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Contribution of the BioFire® FilmArray® Meningitis/Encephalitis Panel: Assessing Antimicrobial Duration and Length of Stay

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ABSTRACT

Introduction. Traditional evaluation of meningitis includes cerebrospinal fluid (CSF) culture and gram stain to pinpoint specific causal organisms. The BioFire® FilmArray® Meningitis/Encephalitis (ME) Panel has been implemented as a more timely evaluation method. This study sought to assess if the BioFire® ME Panel was associated with a decreased length of stay or decreased antimicrobial duration when used in the diagnosis of meningitis or encephalitis.

Methods. A case, historical-control, chart review was performed on patients admitted to a regional medical center with CSF pleocytosis during Cohort 1 (the year prior to BioFire® ME Panel implementation) and Cohort 2 (the year after BioFire® ME Panel implementation). Length of hospital stay, duration of antimicrobials, and BioFire® ME Panel result were gathered and analyzed.

Results. Average length of stay for both cohorts was about four hospital days. Approximately three-fourths of all patients received antibiotic/antiviral treatment with an average of three days duration. No significant differences were observed between groups. The mean (median) duration of antimicrobials in the year prior to and after the BioFire® ME Panel implementation was 3.6 (3) and 3.1 (2) days, respectively (p = 0.835). The mean (median) length of stay in the year prior to and after the BioFire® ME Panel implementation was 5.8 (4) and 5.4 (4) days, respectively (p = 0.941). Among the patients admitted after the implementation of the BioFire® ME Panel, 4.3 % (n = 2) had a positive bacterial result, 38.3% (n = 18) had a positive viral result, and 57.4% (n = 27) had a negative result. Of the 27 negative results, 77.8% (n = 21) were treated with antimicrobial medication.

Conclusions. This study suggested there is no difference between length of stay or antimicrobial duration in presumed meningitis cases assessed with traditional methods as compared to the BioFire® ME Panel. ***Kans J Med 2019;12(1):1-3.***

INTRODUCTION

Meningitis, defined as inflammation of the leptomeninges surrounding the brain and spinal cord, has a worldwide incidence of about 1.2 million cases yearly.[1] Crucial in the evaluation of meningitis cases is the prompt retrieval of cerebrospinal fluid (CSF) via lumbar puncture to assess for organismal etiology of the infection. Evaluation of CSF includes culture and gram stain to pinpoint specific organisms causing infections. These traditional methods often take several days to render results leading to prolonged use of broad spectrum antimicrobials. Use of meningitis/encephalitis polymerase chain reaction (PCR) panels have been implemented as a supplemental organism identification method.

The BioFire® FilmArray® Meningitis/Encephalitis PCR Panel (BioFire® ME Panel) is a multiplex PCR assay that is able to identify 14 viral, bacterial, and fungal organisms that cause meningitis or encephalitis with high diagnostic specificity and sensitivity.[2] This diagnostic test was similar in price per patient when compared to a classic CSF culture.[3] With the BioFire® ME Panel providing a reliable diagnosis and cost effective method, the question arises about the effect the test has on course of treatment. This study assessed if the utilization of the BioFire® ME Panel was associated with a decrease in length of hospital stay and duration of antimicrobials when used in the diagnosis of meningitis or encephalitis.

METHODS

Design. A case, historical-control study design was used to identify medical records for patients who were hospitalized for suspected meningitis. Cohort 1 included patients who were diagnosed using a cerebrospinal fluid culture and gram stain (CSF culture only: Year 1) during a hospital stay from August 7, 2015 through 2016. Cohort 2 included patients from August 8, 2016 through 2017 who were diagnosed with the BioFire® ME Panel: Year 2.

Participants. Patients were included if they were 18 years or older and had white blood cell counts greater than or equal to 10. Patients were excluded if younger than 18 years of age, received antimicrobial therapy for reasons other than meningitis/encephalitis, taking chemotherapy, diagnosed with sepsis, HIV/AIDS, or other non-infectious neurological disorder or condition (Figure 1).

Data Extraction. The OneChart EHR system was utilized to perform a chart review on patients who qualified for inclusion in the study at a regional medical center. Data regarding length of hospital stay in days (LOS), treatment with or without antimicrobials, which included duration use in days, and results from the BioFire® ME Panel (positive-viral, positive-bacterial, negative, not used) were gathered and entered into a REDCap™ database. REDCap is a secure, web-based application that was developed specifically around HIPAA-security guidelines to house patient data. All information transmission is encrypted to protect the identity of study participants.[4]

Analysis Plan. Data were summarized by cohort: CSF culture: Year 1 versus BioFire® ME Panel: Year 2. Continuous variables included LOS and duration of antimicrobials in days. To determine appropriate statistical tests, data were evaluated for normality with the Kolmogorov-Smirnov test. As data were highly skewed, and

test results were significant, variables did not pass the normality assumption. Therefore, these were summarized with medians and interquartile ranges (IQR). Cohort differences were evaluated with Mann-Whitney U tests. Categorical data included one dichotomous variable, treatment with or without antimicrobials, which were summarized by cohort using frequencies and percentages. Pearson Chi-square test was conducted to compare cohorts by treatment. Where data were sparse, exact testing procedures were utilized. Significant group differences were based on test results of $p < 0.05$. All statistical analyses were conducted with IBM SPSS Statistics, Version 23.

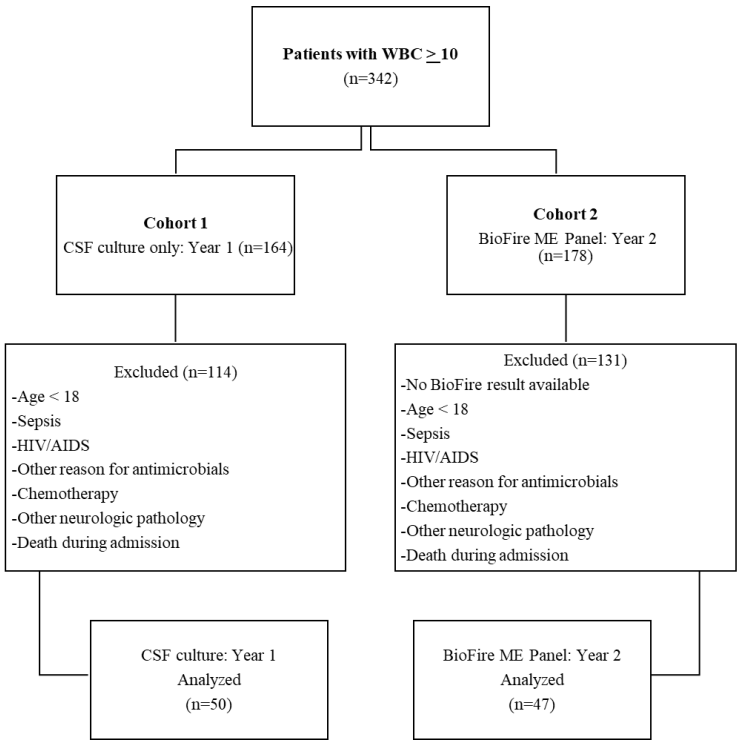

Figure 1. Inclusion and exclusion criteria.

RESULTS

During the two study periods, a total of 342 patients were reported with white blood cell counts greater than or equal to 10: 164 were in Cohort 1 (CSF culture: Year 1), while 178 were in Cohort 2 (BioFire® ME Panel: Year 2; Figure 1). For Cohort 1, 50 patients met all inclusion criteria, with 114 patients being excluded. Of the 178 patients in Cohort 2, 47 met inclusion criteria with 131 patients excluded. Thus, a total of 97 patients were included in the analysis.

Table 1 illustrates group comparisons for hospital stay, antimicrobial treatment, and antibiotic/antiviral duration, along with results for BioFire® ME Panel: Year 2. Groups were similar across all attributes and no significant differences were observed. Average length of stay was about four hospital days per group; approximately three-fourths of all patients received antibiotic/antiviral treatment with an average of three days duration. Among the 47 patients who were evaluated with the BioFire® ME Panel, 4.3% (n = 2) had a positive bacterial result, 38.3% (n = 18) had a positive viral result, and 57.4% (n = 27) had a negative result. Among the 27 participants with a negative panel result, 77.8% (n = 21) were treated with antimicrobial medication for an average of four days (IQR: 2.0, 5.0).

