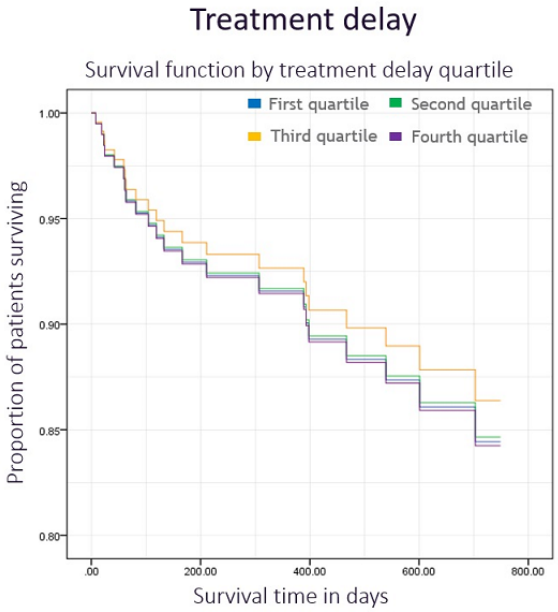


Figure 6. Kaplan-Meier plot illustrating the survival function by treatment delay quartile with time.



Total Delay, Referral Delay, and Other Delay Subdivisions

In the analysis of total delay, treatment modality, intent, and setting were not included as covariates. Total delays were not significantly related to survival in either patients with colon cancer (*P*=.75) or in patients with rectal cancer (*P*=.35). Similarly, referral delays did not affect survival in either patients with colon cancer or patients with rectal cancer (*P*=.74 and *P*=.25, respectively). A summary of the bias and covariate adjusted analyses is shown in Table 3. However, the delay between the first hospital appointment and the date of diagnosis significantly affected the survival in patients with rectal cancer (Figure 2). Patients with the shortest delays were significantly less likely to die than those with the longest delays (hazard ratio 0.325, 95% CI 0.107-0.990; *P*=.048).

Table 3. Patient numbers and significance values for total delay, referral delay, and delay subdivision analyses.

Delay	Patients with colon cancer (N=405)		Patients with rectal cancer (N=243)	
	Patients, n (%)	*P* value	Patients, n (%)	*P* value
T1a[a]	399 (98.5)	.12	243 (100)	.64
T1b (referral delay)[b]	390 (96.3)	.74	237 (97.5)	.25
T1c[c]	344 (84.9)	.29	213 (87.6)	.048
T2a[d]	298 (73.5)	.56	187 (76.9)	.25
T2b (surgical patients only)[e]	237 (58.5)	.89	128 (52.7)	.69
Ttotal (total delay)[f]	375 (92.6)	.75	222 (91.3)	.35

[a]Delay between referral for symptoms and receipt of the referral by the hospital.

[b]Delay between referral based on symptoms and date of hospital appointment (referral delay).

[c]Delay between date of hospital appointment and date of diagnosis.

[d]Delay between date of diagnosis and multidisciplinary meeting date.

[e]Delay between date of diagnosis and admission for surgery.

[f]Delay between referral based on symptoms and date of the first surgical procedure or treatment (total delay).

Sensitivity Analyses

There was good concordance between all models except for the effect of diagnostic delays on survival in patients with rectal cancer. A borderline result was obtained when censored patients were excluded (*P*=.052). Neither stratifying the models by cancer stage nor excluding covariates related to cancer behavior substantively altered the results. The results of the sensitivity analyses are shown in Table 4.

Table 4. Results of the sensitivity analyses.

Types of sensitivity analyses and delays	Patients with colon cancer (*P* value)	Patients with rectal cancer (*P* value)
Sensitivity analysis 1: Excludes patients who do not have either a known follow-up date or date of death		
Diagnostic delay	.10	.05
Treatment delay	.09	.34
Sensitivity analysis 2: Stratifies colon and rectal cancer cohorts by cancer stage		
Diagnostic delay	.24	.01[a]
Treatment delay	.12	.72
Sensitivity analysis 3: Repeats analyses after excluding tumor stage and grade		
Diagnostic delay	.64	.03[b]
Treatment delay	.70	.58

[a]The statistically significant relationship between diagnostic delay and survival in the rectal cancer cohort remained consistent when stratifying by cancer stage, where the first quartile group was significantly less likely to die than the fourth quartile group (hazard ratio 0.141, 95% CI 0.034-0.590; *P*=.01).

[b]When excluding tumor grade and stage, patients with the shortest delays were significantly less likely to die than those with the longest delays (hazard ratio 0.165, 95% CI 0.044-0.616, *P*=.03).

Discussion

Summary and Interpretation of Findings

This observational study investigated the relationship between health care provider delays and survival of patients with CRC. The median diagnostic delays were 34 days for both cancer types, while the median treatment delays for the patients with colon cancer and rectal cancer were 31 and 42 days, respectively. Contrary to the stated hypothesis, the health care provider delays had no effect on survival in this cohort.

Although longer diagnostic delays were associated with worse survival in the rectal cancer cohort, this relationship was statistically nonsignificant when restricting the analysis to patients with a known follow-up date or date of death. Further, although it is necessary to censor the patients who emigrate, are lost to follow-up, or for whom no date of death is recorded but who have not yet had a follow-up appointment, the nonsignificant result in this model may indicate that a disproportionately greater number of patients with shorter diagnostic delays were censored in the initial analysis. Considering this limitation, any conclusion regarding diagnostic delays in the rectal cancer cohort should be made tentatively.

Nonetheless, analysis of the delay subdivisions indicated that the delay between the first hospital appointment and diagnosis significantly affects survival. This may suggest that the effect on outcomes is due to unmeasured confounders relating to the nature of a patient's diagnostic pathway. For example, frail patients may receive a computed tomography colonoscopy prior to an endoscopic procedure. These patients could experience longer diagnostic delays but are more likely to die. Future research should therefore adjust for the nature of the diagnostic testing performed, as this may confound the diagnostic interval and survival, thereby creating a spurious positive correlation between diagnostic delay and risk of death [12,13].

Previous studies have shown longer diagnostic delays in patients with colon cancer [38,39], which have been attributed to the symptoms being presented vaguely [40]. However, median diagnostic delays were the same for both cancers in this study. This may indicate a more homogenous group regarding presenting symptoms. Treatment delays were longer for patients with rectal cancer, and this is likely due to the higher incidence of neoadjuvant therapy [41], which requires oncological referral.

Risk of death increases for each stepwise progression in the cancer stage [42,43] and as expected, tumor stage was a significant predictor of survival in most models. Similarly, tumor grade was a significant covariate in many models; however, often with a smaller effect in increasing the hazard ratio of death. This may be due to the relative inconsequence of tumor grade in early-stage CRC. O'Connell et al [43] investigated the effect of tumor grade on survival by cancer stage and found a significant relationship between grade and survival in TNM stages II to IV but not stage I.

Previous literature has produced mixed results regarding the association between diagnostic delay and tumor stage. Ramos et al [44] found that delay was not significantly correlated with tumor stage. This finding was corroborated by several other researchers [45,46]—though not all the previous studies—with some researchers finding an inverse association between diagnostic delay and tumor stage [14,24,38]. Our study demonstrates no significant relationship between tumor stage and health care provider delays, contending the previously held notion that tumor stage is an intermediate factor between delay and survival [13].

Comparison of the Main Findings with Previous Works

The paucity of evidence for a relationship between delay and survival in this study supports the results of previously published studies [22,47,48]. In a 2007 systematic review, 20 of the 26 studies found no association between delays and survival of patients with CRC [49]. Four studies found that longer delays were associated with favorable prognoses, with only 2 studies demonstrating an inverse relationship with worse outcomes. Studies that reported that longer delays lead to favorable outcomes likely fail to account for tumor aggressiveness either by restricting analysis to nonemergent cases [18] or by accounting for the confounding factor of the tumor grade [44,49].

There have also been various approaches to data analysis in this field. In a general practitioner–based study of 268 patients, a Danish group treated diagnostic delay as a continuous variable and conducted a restricted cubic spline regression analysis. This analysis revealed that patients who experienced >5 weeks of delay had a greater risk of death [13]. The study collected delay data retrospectively, making recall and information bias difficult to avoid. Additionally, they were unable to account for the tumor grade and considered colon and rectal cancers together.

A subsequent study of 958 patients with CRC by Murchie et al [35] also used restricted cubic spline regression analysis, which was adjusted for grade, symptoms, emergencies, and place of presentation. Furthermore, they used registry data and explored the relationship between delay and survival separately for colon and rectal cancers. They found no association between health care provider delay and the survival of patients with CRC.

Such conflicting results indicate that the relationship between health care provider delay and survival of patients with CRC remains uncertain [18]—an issue compounded by the ethical limitations of conducting a randomized control trial. Despite this, the evidence against the influence of delay on survival has remained consistent. However, it is important to note that median delays of 31-42 days for diagnosis and treatment in this study represented a relatively short period of time. It was therefore not possible to investigate the effect of lengthy delays on the survival of patients with CRC. Future research in settings wherein it is possible to measure the diagnostic delay from a patient's subjective experience of symptoms or in areas with longer treatment delays may capture a relationship in the context of extended delays and survival.