Table 1. CSF culture versus BioFire® ME Panel: hospital stay, antiviral duration, antimicrobial treatment.

		Length of Hospital Stay (days)	Treated with Antimicrobials	Antibiotic/ Antiviral (days)
Diagnostic Instrument	**n**	**Median (IQR)**	**n (%)**	**Median (IQR)**
Cohort 1: CSF Culture only	50	4 (3.0, 7.0)	36 (72.0)	3 (2.5, 5.0)
Cohort 2: Bio-Fire® ME Panel	47	4 (2.0, 7.0)	36 (76.6)	3 (2.0, 5.0)
p-value		0.935*	0.648**	0.571*
BioFire® ME Panel results				
Positive Bacterial	2	6 (3.0, 9.0)	2 (100.0)	6 (3.0, 9.0)
Positive Viral	18	2 (2.0, 5.0)	13 (72.2)	2 (2.0, 4.0)
Negative	27	6 (3.0, 10.0)	21 (77.8)	4 (2.0, 5.0)

IQR: Interquartile ranges
*Mann-Whitney U exact test
**Pearson chi-square exact test

Next, cohorts were compared by antimicrobial status. No significant difference was observed in hospital days between Cohort 1 and 2, regardless of treatment status. For those who were administered antimicrobials, Cohort 1 median LOS was 5.0 (IQR: 3.0, 7.0), while Cohort 2 LOS was 4.5 (IQR: 3.0, 9.0); $p = 0.759$. For those who did not receive antimicrobials, Cohort 1 median LOS was 2.5 days (IQR: 1.0, 4.25), and for Cohort 2 it was 1.0 days (IQR: 1.0, 5.0); $p = 0.851$. Although, sample size was small for each cohort without treatment, n = 14 and 11, respectively.

Further, test results showed a significant difference occurred for length of hospital stay between those who received antimicrobial treatment compared to those who did not: median hospital days with antimicrobials was 5.0 (IQR: 3.0, 7.5) versus without LOS was 2.0 (IQR: 1.0, 4.0); $p < 0.001$. Because data were sparse, a generalized linear model using the Gamma distribution and log link function (to account for the skewed LOS data) was conducted with a bootstrap sample of 5,000 (to account for data sparseness). Results showed that antimicrobial treatment was not a significant predictor of LOS; $p = 0.223$. Thus, the significant difference found above may be due to the wide variability of hospital days among participants, along with the small sample size.

DISCUSSION

The purpose of the current study was to determine if the diagnostic utilization of the BioFire® ME Panel decreased hospital length of stay and antimicrobial duration. This study suggested that utilizing this panel has little impact on the number of hospital days or treatment duration. However, data were sparse, and statistical results were inconsistent regarding length of stay with and without treatment.

These findings may be due to several factors. For example, unintentional inclusion of patients without meningitis or encephalitis (conditions would otherwise explain an elevated WBC), insufficient sample size, patient characteristics, such as sex, age, or other comorbidities that might have shed light on these results, and utilization of antimicrobials by clinicians despite negative BioFire® ME Panel results. A larger scale study with similar parameters may reveal significant differences between these groups.

Of the 27 negative BioFire® ME Panel results, 21 (77.8%) were continued on antimicrobial therapy despite the result. Chang et al.[5] found similar results when assessing the BioFire® ME Panel's role in antibiotic stewardship. The current study suggested that clinicians proceed with antimicrobial treatment regardless of a negative result. This may be due to clinicians' concerns with risk of mortality without treatment or other healthcare-related concerns.[6]

CONCLUSIONS

The BioFire® ME Panel as a diagnostic tool has the potential to target antimicrobial treatment in a timely and cost effective manner. However, evidence of its potential to decrease the use of unnecessary antimicrobials is lacking. Future investigations into antimicrobial treatment in lieu of a negative result on the BioFire® ME Panel are warranted. With altered management of meningitis and encephalitis cases worked up with BioFire® ME Panels and a similar study of larger caliber, the potential may exist to shorten antimicrobial duration and length of hospital stay for patients hospitalized with meningitis/encephalitis.

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Keywords: anti-infective agents, meningitis, encephalitis, length of stay

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Can the Federal Baldrige Survey Measure Workforce Well-being in an Academic Health Center?

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ABSTRACT

Introduction. Experts suggest health care institutions switch focus from measuring burnout to measuring positive organizational psychology. Concerns include burnout being a late sign of organizational decline. The Baldrige survey is promoted by the U.S. Department of Commerce to measure positive worksite conditions (e.g., workforce wellbeing of industries, including health care and education). For years, the survey has been completed by managers within organizations, but now the same survey is promoted for completion by an organization's workforce. We tested the structure of the Baldrige survey when completed by an academic health care workforce. In addition, we tested whether the results in an academic worksite correlate with an example metric of an organizational mission.

Methods. In 2015, our academic health center surveyed faculty and staff with the Baldrige survey. The validity of the Baldrige was tested with confirmatory factor analyses. Within the School of Medicine, responses for the Baldrige's concepts were correlated against a measure of organizational outcome: graduates' assessments of Departmental educational quality.

Results. The structure of the Baldrige survey did not validate when assessed by a workforce (RMSEA = 0.086; CFI = 0.829; TLI = 0.815). None of its concepts correlated with learner reported educational quality.

Conclusions. The Baldrige survey, when administered to a workforce rather than managers, did not appear to measure workforce well-being within an academic health care center. We discourage use of the current survey for this purpose. ***Kans J Med 2019;12(1):4-6.***

INTRODUCTION

The well-being of physicians in the United States, as measured by rates of burnout, is declining.[1] Accordingly, the well-being of health care personnel has been proposed as a fourth aim of health care in addition to the health of a population, the patient experience of care, and the cost of care.[2,3] The health care system's focus on burnout, rather than positive organizational psychology, has been questioned.[4,5] Burnout is likely an end state in organizational decline, so focusing on burnout may delay detection of organizational dysfunction.

The Baldrige survey is an excellent candidate for measuring positive organizational health and has been used by industries, including healthcare and education.[6] The Baldrige framework and criteria for performance excellence was created by the Malcolm Baldrige National Quality Improvement Act of 1987 and is managed and its use encouraged by the National Institute of Standards and Technology (NIST) within the U.S. Department of Commerce. The survey and national benchmarks are freely available. The Baldrige institutional assessment includes a questionnaire that measures seven concepts of organizational tactics. While the survey was originally intended to be completed by managers within an organization applying for the Malcolm Baldrige National Quality Award, administration of the survey to front-line personnel is now encouraged by the NIST.[7] Although the survey is encouraged for front-line personnel by the NIST, the survey's structure has not been validated for this purpose. The objective of this study was to assess the structural validity of the Baldrige questionnaire when front-line personnel of an organization are queried. In addition, we correlated the concepts within the Baldrige with a measurement of an institutional goal.

METHODS

Study design and setting. An analysis of existing, anonymous data that had been collected for operational purposes by the Organizational Improvement Office (OIO) at the University of Kansas Medical Center was performed.

Participants. Invitations to the online, anonymous survey were emailed by OIO to all faculty and staff in 2015. One reminder email was sent.

Measurements. We used the Baldrige "Are We Making Progress" 2011 questionnaire (Table 1). The questionnaire contains 40 Likert questions that query the presence of four to nine positive attributes per seven concepts (leadership, strategy, customer focus, workforce focus, information management, operations, and results).

The organizational outcome of interest was educational quality which was measured using the ratings of clinical clerkships by recent graduates of the school. The ratings were gathered from the 2014 Association of American Medical Colleges graduation questionnaire (AAMC-GQ).[8] The AAMC-GQ provides separate ratings for clerkships in internal medicine, family medicine, surgery, pediatrics, psychiatry, and obstetrics and gynecology. The ratings were normalized by using the national percentile ratings for each clerkship rather than use the raw ratings by our graduates.

Statistical methods. A confirmatory factor analysis (CFA) validated the structure of the Baldrige questionnaire. Statistical fit of the model was evaluated with the root mean square error of approximation (RMSEA), comparative fit index (CFI), and the Tucker-Lewis index (TLI). Acceptable fit is indicated by RMSEA less than 0.06, CFI above 0.90, and TLI above 0.90.[9] Analyses were done with the Lavaan Package for R Programming Language.[10]

Table 1. The Baldrige "Are We Making Progress" 2011 questionnaire.

Baldrige Concept	Questions
Leadership	1. I know my organization's mission (what it is trying to accomplish). 2. I know my organization's vision (where it is trying to go in the future). 3. My senior (top) leaders use our organization's values to guide us. 4. My senior leaders create a work environment that helps me do my job. 5. My organization's leaders share information about the organization. 6. My organization asks what I think.
Strategic planning	1. As it plans for the future, my organization asks for my ideas. 2. My organization encourages totally new ideas (innovation). 3. I know the parts of my organization's plans that will affect me and my work. 4. I know how to tell if we are making progress on my work group's part of the plan. 5. My organization is flexible and can make changes quickly when needed.
Customer focus	1. I know who my most important cutomers are. 2. I regularly ask my customers what they need and want. 3. I ask if my customers are satisfied or dissatisfied with my work. 4. I am allowed to make decisions to solve problems for my customers. 5. I also know who my organization's most important customers are.
Measurement, analysis, and knowledge management	1. I know how to measure the quality of my work. 2. I can use this information to make changes that will improve my work. 3. I know how the measures I use in my work fit into the organization's overall measures of improvement. 4. I get all the important information I need to do my work. 5. I know how my organization as a whole is doing.
Workforce focus	1. The people I work with cooperate an work as a team. 2. My bosses encourage me to develop my job skills so I can advance in my career. 3. I am recognized for my work. 4. I have a safe workplace. 5. My bosses and my organization care about me. 6. I am committed to my organization's success.
Operations focus	1. I can get everything I need to do my job. 2. We have good process for doing our work. 3. I have control over my work processes. 4. We are prepared to handle an emergency.
Results	1. My work products meet all requirements. 2. My custormers are satisfied with my work. 3. I know how well my organization is doing financially. 4. My organization has the right people and skills to do its work. 5. My organization removes things that get in the way of progress. 6. My organization obeys laws and regulations. 7. My organization practices high standards and ethics. 8. My organization helps me help my community. 9. My organization is a good place to work.

For departments or divisions that sponsor a clinical clerkship within the School of Medicine, mean values of responses were calculated by personnel within the work unit to each item within the seven Baldrige concepts. Then, a mean for each Baldrige concept was calculated. The means of the responses were correlated for each concept to graduates' assessments of departmental educational quality. Calculations were done with the R Programming Language.[11]

RESULTS

Responses were received from 877 faculty and staff for a response rate of 21%. The Baldrige did not validate by confirmatory factor analysis with all measures of fit not meeting thresholds for validity (RMSEA = 0.086; CFI = 0.829; TLI = 0.815).

None of the seven concepts of the Baldrige as assessed by departmental personnel significantly correlated with educational quality as assessed by recent graduates (Table 2). The range of correlation coefficients ranged from -0.01 for the concept of "Results" to 0.58 for the concept of "Customer Focus".

Table 2. Correlations of the seven concepts of the Baldrige as assessed by departmental personnel with educational quality as assessed by recent graduates.

Baldrige Concept	Correlation with recent graduates' satisfaction with departmental clerkships	p - value
Leadership	0.12	0.72
Strategic planning	0.138	0.71
Customer focus	0.58	0.06
Measurement, analysis and knowledge management	0.40	0.22
Workforce focus	0.07	0.83
Operations focus	0.31	0.37
Results	-0.01	0.98

DISCUSSION

Our academic health center, which like all academic health centers combines both delivery of health care and provision of higher education, did not validate the structure of the Baldrige for measuring its seven concepts. In addition, the Baldrige concepts did not correlate with our measure of an organizational goal, the AAMC-GQ. The negative results may reflect that most prior studies of the Baldrige queried managers and external assessors of organizations rather than front-line personnel.[12-22] In addition, most of these studies created custom surveys based on Baldrige concepts.[13,14,16,20,22]

Four previous studies attempted validation of the original Baldridge questions.[12,15,21] Two studies surveyed leaders or managers in diverse industries and were able to validate the survey after modifying the structure.[12,15] In a third study, Jayamaha et al.[21] surveyed Baldrige personnel who formally assessed companies that applied for the Baldrige award. They found low discriminant validity suggesting questions belonged to multiple concepts. The only study that surveyed front-line personnel, like our study, was not able to validate the relationships between concepts of the Baldrige model.[23]

Workforce conditions should move beyond current recommendations to measure burnout and instead measure positive organizational

psychology.[4,5] Unfortunately, the Baldrige does not support this goal. Other studies support the concept of thriving (defined as a workforce that is both engaged and learning or improving) should be measured.[24,25] Thriving has been studied in industries other than health care and found to correlate with job performance of both individuals and groups.[24,25] On the other hand, burnout, while correlated with quality of care as perceived by physicians,[26] did not correlate with measured quality of care in the "Minimizing Error, Maximizing Outcome" study[27] or Healthy Work Place trial.[28] In addition, as previously noted, focusing on burnout may delay detection of organizational dysfunction. In addition to helping academic health centers meet organizational goals, successful measurement of workforce well-being may have larger impact by using controlled, public reporting to address physician burnout in clinical practice.[3]

Our study is limited by a low response rate. However, this rate is typical of national studies of burnout.[1] With a larger study size, our correlation of 'customer focus' of departments with recent graduates' satisfaction with departmental clerkships might become statistically significant. However, even if this correlation is significant, the structure of the Baldrige does not validate and better surveys should be sought. In 2015, the Baldrige survey was revised; however, only a single question was reworded.

Our negative finding regarding the Baldrige's inability to measure the perspective of front-line personnel should not be generalized to other roles of the Baldrige framework and awards. For example, other studies using external examiners show receipt of the Baldrige award in health care correlates with organizational financial performance[29] and positive experiences by patients.[30] However, as noted previously, the only prior study that attempted validation of the structure of the Baldrige survey to measure the perspective of front-line personnel using the original questions in the survey was also negative.

CONCLUSIONS

We discourage use of the Baldrige survey to measure employee perceptions of well-being in academic health centers. The lack of validation studies of front-line personnel in any industry questions the use of the Baldridge by frontline personnel in any setting. Our negative findings are important as workforce well-being is an emerging issue and the NIST is promoting the Baldrige "Are we making progress" survey for measuring the front-line perspective.

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Keywords: academic medical centers, professional burnout, workplace, health promotion, surveys and questionnaires

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Computed Tomography in Trauma Patients Accepted in Transfer: Missed Injuries and Rationale for Repeat Imaging. Can we do Better?

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ABSTRACT

Introduction. Computed tomography scans often are repeated on trauma patient transfers, leading to increased radiation exposure, resource utilization, and costs. This study examined the incidence of repeated computed tomography scans (RCT) in trauma patient transfers before and after software upgrades, physician education, and encouragement to reduce RCT.

Methods. The number of RCTs at an American College of Surgeons Committee on Trauma verified level 1 trauma center was measured. The trauma team was educated and encouraged to use the computed tomography scans received with transfer trauma patients as per study protocol. All available images were reviewed and reasons for a RCT when ordered were recorded and categorized. Impact of system improvements and education on subsequent RCT were evaluated.

Results. A RCT was done on 47.2% (n = 76) of patients throughout the study period. Unacceptable image quality and possible missed diagnoses were the most commonly reported reasons for a RCT. Preventable reasons for a RCT (attending refusal to read outside films, incompatible software, and physician preference) decreased from 25.8 to 14.3% over the study periods.