Few studies have explored the effect of delays on postoperative outcomes such as readmission or complication rates. Psychosocial factors such as quality of life and anxiety are seldom assessed. Such outcomes should increasingly become the focus of future research.

Context of the Findings

Timeliness and quality are not necessarily congruent and expediting the care of patients may be detrimental in certain circumstances. For example, McConnell et al [50] found that patients with CRC achieving a 4-week benchmark between diagnosis and surgery were less likely to have had preoperative staging. Although longer delays are undesirable, the 2-week wait pathway has not appreciably improved the outcomes and has increased the wait times for routine referrals, which remains the most common pathway for CRC diagnosis [51]. However, there is evidence that diagnosing CRC prior to symptom onset considerably improves survival. Annual occult blood tests reduce the 13-year cumulative mortality by 33% [52], and a single screening by sigmoidoscopy achieves similar results [53]. Public health initiatives should focus on improving compliance with screening programs, wherein prompt intervention improves outcomes.

Strengths and Limitations

The Kaplan-Meier and Cox regression methods assume that censoring is independent of a patient's risk of death. This may not have been the case, given the change in the significance between diagnostic delay and survival in the sensitivity analysis, which excluded censored patients. This suggests that the initial

model underestimated the survival of patients with the shortest delays. However, others utilizing this technique have found the opposite, with censored patients being less likely to die, and therefore may have overestimated mortality in their analyses [12,54,55]. The magnitude and direction of this bias is therefore difficult to predict.

It was not possible to consider the initial presenting symptoms in this study. However, rectal bleeding has been associated with both poor [45] and improved [22] outcomes. Pruitt et al [14] stratified their cohort into 4 groups representing common presenting symptoms and found that this made no difference to their results. The effect of symptoms on survival is likely mediated by the cancer stage, which has been controlled for in this study.

There were also limitations associated with utilizing registry data. First, an analysis of patient delay was not possible, which is defined as the time between a patient noticing symptoms and presenting these symptoms to the general practitioner. However, patient delay data is often accrued through interviews or questionnaires, making recall bias difficult to avoid [18]. Even in prospective studies utilizing a structured interview format, there is often disagreement between patient responses and the clinical history [56,57]. Conclusions regarding patient delays should therefore be made cautiously. Secondly, survival should ideally be measured from the date of the first symptom presentation for diagnostic delay analysis [58,59]; however, this was not recorded in the Somerset Cancer Register. Finally, there was a short mean follow-up period of survival in this study, indicating that the conclusions are most relevant to 1-year survival rates. Continued follow-up of patients would allow for 5-year and 10-year survival trends to be analyzed in the future.

Despite these limitations, this study has several strengths. Registry data was entered synchronously with clinical practice, making this analysis resilient to recall bias [18]. Utilizing a population-based sample not restricted to those in tertiary care ensures more generalizable results. Unlike many previous studies, tumor aggressiveness and emergencies were controlled for, thereby minimizing the wait-time paradox. This study adjusted for several important biases and considered patients with colon cancer and rectal cancer separately. The Somerset Cancer Register data allowed an analysis of delay subdivisions, which ensured that important trends were not subsumed in a monotonic or a dichotomized delay model, while allowing clinically relevant conclusions about delays and their causes to be made. Finally, sensitivity analyses ensured the internal validity of the results.

Conclusion

This observational study investigated the effect of health care delays on survival in patients with CRC. It is reasonable to conclude that the relatively short health care provider delays experienced by patients in the United Kingdom are not likely to affect the outcomes. Promoting effective screening programs should remain a high public health priority.

Authors' Contributions

AA was involved in data acquisition, study design, statistical analysis, and write-up of this manuscript. CA was involved in data acquisition, preprocessing, and a full review of the work. PZ was involved in the study design and many of the research study's conclusions.

Conflicts of Interest

None declared.

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Abbreviations

CRC: colorectal cancer
E(s): exponential distribution of the sojourn time

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Original Paper

Exploring the Usage Intentions of Wearable Medical Devices: A Demonstration Study

Chiao-Chen Chang[1], PhD

Executive Master Program of Business Administration in Biotechnology, College of Management, Taipei Medical University, Taipei City, Taiwan

Corresponding Author:
Chiao-Chen Chang, PhD
College of Management
Taipei Medical University
11F, No 172-1, Sec 2, Keelung Rd
Da an Dist
Taipei City, 10675
Taiwan
Phone: 886 266382736 ext 1128
Email: ariel66@tmu.edu.tw

Abstract

Background: In the face of an aging society, an immediate and preventive medical system urgently needs to be established, and the application of wearable devices is essential. However, the application of smart medical care in Taiwan is still not widespread, and few studies have explored the related issues of wearable medical device usage. Thus, determining the success of a wearable medical device mainly depends on the degree of user adoption and use.