Conclusions. The volume of unnecessary RCT can be reduced primarily through software updates and physician education, thereby decreasing radiation exposure, patient cost, and inefficiencies in hospital resource usage. ***Kans J Med 2019;12(1):7-10.***

INTRODUCTION

Regional Trauma Centers (RTCs) accept a large number of trauma patients in transfer, many of whom arrive with imaging studies, in part, due to the increasing number of computed tomography (CT) scanners that have become available throughout rural America.[1,2] What formerly was "stabilize and ship" has morphed into "stabilize, CT scan, and ship." Justifiable reasons for obtaining CTs at outlying hospitals prior to transfer include the need to identify injuries, properly triage patients, determine the appropriate transport method,[3] and document the need for referral to a RTC.[4] Many RTCs have formal or informal protocols to perform a total body CT or pan-scan on all trauma patients accepted in transfer, which often duplicates some or all of the imaging performed pre-transfer. The preconceived notion that rural hospitals produce suboptimal CT images may have contributed to these strategies.

There are multiple interests driving the effort to decrease duplicate imaging.[5] One reason is a heightened public awareness of the risks associated with CT, primarily the exposure to ionizing radiation and increased risk of malignancy.[6-9] In addition to radiation exposure, intravenous contrast administration often is duplicated. The overall volume of contrast infused is an independent risk factor for contrast-induced nephropathy and should be minimized.[10,11] Uncommon but potentially devastating, non-renal sequelae of intravenous contrast such as allergic reactions and intravenous access site extravasations also can occur.[12,13] Another major factor driving efforts to reduce unnecessary repeat imaging is the awareness of the over-consumption of resources. Many institutions recognize the financial burden of duplicated imaging of trauma patients.[6-9,14] In response to the widespread concern regarding repeat imaging, multiple professional societies have responded by publishing recommendations regarding minimizing radiation dose and educating patients prior to imaging.[15]

The purpose of this study was to determine if CT scans from transferring hospitals can be used at the time of patient evaluation, identify any obstacles that impair the effective use of those CT scans, determine physician reasoning behind repeating CT scans, identify any missed injuries or complications associated with using pre-transfer CT scans, and determine if software updates and physician education can reduce RCT effectively for preventable reasons.

METHODS

As part of a quality improvement initiative, we prospectively collected data on all trauma patients accepted in transfer to our American College of Surgeons Verified Level I Trauma Center during two time periods in 2009 and 2010. During time period 1 (T1: July 1, 2009 to November 30, 2009), the importance of use of outside imaging studies was addressed with the surgery residents and trauma attendings at peer review as a quality initiative. During T1, physicians were aware that they were being observed. During a subsequent five-month wash-out interval, this education was followed by installing imaging software on all trauma bay computers to speed image loading and ease of use. These software upgrades were intended to reduce the number of transferred scans that were unreadable due to hardware or software incompatibility. Finally, hands on training was performed with technologists, residents, and attendings, who then provided training to those that followed. Following the wash-out period of five months, a second time period (T2: March 11, 2010 to May 3, 2010) of follow-up data collection was performed to compare findings from T1. The data from T2 was collected retrospectively, and physicians were unaware that data from T2 were being evaluated in order to assess the effectiveness of software upgrades and additional training and physicians were blinded to study purpose.

The attending trauma surgeon or resident collected quality assurance data at the time of patient arrival in the trauma bay during T1. Each patient was evaluated and the accompanying image(s) reviewed. A data sheet was completed on all patients accepted in transfer who underwent pre-transfer CT imaging. Data variables included patient

demographics (age, race, and gender), trauma activation level, which body region(s) were CT imaged prior to arrival, presence of CD containing images (radiology report alone was unacceptable), if the image was read by a resident or attending physician, if a repeat CT was ordered and what type of CT it was, and the reasoning given for the repeated CT.

Reasons for performing another CT are detailed in Table 1. Physicians were allowed to give more than one reason for repeating a scan.

Table 1. Reasons for performing a repeat CT.

Poor quality/unacceptable images, including CTs with poorly timed contrast, non-contrasted scans of the chest/abdomen/pelvis, no neck reconstructions, or blurry images from excessive motion artifact.
Possible missed injury, including patients with cervical spine fractures that needed a CT angiogram of the neck or those patients with pelvic fractures, lower rib fractures or spine fractures that needed CT imaging of their abdomen/pelvis.
Incompatible software, including images that could not be loaded, windowed, scrolled, or viewed satisfactorily due to software issues.
Additional studies were needed for patients who had incomplete imaging, including CTs of the upper abdomen that did not include the pelvis or a patient with an adequate CT chest, but also needed an abdomen/pelvis scan.
Progression of injury, including patients who arrived with a worse clinical picture, inconsistent with their imaging.
Physician preference/other served as a miscellaneous category to repeat a scan for an unclassified reason.

The data collected during T1 were used to generate a quality assurance database to evaluate resource utilization with regard to CT scans. The database was reviewed retrospectively in conjunction with each patient's electronic health record and trauma registry. We hypothesized there would be an overall decrease, from T1 to T2, in the number of CTs repeated and the pre-transfer CT scans could be used safely during real-time patient evaluation with a low risk of missed injuries.

Satistical Analysis

Data were analyzed using chi-square analyses on SPSS release 19.0 (IBM Corp., Somers, New York). All statistical tests were two-sided and considered significant when the resultant p value was ≤ 0.05. This study was approved by the Institutional Review Board of Via Christi Hospitals Wichita, Inc. and the Human Subjects Committee of the University of Kansas School of Medicine-Wichita.

RESULTS

The quality assurance database included 142 patients during T1 and 27 patients during T2 for a total of 169 patients (Table 2). During T1, three patients did not arrive with a CD containing their images, and five patients arrived with a CD that did not include all the documented scans. During T2, one patient did not arrive with a CD containing their images. Therefore, 94.4% (n = 134) and 96.3% (n = 26) of our trauma patients, respective to T1 and T2, arrived in the trauma bay with a CD that contained all of their locally obtained scans.

Table 2. Comparison of computed tomography (CT) scans received in transfer, proportion receiving repeat CT and ordering patterns of repeat CTs for patients injured in time periods 1 and 2.

Parameter	Period I Number (%)	Period II Number (%)	p value
Number of observations	142 (84.0)	27 (16.0)	
Status of CT's			0.548
All arrived with patient	134 (94.4)	26 (96.3)	
Some, but not all, arrived with patient	5 (3.5)	0 (0.0)	
None arrived with patient	3 (2.1)	1 (3.7)	
Patient CT's repeated	62/134 (46.3)	13/26 (50.0)	0.727
CT reordered by	N = 61	N = 13	0.824
Resident	40 (65.6)	9 (69.2)	
Attending surgeon	17 (27.9)	4 (30.8)	
Radiologist	3 (4.9)	0 (0.0)	
Neurosurgeon	1 (1.6)	0 (0.0)	

Of those patients that arrived with pre-transfer CTs, 46.9% (n = 75) went from our trauma bay to radiology to obtain a repeat CT scan. No statistically significant difference was observed in the repeat CT rate between T1 and T2 (46.3 vs 50.0%, p = 0.727); however, the reasons behind repeating scans changed. Table 3 includes a comparison of the reasons given for repeating CT scans between T1 and T2. The most common reasons for repeat CT in T1 were unacceptable image quality (47.0%) and possible missed diagnosis (36.4%). In T2, the most common reasons for repeat imaging were possible missed diagnosis (42.9%), progression of injury (21.4%), and additional studies needed (21.4%). From T1 to T2, there was a significant decrease in repeat imaging for unacceptable image quality (47.0 to 14.3%, p = 0.024) and a concurrent increase in repeat imaging due to progression of injury (3.0 to 21.4%, p = 0.035) and additional studies needed (3.0 to 21.4%, p = 0.035).