Objective: The purpose of this study was to examine the factors that influence the intention to use wearable medical devices.

Methods: This study applied the unified theory of acceptance and use of technology (UTAUT) to build a comprehensive model that explains intentions to use wearable medical devices.

Results: The research findings showed that health consciousness and trust were the strongest predictors of intentions to use wearable medical devices.

Conclusions: The results reveal the magnitudes of the impacts of the variables in a well-accepted revised UTAUT model in the context of the medical industry, particularly in the setting of wearable medical devices. Several important implications for academics and industry decision-makers can be formulated from these results.

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KEYWORDS

wearable medical device; unified theory of acceptance and use of technology; usage intention; health consciousness; trust

Introduction

Background

With the emergence of various wearable devices in recent years, the concept and statement of “smart medical care” are gradually emerging in medical innovation. The development of smart medical care has a long history. In addition, with the advancement and rapid rise of the internet of things (IoT) technology, a large amount of medical information has been exchanged and analyzed, which has become the basis of medical big data. Artificial intelligence, which has developed rapidly in recent years, has been introduced as an inductive use of these data. After the combination of the IoT and artificial intelligence, instant mobile medical care emerged, which is the core concept of smart medical care.

Wearable devices can detect the physical condition, use real-time perception, and compare and analyze a large amount of data for analysis, interpretation, and response and can then select the most appropriate current processing and support. Through smart medical care, many dilemmas faced by the current medical system have been resolved. The global market for wearable medical devices is expected to increase from US $6.22 billion in 2017 to nearly US$ 14.41 billion in 2022 at a compound annual growth rate of 18.3% (2017-2022) [1]. Furthermore, the emerging market demand introduced by smart health care is also a big business opportunity.

Further, according to Gartner's latest forecast [2], by 2020, global end user spending on wearable devices will reach US $51.545 billion, up 27% from US $40.581 billion in 2019. Among them, consumers will spend the most on smartwatches and smart clothing, growing 34% and 52%, respectively. In the past few years, the improvement of sensor accuracy, the development of miniaturization, and better user data protection have made more consumers willing to buy wearable devices. As for hardware manufacturers, they are focusing on sensors that are smaller and smarter, so that the sensors built into wearable devices can obtain more accurate readings, and more usage examples continue to appear. Previous literature has focused on a single form of smart medical service, such as discussing the application of wearable medical services from the perspective of developers [3]. There are few studies considering wearable medical devices from the perspective of users. To fill the abovementioned research gaps, this study developed and validated empirically a model that explicates users' intentions to use wearable medical devices. Specifically, it revisits a popular contemporary adoption theory (unified theory of acceptance and use of technology [UTAUT] [4]) by augmenting it to better capture wearable medical device environments. Recently, Zhou [5] added a health consciousness construct to the UTAUT in a wearable medical device context. Zahir and Gharleghi [6] also effectively introduced an innovation-related construct (trust), which influences users to adopt the technology. Thus, these two constructs are especially relevant when identifying users' characteristics regarding the adoption of information technology (IT).

Hence, this study augments the application of the UTAUT and adds two individual factors (health consciousness and trust) to explain users' intentions regarding wearable medical devices. The purpose of this study was to combine the UTAUT and the two specific factors to improve the IT adoption model and explain the users' intentions for wearable medical devices.

Literature Review

Wearable Medical Devices

In the face of an aging society, an immediate and preventive medical system urgently needs to be established, and the application of wearable devices is essential. Wearable devices can help patients to detect more serious medical conditions early and then provide early assistance and warning to patients with diseases such as diabetes. This provides an opportunity for people to analyze solutions in health care.

Wearable medical devices include a cardiac sensing electrode, a behavior electrode, a user interface, and a sensor. Indeed, wearable medical devices are designed to diagnose, prevent, and avoid diseases. According to the Food and Drug Administration (FDA), a medical device should not achieve its purposes through chemical action within or on the body, and an agent achieving its purpose through chemical action is termed as a drug.

Conceptual Model

Revisiting the Main UTAUT

The UTAUT [4] is a technology acceptance model that aims to provide a rough framework specifically designed to explain technology acceptance and use. In particular, this theoretical framework introduces the following two main aspects regarding its predecessor: (1) redefining the four explanatory variables included in the original UTAUT of performance expectancy (PE), effort expectancy (EE), social influence (SI), and facilitating conditions (FC) to adapt them to the consumption context; and (2) identifying three additional key constructs from prior research on both general adoption and use of technologies and consumer adoption and use of technologies. The main constructs in the UTAUT are as follows: PE, EE, SI, and FC. Despite its recent adoption in the literature, the UTAUT has already been tested in some studies that have confirmed its validity to explain technology adoption in consumption contexts, including the wearable medical device industry [7].