Adverse outcomes related to using pre-transfer CT scan were defined as injuries not visualized on the outside CT scan or injuries incorrectly characterized on that imaging, effecting management. After reviewing the trauma registry and medical records, no missed injuries or adverse outcomes related to using pre-transfer CT scans were identified.

Table 3. Comparison of reasons for repeat computed tomography (CT) scans for patients injured in time periods 1 and 2.

Parameter	Period I Number (%)	Period II Number (%)	p value
Number of observations*	N = 66	N = 14	
Reason for repeat CT			
Unacceptable quality	31 (47.0)	2 (14.3)	0.024
Possible missed diagnosis	24 (36.4)	6 (42.9)	0.649
Attending refused to read outside film	10 (15.2)	0 (0.0)	0.196
Incompatible software	6 (9.1)	2 (14.3)	0.624
Additional studies needed	2 (3.0)	3 (21.4)	0.035
Progression of injury	2 (3.0)	3 (21.4)	0.035
Physician preference	1 (1.5)	0 (0.0)	1.000
Patient condition	1 (1.5)	1 (7.1)	0.321
Radiologist refused to read outside film	0	0	----

*Multiple reasons for repeating a CT image or set of images sometimes were given for a single patient.

DISCUSSION

The overall rate of patients undergoing repeat CT scans was 46.9%, which was similar to other recently published data of 53 to 58%.[1,7,14] Haley et al.[7] found that 53% of referrals underwent repeat imaging at their trauma center, costing an additional $610,000 on duplicated CT imaging at an average cost of $2,985 per patient. These findings were comparable to those from Cook et al.[8] in which the additional charge generated from repeating a CT scan of the abdomen was $3,055 per scan. Most recently, Gupta et al.[14] highlighted this "inefficiency in rural trauma" with regard to repeat CT imaging. They found that 58% of their patients underwent a repeat CT scan with reasons similar to those reported in our study. Our findings are congruent and suggest repeat imaging is prevalent among rural trauma centers and not isolated to any geographic region of the United States.

Surprisingly, 95.3% of our patients arrived with a CD containing all their pre-transfer CT imaging. In similar studies, 12 to 20% of scans were not sent with the patient or not viewable due to software incompatibility.[5,14] Our "incompatible software" category accounted for 10.0% of the overall reasons for repeating a CT and was not significantly different between study time periods. Our observed decrease in "unacceptable" images was likely due to the persistent intervention occurring throughout our study time periods involving increased physician awareness, computer literacy, and software upgrades.

One of the most important issues surrounding pre-transfer CT scans was the potential for missed injuries because rural imaging was purported to be sub-optimal or inadequate. A recent survey indicated that while greater than 90% of rural critical access hospitals have access to CT, the equipment is more likely of lower quality with less resolution, such as 1 to 4 slice scanners.[2] Despite the disclaimer printed on the CD that "these images should not be used for diagnostic purposes", our experience was that the overall resolution and quality was acceptable. During T2, 14.3% of the imaging studies fell into the "unacceptable quality" category. Anecdotally, this related more to contrast timing or motion artifacts, which are technologist dependent, as opposed to hardware or software issues. After reviewing patient medical records and the trauma registry, no missed injuries related to using pre-transfer CTs were identified.

When considering the use of repeat CT scans, the risk of missed injuries must be weighed against increased radiation exposure. The increased risk of radiography-induced cancer from CT scans is well documented in the younger population.[16] Recent computer models indicate middle-aged individuals are susceptible to radiography-induced cancer, and the risk may be twice what was thought previously.[16,17] Decreasing the rate of repeating those particular studies would decrease the patient's cumulative radiation dose and contrast exposure.[18] While repeated CTs were done less often for unacceptable images during T2, the proportion of "additional studies needed" increased. Additional studies were included as repeat scans because there was considerable overlap in the scan itself with duplicated radiation and risks. As an example, patients included in this category may have arrived with only a chest CT, but also needed imaging of the abdomen/pelvis. The anatomic overlap of separately imaging the neck, chest, abdomen, and pelvis results in an increased radiation dose to bordering tissues. Due to both observed decreases in some reason categories, such as "unacceptable quality," and concurrent increases in others, such as "additional studies needed," there was no overall decrease in RCT in the current study. We deem our findings still to indicate success as we observed decreased RCT for preventable reasons while seeing a concurrent increase in nonpreventable reasons that may have multiple explanations.

Our current practice has evolved based on the results of this study. For patients arriving in transfer with a CD, the images are viewed immediately on the trauma bay computer, then given to the radiology technologist to upload into our Picture Archiving and Communication System (PACS). Within 30 minutes, the images are viewable through our local software on any hospital computer. Our radiologists do not over-read outside CT scans routinely unless a clinical scenario prompts a special request from the trauma team. However, the images are archived and follow-up images are compared to the pre-transfer imaging, which is often the case for follow-up head CTs.

Teleradiology, which allows digital transfer of images from the referral hospital for review by the receiving in-house trauma team, will influence interfacility transfer and management of acutely injured patients.[3] One study showed that an integrated trauma system that utilizes PACS has significantly fewer repeat CT scans (16%) when compared to a non-integrated system (48%).[19] Because the integrated trauma center received a third of patients from hospitals outside the integrated trauma system, the authors suggested that the 16% of scans repeated at the integrated hospital may be much lower for populations transferring from hospitals within the integrated trauma system.

Several limitations existed within this study. First, the findings came from a single RTC within a small time period. Second, we did not know which, or how many, pre-transfer CT scans were indicated

based on Advanced Trauma Life Support or current trauma practices. Perhaps some scans were not repeated because they were not indicated to begin with. However, our findings were comparable to those previously reported at other institutions from various geographic regions.[5,7,14] We did not measure or quantify radiation exposure or IV contrast exposure nor their associated complications. We also defined "repeat" as any trip to the CT scanner from our trauma bay after the patient was scanned at the transferring facility previously. The "progression of injury" category contained five patients and could be excluded, because the reason for their trip to the scanner is independent of pre-transfer imaging. Additionally, the number of observations in some categories evaluated, as well as in T2, were low enough that it may limit their generalizability.

Future work on this topic revolves around educating our transferring hospitals with regard to CT imaging protocols. The idea that small rural hospitals do not have adequate technology to produce quality CT scans is not supported by our findings. It seems unreasonable to suggest that rural hospitals not perform CT scans on trauma patients. Rather, they should be educated with regard to current imaging protocols, and our trauma systems should be refined to incorporate teleradiology programs that will aid triage and transfer.

CONCLUSIONS

With appropriate software and practitioner effort pre-transfer, the majority of CTs may be used effectively and safely at the time of patient presentation to regional trauma centers and need for RCT for preventable reasons can be minimized.

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Assessing Work-Related Burnout and Job Satisfaction among Obstetrics and Gynecology Residency Program Coordinators

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ABSTRACT

Introduction. This study explored the prevalence of and the relationship between job satisfaction and burnout among obstetrics and gynecology residency program coordinators.

Methods. This cross-sectional study involved members of the American Program Managers of Obstetrics and Gynecology. The Copenhagen Burnout Inventory and Spector's Job Satisfaction Survey were used to measure the participants' burnout and job satisfaction rates respectively. Data were collected between August 2017 and December 2017. The authors used Fisher's exact tests, Spearman's *r* correlations, and multiple linear regression to analyze the data.

Results. There was an 83% (171/207) response rate. Thirteen percent of the coordinators reported high, 70% moderate, and 17% low job satisfaction scores. Thirty-nine percent of the coordinators reported high, 25% moderate, and 36% slight work-related burnout rates. Correlation coefficient showed a significantly negative relationship between job satisfaction and work-rated burnout, (r_s[169] = -0.402, $p < 0.01$). Regression analysis showed co-workers ($\beta = -0.47$) and supervision ($\beta = -0.16$) domains of the job satisfaction scale were significant predictors of work-related burnout ($R = 0.55$; F[5, 195] = 11.05; $p < .001$).