Intention to Use

Intention to use refers to "the degree to which a person has formulated conscious plans to perform or not perform some specified future behavior" [8]. Furthermore, Venkatesh et al [4] indicated that intention to use is the main indicator of the effectiveness of an information system. The usage intention of wearable medical devices is also a form of information system adoption.

Performance Expectancy

PE refers to an individual's perception that information service (IS) facilitates the completion of a task [4], that is, it means the degree to which users perceive that using wearable medical devices will enable them to achieve improved health management. PE is of direct relevance to the use of wearable devices for medical management in life. This is because users rely on the use of wearable devices to access adequate information. As a result, this study assumed the following hypothesis: hypothesis 1 (H1), PE has a positive influence on the intention to use wearable medical devices.

Effort Expectancy

EE is defined as an individual's evaluation of the effort necessary to complete a task using a given IS [4]. Venkatesh et al [4] viewed EE as the degree of ease associated with the use of an information system. EE is also based on the idea that there are relationships among the effort put forth at work, the performance achieved from that effort, and the rewards received from the effort [9]. Thus, this study proposed the following hypothesis: hypothesis 2 (H2), EE has a positive influence on the intention to use wearable medical devices.

Social Influence

SI refers to how an individual perceives the degree of approval of a certain behavior from important referents [4,10]. In addition, SI has a strong origin in attitudinal-behavioral theories (eg, Theory of Reasoned Action [11]), although it was not present in the preceding theories of IS adoption, such as the technology acceptance model (TAM) [12]. Taylor and Todd [13] indicated that peer influence from friends and classmates and superiors'

influence from professors indirectly influenced behavioral intention through the mediator of subjecting norms. Using the medical wearable device would be affected by influences from superiors or important people; therefore, the following hypothesis was proposed: hypothesis 3 (H3), SI has a positive influence on the intention to use wearable medical devices.

Facilitating Conditions

FC refers to the degree to which an individual believes that a technical infrastructure exists to support technology use [14]. In commercial settings, FC represents the extent to which a consumer believes that resources exist, and they facilitate the task completion while adopting IS [13]. This construct was introduced more recently in the IS adoption literature to overcome the narrower focus of previous research almost exclusively on a user's internal belief system [4]. Hence, the following hypothesis was proposed: hypothesis 4 (H4), FC has a positive influence on the intention to use wearable medical devices.

Health Consciousness

Health consciousness refers to the degree to which health concerns are integrated into a person's daily activities and health conscious people are aware of and concerned about their wellness, resulting in better motivation to improve or maintain their health [15]. That is, health consciousness is the degree to which health concerns are integrated into a person's daily actions [16]. Health conscious people are aware of and concerned about their wellness; therefore, they are motivated to improve and/or maintain their health. The following hypothesis was proposed: hypothesis 5 (H5), health consciousness has a positive influence on the intention to use wearable medical devices.

Trust

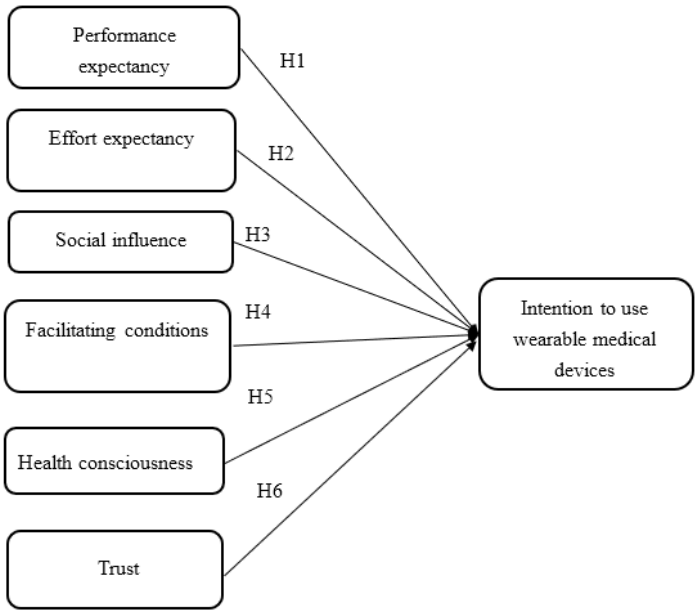
Trust refers to the belief that someone or something is honest, reliable, good, and operative or the wish to depend on someone or something for security. It represents the intention of a party to be vulnerable to the actions of other parties [17]. Trust becomes a critical issue for research because it plays a role in building satisfied and expected outcomes as a result of a transaction [18]. In the context of mobility, trust has played an important role in explicating the adoption of mobile payment [19]. Similar to other online contexts, trust is a relevant determinant of adoption in the wearable medical device scenario owing to the impersonal nature of the mobile internet environment and the uncertainties involved in such transactions. In line with this assumption, this study proposed the following hypothesis: hypothesis 6 (H6), trust has a positive influence on the intention to use wearable medical devices.