Conclusions. The findings highlight the importance of job satisfaction factors, such as support from coworkers and supervisors, in dealing with work-related burnout among residency coordinators.
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INTRODUCTION

Obstetrics and gynecology (Ob-Gyn) residency program coordinators play an integral role in day-to-day operations of Ob-Gyn graduate medical education. There are different job titles of Ob-Gyn residency coordinators including program administrator, residency manager, residency program manager, and resiliency coordinator. For consistency purposes, we used "residency program coordinators" to refer to all the Ob-Gyn coordinators irrespective of their job title. Residency program coordinators have multiple roles and responsibilities that include providing administrative support to program directors, faculty, fellows, and residents; scheduling and assisting with program accreditation; and maintaining files and databases that contain faculty, fellow, and resident information. These coordinators often work in an environment that can be stressful.[1,2] Increased job responsibilities could result in increased job stress if these coordinators do not receive an adequate level of institutional support.[3,4]

A study that included 56 residency coordinators from 21 specialties, including obstetrics and gynecology, revealed 72% were overwhelmed by job duties and responsibilities and 39% considered quitting their job.[5] Similar sentiments were shared by family medicine residency coordinators where 81% reported they are overwhelmed by their workload and 71% indicated their work wore them out.[6]

Burnout has been associated with long-term exposure to work-related stress[7,8] and low job satisfaction.[9,10] Job satisfaction is multi-faceted, but can be broken into nine meaningful domains: satisfaction with pay, opportunities for promotion, fringe benefits, contingent rewards, supervision, co-workers, nature of work, communication, and work conditions. These domains are the basis for the commonly used job satisfaction survey.[11] Work-related burnout is "the degree of physical and psychological fatigue and exhaustion that is perceived by a person as related to his/her work."[12]

Even though burnout rate among physicians is studied widely, a review of the literature indicated little information regarding job satisfaction and work-related burnout studies involving Ob-Gyn residency program coordinators who play a pivotal role in postgraduate medical training. Therefore, the purposes of this study were to:

1. explore the prevalence of job satisfaction and work-related burnout among Ob-Gyn residency program coordinators;
2. assess if there is a relationship between job satisfaction and work-related burnout among the Ob-Gyn residency program coordinators. We hypothesized that the coordinators who are satisfied with their jobs will report low work-related burnout scores on the burnout scale; and
3. determine predictors of Ob-Gyn residency program coordinators' work-related burnout using job satisfaction domains: pay, promotion, supervision, co-worker, and nature of work.

METHODS

Study Design and Participants

This cross-sectional study included data from Ob-Gyn residency program coordinators who were active members of the American Program Managers of Obstetrics and Gynecology (APMOG). Among other functions, the APMOG is a professional organization dedicated to professional growth of residency program coordinators. Study participants completed an anonymous, 43-item online survey that included questions from the Copenhagen Burnout Inventory[12] and the Spector's Job Satisfaction Scale,[11] as well as questions used to construct the demographic profile of the participants. The University of Kansas School of Medicine-Wichita Institutional Review Board granted exemption for the study. A sample size of 100 was calculated as necessary for adequate power (> 0.85) to detect significant correlations of 0.5, $p < 0.01$ between variables.[13]

Study Instruments

Job Satisfaction. The first outcome measure for the study was job satisfaction, which was defined as pleasure people derive from their work, including their ability to affect the lives of people through work positively.[14] The job satisfaction measure was assessed using the Job Satisfaction Scale,[11] which is a validated research tool used widely. The Job Satisfaction Scale has a set of nine domains designed to measure employee attitudes about their job and aspects of the job that include Pay, Promotion, Supervision, Fringe Benefits, Contingent Rewards (performance based rewards), Operating Procedures (required rules and procedures), Co-workers, Nature of Work, and Communication.[11] Based on the research goal, the current study utilized statements from five of the nine domains to include:

Pay. This job satisfaction domain consists of four statements that measure workers perception of the pay and remuneration they receive from the work they do. An example of a statement under this domain is, "I feel I am being paid a fair amount for the work I do."

Promotion. The Promotion domain of the job satisfaction has four statements that measure how workers perceive promotion opportunities they have at work. An example of a statement under this domain is, "Those who do well on the job stand a fair chance of being promoted."

Supervision. This domain has four statements that measure workers perceptions of their immediate supervisor. An example of a statement under this supervision construct is, "My supervisor shows interest in the feelings of subordinates."

Co-workers. This job satisfaction domain measured workers perceptions of the people with whom they work. It consists of four statements. An example is, "People I work with get along very well."

Nature of Work. The four statements under this domain measured the participants' job tasks. An example of a statement under this domain is, "I feel a sense of pride in doing my job."

For each domain, respondents recorded how much a statement applied to them using a 6-point Likert scale ranging from disagree very much to agree very much. The scores from all the five domains were summed to form the overall job satisfaction score with higher scores indicating high job satisfaction. Consistent with convention,[15] the job satisfaction composite score was categorized into low (< 53), moderate (53 - 88), and high (> 88).

Burnout. The second outcome measure for the study was burnout, which can be associated with a "very high workload or a non-supportive work environment".[8] The personal and work-related burnout sub-scales of the Copenhagen Burnout Inventory were used to measure the respondents' burnout scores. Personal burnout is a state of prolonged physical or psychological fatigue and exhaustion. Work-related burnout occurs when the degree of the physical and emotional exhaustion is attributed to one's work.[12] By comparing the personal burnout and work-related burnout, individuals who attributed their fatigue to personal factors, such as family demands, were identified. The Copenhagen Burnout Inventory is used worldwide and has been validated in samples of administrative staff.[12]

For personal burnout, respondents recorded how often they experience physical or psychological fatigue and exhaustion using a 5-point Likert scale ranging from never/almost never to always. The overall personal burnout score is the average of the scores on the items with higher scores indicating higher degree of burnout on the personal burnout scale. Consistent with convention,[16] the personal burnout composite score was categorized into slightly (< 50), moderate (50 - 70), and high (> 70).

For work-related burnout, respondents reported how often or the degree to which they experience work-related physical or psychological fatigue and exhaustion using a 5-point Likert scale ranging from never/almost never/to a very low degree to always/to a very high degree. One item was reverse scored. The overall work-related burnout score was computed as the average of the scores on the items with higher scores indicating higher degree of burnout on the work-related burnout scale. Consistent with convention,[16] the work-related composite score was categorized into slightly (< 45), moderate (45 - 60), and high (> 60).

Data Collection

There are 277 accredited obstetrics and gynecology programs nationally.[17] Due to logistical reasons (i.e., the inability to know the total number of the Ob-Gyn residency program coordinators and their contact information), the current study included only active members of the APMOG at the time of the study. SurveyMonkey® was used to host the survey and a generated link was sent via email to all of the 207 registered members of the APMOG. Data were collected between August 2017 and December 2017.

Statistical Analyses

Standard descriptive summary statistics were used to examine the respondents' job satisfaction rates, burnout prevalence, and to create demographic profiles of the respondents. Fisher's Exact tests were conducted to determine the relationship among variables (job satisfaction, work-related burnout, years on the job, gender [male vs female], residency program type, and location of program). Correlations determined association between the variables, and multiple regression using the five domains of the Job Satisfaction Scale determined the best predictors of the respondents' work-related burnout. A statistical critical value of 0.05 was specified for all tests.

RESULTS

Of the 207 Ob-Gyn residency program coordinators surveyed, data from 171 were collected, a response rate of 83%. As shown in Table 1, 94% of the respondents were females. Thirty-nine percent of the respondents have been in their current job for less than five years; 52% were working in university-based programs; and 61% of the programs were located in urban areas. Fisher's Exact tests showed no significant relationship among the variables.

Job Satisfaction Results. Overall, 13% of the Ob-Gyn residency program coordinators reported high, 70% moderate, and 17% low job satisfaction scores (Table 2).

Burnout Results. The burnout results are presented in Tables 2 and 3. Thirty-nine percent of the Ob-Gyn residency program coordinators reported high, 25% moderate, and 36% slight work-related burnout scores (Table 2). In particular, 56% of participants reported a high or very high score in the category measuring the degree to which participants were worn out at the end of the working day. Further, 39% reported high or very high scores describing their work as emotionally exhausting and 36% felt burnout because of their work (Table 3).