Methods

Research Model

The conceptual model for the study was developed from the researcher's view of the interactions that could exist between the variables of the study based on a review of the literature. The model proposes a direct relationship between the independent variables and the dependent variable. Specifically, it is assumed that there is a relationship between PE and the use of wearable medical devices. In addition, there could be a link between EE and the use of wearable medical devices. It is also evident from the model that a relationship could be proposed between FC and the use of wearable medical devices. In addition, the model also seeks to test the influence of the three independent variables on the dependent variable (Figure 1).

Figure 1. Research model.



Instrument Development

For data collection, this study developed a self-administered online survey. Measurement scales for all construct items were taken from existing scales based on prior work [4,20], with modified wordings to adapt the items to the topic area. In the pretest phase, the questionnaire was reviewed by a small group of IS faculty and management students. The scales were modified as a result of their suggestions. The questionnaire was

then tested with a sample of medical and business school students and personnel. This resulted in further modifications to the questions. The purposes of these pretests were to confirm that relevant aspects were included and to enhance the clarity and readability of the questionnaire.

Measurements

To ensure the content validity of the scales used, the items selected should represent the concept around which generalizations are to be made. Items selected for the constructs were therefore largely adapted from prior studies [4] to ensure content validity. In this study, the constructs of the UTAUT were taken from the study by Venkatesh et al [4] and modified to reflect the utility of wearable medical devices, whereas the constructs of health consciousness and trust were taken from the studies by Ahadzadeh et al [15] and Safa and Solms [21].

The participants were instructed to rate each item of the dependent variables on a 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree).

Procedures and Participants

This study posted an electronic survey through an online survey platform (Survey Cake) to obtain a sample from the mass population of wearable medical device users. The wearable medical devices included devices and technologies (eg, wearable glucose monitoring and drug delivery devices, activity monitors, smart clothing, smart equipment, wearable vital sign monitors, and smartwatches). Using Facebook, a popular social networking site, potential participants were chosen to complete surveys. After clicking on the link and entering the questionnaire website, participants were considered wearable medical device users or potential users.

Data Collection and Samples

An online self-administered survey questionnaire was considered an appropriate instrument to identify wearable medical device users. All questions in the questionnaire were measured on a 5-point Likert scale, ranging from “1” (strongly disagree) to “5” (strongly agree). The time required to complete the questionnaire was almost 3 to 5 minutes. The final questionnaire of items is presented in Multimedia Appendix 1 [4,20,21].

All subjects participated in the study voluntarily during the period from July 20 to August 20, 2019. There were 452 participants overall (252 male and 200 female participants). The mean age was 47.8 years, and participants aged 39 to 55 years accounted for 53.1% (240/452) of the study sample. Most of the participants (344/452, 76.1%) stated that they were familiar with the term “wearable medical devices” prior to completing the survey.

Data Analysis

Structural equations among latent constructs were examined to test the conceptual structural equation model (SEM). The SEM was used to analyze causal models and simultaneously estimate a series of interrelated dependence relationships. Thus, data analysis was carried out using structural estimation modeling. Before this study tested the research model, SPSS 25.0 for Windows (IBM Corp) was used to show the important descriptive information on demographic variables, including participant characteristics such as gender, age, and educational background. This information also included behaviors related to the use of wearable medical devices, such as the time spent on the internet, the preferred online medical platform provider, and the frequency of using wearable medical devices. Model evaluation involved a two-step analysis [22] using the software IBM Amos 21.0. For this purpose, the author first built a measurement model using confirmatory factor analysis for the model to check its fit and then built the SEM and examined the hypothesized causal paths among the constructs by performing a simultaneous test. This helped to observe whether the conceptual framework had provided an acceptable fit to the empirical data.

Measurement Model

The validity of the measurement model was evaluated by investigating convergent validity, discriminant validity, and reliability. Structural equation modeling has been used to evaluate the plan’s research model and hypotheses. Simultaneously, for assessing the reliability of measurement items, this research computed composite construct reliability coefficients. Therefore, all the average variances extracted exceeded 0.50, all composite reliabilities were larger than 0.70, the factor loadings of all items exceeded the recommended level of 0.60, and all values were significant at .001, demonstrating that the scales had good convergent validity. In addition, the Cronbach α of the seven constructs ranged from .81 to .89. All composite reliabilities were larger than 0.70, displaying good reliability [23]. The results confirmed good reliability (Table 1).

Discriminant validity is shown when (1) measurement items load more strongly on their assigned construct than on the other constructs in a confirmatory factor analysis and (2) the square root of the average variance extracted of a construct is larger than its correlations with the other constructs [24]. To test the discriminant validity, this research computed the square root of the average variance extracted and factor correlation coefficients. For each factor, the square root of the average variance extracted should be greater than its correlation coefficients with other factors to show that the scale has a worthy discriminant validity [25]. As shown in Table 2, all constructs had an average variance extracted value higher than the threshold of 0.50, confirming the convergent validity of the constructs.

Table 1. Loading and composite reliability values for the items.

Item	Loading	Composite reliability
Performance expectancy (PE)		0.81
PE1	0.80	
PE2	0.82	
PE3	0.81	
PE4	0.84	
Effort expectancy (EE)		0.84
EE1	0.79	
EE2	0.86	
EE3	0.84	
EE4	0.81	
Social influence (SI)		0.86
SI1	0.83	
SI2	0.89	
SI3	0.89	
Facilitating conditions (FC)		0.83
FC1	0.82	
FC2	0.80	
FC3	0.85	
Health consciousness (HC)		0.89
HC1	0.90	
HC2	0.89	
Trust (TR)		0.87
TR1	0.86	
TR2	0.88	
TR3	0.88	
Intention to use (INT)		0.86
INT1	0.87	
INT2	0.80	
INT3	0.81	
INT4	0.86	

Table 2. Correlations between constructs.

Variable[a]	PE[b]	EE[c]	SI[d]	FC[e]	HC[f]	TR[g]	INT[h]
PE	0.73	__[i]	—	—	—	—	—
EE	0.59	0.79	—	—	—	—	—
SI	0.62	0.63	0.84	—	—	—	—
FC	0.58	0.71	0.82	0.82	—	—	—
HC	0.71	0.70	0.77	0.68	0.83	—	—
TR	0.61	0.60	0.71	0.80	0.77	0.84	—
INT	0.58	0.59	0.58	0.75	0.71	0.78	0.78

[a]Values on the diagonal are the square roots of average variance extracted and the off-diagonal values are the correlation coefficients between the construct variables.

[b]PE: performance expectancy.

[c]EE: effort expectancy.

[d]SI: social influence.

[e]FC: facilitating conditions.

[f]HC: health consciousness.

[g]TR: trust.

[h]INT: intention to use.

[i]not applicable.

Structural Model

After the measurement model was satisfied, the structural model was evaluated, and it was well converged. The results investigated the chi-square of the structural model, ratio of chi-square to *df*, goodness-of-fit index, adjusted goodness-of-fit index, normed fit index, comparative fit index, root mean square residual, and root mean square error of approximation. Table 3 presents the model fit indicators with their respective criteria as follows: (1) the comparative fit index was 0.91 (greater than 0.90), (2) the root mean squared error of approximation was 0.03 (smaller than 0.08), and (3) the goodness-of-fit index was 0.93 (greater than 0.90) [25-29]. These indicators were acceptable and showed good fit of the model to the data.

Table 3. Fit statistics.

Fit measures	Sample value	Recommended value
χ^2/df [a]	2.71	<5.0 [26]
Goodness-of-fit index	0.93	≥0.90 [27]
Adjusted goodness-of-fit index	0.94	≥0.90 [27]
Normed fit index	0.91	≥0.90 [25]
Comparative fit index	0.91	≥0.90 [28]
Root mean square error of approximation	0.03	<.08 [29]
Square multiple correlation intention	0.76	N/A[b]

[a]χ^2/df: chi-square distribution is a special gamma distribution, which is one of the most widely used probability distributions in statistical inferences, such as hypothesis testing and CI calculations.