As shown in Table 3, 64% of the coordinators reported that they often/always feel tired; 52% often/always feel emotionally exhausted; and 52% often/always feel worn out. The overall work-related score positively correlated with the overall personal burnout score ($r_s[169] = 0.913$, $p < 0.01$; Table 4).

Job Satisfaction and Burnout Results. To test the study's hypothesis that Ob-Gyn residency program coordinators who are satisfied with their job would report fewer symptoms of work-related burnout, a correlation coefficient was calculated. The results showed a statistically significant negative relationship between the variables ($r_s[169] = -0.402$, $p < 0.01$; Table 4), suggesting that the Ob-Gyn residency program coordinators who reported satisfaction with their jobs scored low on the work-related burnout scale. As shown in Table 4, the overall work-related burnout score negatively correlated with two job satisfaction domains: co-workers ($r_s[169] = -0.460$, $p < 0.01$) and supervision ($r_s[169] = -0.163$, $p < 0.05$). Multiple linear regression analysis was conducted to determine the job satisfaction factors that best predicted work-related burnout. The results showed 30% of the variance was explained by the model. Co-workers ($\beta = -0.47$) and supervision ($\beta = -0.16$) domains were significant predictors of work-related burnout ($R = 0.55$; $F[5, 195] = 11.05$; $p < .001$; Table 5).

DISCUSSION

The study provided information regarding job satisfaction and burnout among residency program coordinators who are an integral part of the residency education team. Our results indicated that moderate to high levels of burnout exist among Ob-Gyn residency program coordinators in both work-related and personal domains. Burnout was associated with high workload or non-supportive working environment.[6] Our data showed 39% of the Ob-Gyn residency program coordinators reported the highest rates of work-related burnout and only 13% reported high job satisfaction. Job satisfaction and work-related burnout negatively correlated. These findings suggested that increased rates of burnout are associated with job dissatisfaction among the Ob-Gyn residency program coordinators, which is consistent with a study that has shown inverse relationship between burnout and job satisfaction.[6]

With co-workers and supervision domains of job satisfaction being predictors of work-related burnout with negative beta coefficient, an opportunity exists to modify the Ob-Gyn residency program coordinators working environment to improve factors causing the job dissatisfaction and high work-related burnout scores. An area of attention should include providing an environment that fosters positive feeling about work, good working relationships, support, and teamwork from co-workers. Consistent with findings of a previous study, co-workers and supervision domains are related most closely to job satisfaction scores and have shown to be best predictors of work-related burnout among nonclinical workers in a medical education center.[15]

Table 1. Demographic profile of participants (N = 171).

Demographic of Participants	Measure
Sex, no. (%)	
Male	9 (5.6)
Female	152 (94.4)
Missing	10
Years on the job, no. (%)	
< 2 years	17 (10.5)
2 - 5 years	46 (28.4)
6 - 10 years	31 (19.1)
11 - 15 years	25 (15.4)
16 - 20 years	20 (12.3)
21 - 25 years	13 (8.0)
≥ 26 years	10 (6.2)
Missing	9
Residency program type, no. (%)	
Community-based, medical school administered	13 (8.1)
Community-based, medical school affiliated	48 (29.8)
Community-based, non-affiliated	15 (9.3)
University	83 (51.6)
Military program	0 (0.0)
Other	2 (1.2)
Missing	10
Community location of program, no. (%)	
Suburban	39 (24.2)
Rural	24 (14.9)
Urban	98 (60.9)
Missing	10

Table 2. Level of burnout and job satisfaction among the respondents.

Levels	Personal Burnout Scale (PBS)[a] (n = 162)	Work-related Burnout Scale (WBS)[b] (n = 161)	Job Satisfaction Scale (JSS)[c] (n = 171)
Slightly or low*	60 (38%)	60 (36%)	29 (17%)
Moderately or moderate*	57 (36%)	41 (25%)	120 (70%)
Highest or high*	42 (26%)	64 (39%)	22 (13%)

*Response category for job satisfaction scale.
[a]PBS level scoring: slightly burnout, < 50; moderately burnout, 50 - 70; highest burnout, > 70.
[b]WBS level scoring: slightly burnout, < 45; moderately burnout, 45 - 60; highest burnout, > 60.
[c]JSS level scoring: low satisfaction, < 53; moderate satisfaction, 53 - 88; highest satisfaction, >88.

Table 3. Participants' burnout inventory: Scales, items and response frequencies.

	Response Category and Scoring						
	Never/almost never[a] or to a very low degree[b]	Seldom[a] or to a low degree[b]	Sometimes[a] or somewhat[b]	Often[a] or to a high degree[b]	Always[a] or to a very high degree[b]		Score
	(Scoring 0)	(Scoring 25)	(Scoring 50)	(Scoring 75)	(Scoring 100)	Missing	Mean
Survey Items	%	%	%	%	%	*n*	(SD)
Personal burnout (α = 0.92) (N = 168)							
How often do you feel tired?[a]	2.3	5.8	28.1	45.0	18.7	-	68.1 (22.8)
How often are you physically exhausted?[a]	4.7	17.5	32.2	34.5	11.1	-	57.4 (25.7)
How often are you emotionally exhausted?[a]	2.3	10.5	35.1	36.3	15.8	-	63.3 (24.0)
How often do you think: "I can't take it anymore"?[a]	15.9	17.1	33.5	21.8	11.8	1	48.7 (30.4)
How often do you feel worn out?[a]	4.1	13.6	30.2	38.5	13.6	2	60.0 (25.6)
How often do you feel weak and susceptible to illness?[a]	19.3	28.7	29.2	15.2	7.6	1	41.1 (29.5)
Total average score							**56.6 (22.2)**
Work-related burnout (α = 0.93) (N = 170)							
Do you feel worn out at the end of the working day?[a]	3.5	9.9	30.4	35.7	20.5	1	65.0 (25.9)
Are you exhausted in the morning at the thought of another day at work?[a]	16.4	17.5	26.9	27.5	11.7	1	50.1 (31.5)
Do you feel that every working hour is tiring for you?[a]	23.4	19.9	29.2	18.1	9.4	1	42.6 (31.7)
Do you have enough energy for family and friends during leisure time? (Reverse scored)[a]	9.4	31.6	35.7	13.5	9.9	1	45.7 (27.5)
Is your work emotionally exhausting?[b]	8.8	18.2	33.5	21.8	17.6	2	55.3 (29.8)
Do you feel burnt out because of your work?[b]	11.7	18.7	33.3	17.5	18.7	1	53.2 (31.4)
Does your work frustrate you?[b]	7.0	18.1	33.3	21.1	20.5	1	57.5 (29.8)
Total average score							**52.8 (24.8)**

Possible score range for all scales: 0 - 100
a = response categories for items denoted with [a].
b = response categories for items denoted with [b].

Table 4. Correlation coefficients of job satisfaction and burnout of respondents (N = 171).

Variables		Personal Burnout	Work-Related Burnout	Job Satisfaction
Personal burnout	Spearman's Correlation	——		
	Sig. (2-tailed)			
Work-related burnout	Spearman's Correlation	0.913**	——	
	Sig. (2-tailed)	0.000		
Job satisfaction	Spearman's Correlation	-0.412*	-0.402**	——
	Sig. (2-tailed)	0.012	0.008	
Promotions	Spearman's Correlation	-0.060	-0.016	0.684**
	Sig. (2-tailed)	0.440	0.838	0.000
Pay	Spearman's Correlation	0.084	0.019	0.674**
	Sig. (2-tailed)	0.285	0.803	0.000
Supervision	Spearman's Correlation	-0.58	-0.163*	0.738**
	Sig. (2-tailed)	0.094	0.036	0.000
Nature of work	Spearman's Correlation	0.011	0.053	0.528**
	Sig. (2-tailed)	0.885	0.496	0.000
Co-workers	Spearman's Correlation	-0.424**	-0.496**	0.263**
	Sig. (2-tailed)	0.000	0.000	0.001
Mean		56.6	52.8	68.8
Standard deviation		22.3	24.8	17.8
Range		0 - 100	0 - 100	20 - 120

**Correlation is significant at the 0.00125 (0.01/8) level (2-tailed).
*Correlation is significant at the 0.00625 (0.05/8) level (2-tailed).