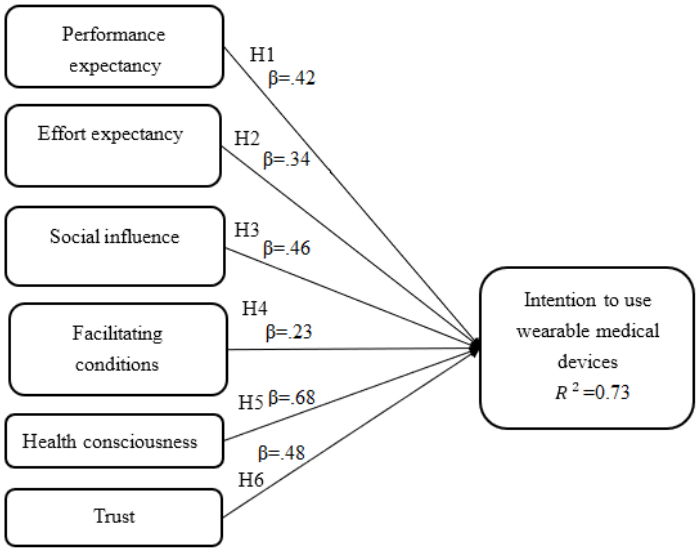
[b]N/A: not applicable.

Hypothesis Testing

Significance was determined by running bootstrapping calculations with 352 samples and no sign variation. Four paths were relevant as shown in Figure 2.

Figure 2 shows the graphic description and the numerical results of the path coefficients. There were significant effects by PE (β=.42; *P*<.001), EE (β=.34; *P*<.001), SI (β=.46; *P*<.001), FC (β=.23; *P*<.001), health consciousness (β=.68; *P*<.001), and trust (β=.48; *P*<.001). The coefficients of these variables were statistically significant (*P*<.001) and had the expected signs (Figure 2). All hypotheses were supported.

Figure 2. Results of the testing model. For all values, *P*<.001.



Results

According to the research findings, the various statistics confirmed that the revised UTAUT model was supported. The study provided some valuable insights into users' intentions of wearable medical devices from their perspectives. PE, EE, SI, FC, health consciousness, and trust greatly influenced the intention to use wearable medical devices.

Discussion

Implications for Research

The results of this study provide several implications for researchers and practitioners. First, the results reveal the magnitudes of the impacts of the variables in the well-accepted revised UTAUT model in the context of the medical industry, particularly in the setting of wearable medical devices. Indeed, PE, EE, SI, and FC lead to positive intentions to use wearable medical devices, supporting H1, H2, H3, and H4.

Second, the impact of SI on adoption intention was more than that of FC, PE, EE, health consciousness, and trust, which is highly relevant in explaining the use of wearable medical devices. This implies that SI is an important factor affecting technology usage intention, that is, SI has positive effects on the intention of using wearable mobile devices. This finding differs from that of most studies on new health care technology acceptance and could reflect the culture, regulations, or rules in the Chinese social context. The result is also consistent with the findings of Ye et al [30]. Compared with another report by the author [31], PE has more positive effects on the intention to use library apps than UTAUT factors. Perhaps in different research backgrounds, the explanatory power of each factor of UTAUT would also be different.

Finally, this study modified the UTAUT by including constructs from health consciousness and trust. H5 and H6 were supported. The path coefficients were relevant, so the additional effects of health consciousness and trust were present. In particular, the degrees of health consciousness and trust were positive for strongly influencing the effects of the usage intention of wearable medical devices. In other words, this study demonstrated that higher health consciousness and trust can lead to much stronger intentions for using wearable medical devices. This study introduced health consciousness and trust as predictors in the Chinese social context to reflect the health care context, and this result is consisted with the findings in the studies by Dou et al [32] and Andrews et al [33].

Implications for Practice

The implications of this study for practice are twofold. One practical implication is that based on the findings of the research model, service providers can make an effort to design a frequently well-used interface in order to enhance users' PE, EE, and FC regarding the intentions of using wearable medical devices. In addition to the roles of PE, EE, and FC in usage intentions, SI has a positive effect on the intentions of using wearable medical devices. Service providers may still encourage users to spread positive word-of-mouth information (eg, positive ratings) to increase peer use. Another practical implication is that the research presented in this paper demonstrates the effects of health consciousness and trust in the use of wearable medical devices. Service providers can consider how to develop a very complicated device that takes into account an individual' s ability and cognition in order to better match the wearable medical device user's needs.

Limitations and Future Research

Although the research findings contribute to the practice of marketing, the study is characterized by several limitations that may provide opportunities for future research. One limitation of this study is that as the sample was obtained by considering wearable devices or websites, the number of participants aged above 50 years was relatively low. Their behavior might differ somewhat from the population average, and this may have biased the results. Another limitation is that our study was limited to the customer base of one country. Further research

is needed to examine differences in the effects of consumer characteristics across cultures.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Final questionnaire.
[DOCX File , 19 KB - ijmr_v9i3e19776_app1.docx]

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Abbreviations

EE: effort expectancy
FC: facilitating conditions
IoT: internet of things
IS: information service
IT: information technology
PE: performance expectancy
SEM: structural equation model
SI: social influence
UTAUT: unified theory of acceptance and use of technology

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