Table 5. Summary statistics: Results from regression analysis.

	Work-Related Burnout				
Variables	*M*	*SD*	*b*	*b*	**95% CI for *b***
(Constant)			102.33		82.42, 122.24
Promotion	7.7	4.1	0.03	0.01	-0.99, 1.05
Pay	8.8	5.1	0.11	0.02	-0.71, 0.93
Supervision	17.2	6.5	-0.61	-0.16*	-1.19, -0.03
Nature of work	18.9	4.7	0.37	0.07	-0.41, 1.14
Co-workers	18.0	4.4	-2.63	-0.47**	-3.39, -1.88
F			11.05**		
R			0.55		
R^2			0.30		

M = Mean, SD = Standard deviation
*p < 0.05, **p < 0.001

Additionally, focusing on factors that contribute to emotional exhaustion may improve burnout scores for these coordinators. Emotional exhaustion has been demonstrated to be a major contributor of burnout among faculty,[18] suggesting that faculty development programs to address this may be applicable to residency program coordinators as well. Residency program coordinators may anticipate growth in job responsibilities as graduate medical education continues to emphasize outcomes-based performance metrics and increased tracking of data for each individual resident and fellow.[19,20] The additional job responsibilities could contribute to higher burnout and lower job satisfaction if programs do not analyze current stressors and workload and adjust accordingly to promote the wellbeing of residency program coordinators.[3,15]

The study has limitations. First, only members of the APMOG were included in the study and the results may not be reflective of all Ob-Gyn residency coordinators. However, our findings of Ob-Gyn program coordinators' job satisfaction and burnout are similar to the findings of family medicine residency program coordinators' job satisfaction and burnout.[6] The survey also provided a single snapshot of Ob-Gyn residency program coordinator's subjective responses. Although the study had a high response rate, the findings could be limited by self-report, and there is a possibility of response bias. The adaption of the modified job satisfaction scale also could limit the study findings. The original scale comprised of nine domains, but the modified scale used for this study included five domains.

CONCLUSIONS

In conclusion, the findings of this exploratory study highlights the importance of job satisfaction factors, such as support from co-workers and supervisors among Ob-Gyn residency program coordinators. Given that job satisfaction and work-related burnout are related negatively, residency program coordinators should not be bystanders in wellness initiatives. Residency program coordinators' wellness should be a priority and efforts to improve their job satisfaction be considered.

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Keywords: professional burnout, job satisfaction, internship and residency, administrative personnel, obstetrics and gynecology departments

KANSAS JOURNAL of MEDICINE

A Non-Operative Approach to Rectal Cancer after Chemo-Radiotherapy: Case Series and Review

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ABSTRACT

Introduction. Chemotherapy administered concurrently with radiotherapy for locally-advanced rectal cancer prior to surgery is a standard of care approach. A fraction of patients after chemo-radiotherapy achieve pathological complete remission. Our aim was to evaluate patients treated only with a non-operative approach of only chemo-radiotherapy followed by observation at a community cancer center.

Methods. Medical charts of the patients who were treated for locally advanced rectal cancer and treated with chemo-radiation therapy alone from January 1, 2000 through May 1, 2017 at a Midwestern cancer center were reviewed. The clinical course of the patients was followed from the time of the cancer diagnosis through their last available clinical record.

Results. A series of three cases were reviewed with locally-advanced distal rectal cancers treated with a non-operative approach.

Conclusions. Watchful waiting for patients with locally advanced distal rectal cancer who have complete clinical response with neoadjuvant chemotherapy and radiation might be an effective treatment strategy. ***Kans J Med 2019;12(1):17-19.***

INTRODUCTION

Post-operative morbidity secondary to total mesorectal excision in rectal cancer patients has increased the interest in organ preserving strategies significantly.[1] Alternative treatment strategies without radical surgery not only reduces the post-operative morbidity, but also lowers the need for intestinal stomas and functional disorders of the anorectal tract.[2] Several European trials have documented watch-and-wait approaches that include treatment with chemo-radiation followed by regular surveillance and monitoring for tumor recurrence.[3,4] The complete response rate with watch-and-wait approaches has ranged from 5 to 60%.[3,4] This variation may be due to different follow-up durations and surveillance intensity.

A study by Habr-Gama et al.[5] reported local recurrence in 31% of patients with initial regrowth and late recurrences. More than half of the recurrences developed in the first 12 months. The authors described that "salvage therapy is possible in > 90% of recurrences, leading to 94% local disease control and 78% organ preservation". The same authors conducted a prospective study on 70 patients with T2-T4, N0-2, M0, neoadjuvant chemo-radiotherapy that included 54 Gy and 5-FU/leucovorin delivered in six cycles.[6] Patients in this study were assessed for tumor response at 10 weeks from radiation therapy. About 47 patients had initial complete response and about eight patients developed regrowth in the first 12 months of follow-up.

The aim of this case-series was to review and report the number of cases treated for T2-T4, N0-N2, and M0 rectal cancer with a non-surgical approach and to evaluate the clinical outcome. Our goal was to augment the findings from the existing literature on the watch-and-wait management of locally advanced distal rectal cancer patients.

METHODS

This study was a case series consisting of three patients. All of the patients included in the study had rectal cancer treated with chemotherapy and radiation with no surgical intervention. The patients were identified using cancer registry databases and the clinical course was retrospectively followed from the time of their histologically proven malignancy until their last available clinical record.

Medical charts of the patients who were treated for locally advanced rectal cancer and treated with chemo-radiation therapy alone from January 1, 2000 through May 1, 2017 at Our Community Cancer Center at Carle Foundation Hospital were reviewed. Seventeen patients were identified, but three presented without metastatic disease and were included in the case series. Patient inclusion required a diagnoses of rectal cancer, treated only with chemotherapy and radiation and no surgical intervention. All or part of the cancer treatment was received at the Carle Foundation Hospital. Patients who did not meet the above criteria were excluded from the case-series.

The clinical course of the patients was followed from the time of the cancer diagnosis through their last available clinical record (Table 1). Approval from the institutional review board committee of Carle Foundation Hospital was obtained prior to the study.

Table 1. Patient diagnosis, treatment regimen, and follow-up.

	Patient 1	Patient 2	Patient 3
Age	93	84	65
Sex	Female	Male	Male
State of the disease upon diagnosis	T3N0M0	T3N1M0	T3N1M0
Chemotherapy and radiation regimen	Capecitabine with radiation	Capecitabine with radiation	5FU with radiation
Average length of follow-up	24 months	24 months	30 months

RESULTS

Case 1. A 92-year-old female presented to her primary care physician with rectal bleeding. A 3 cm mass at the distal rectum was found on colonoscopy. Needle biopsy of the mass revealed moderately differentiated rectal carcinoma at the lower rectal valve. Baseline computed tomography (CT) diagnostic imaging of the chest, abdomen, and pelvis indicated wall thickening of the distal rectum with no significant pelvic adenopathy and no overt findings for metastatic disease. The patient had T3N0M0 adenocarcinoma of the distal rectum by transrectal ultrasound. Based on her poor cardiac health due to a recent myocardial infarction and advanced age, the patient was regarded as high-risk for the hemicolectomy. She was started on capecitabine chemotherapy along with radiation therapy. She completed 25 fractions of radiation therapy. A total of 50 Gy of radiation treatment was administered to her rectum. The patient tolerated the treatment well with improvement

in her rectal bleeding and gradual recovery to baseline. The patient continued to be in remission at 24 months post-treatment without evidence of metastasis on surveillance scans.

Case 2. An 84-year-old male was found to have adenocarcinoma of the distal rectum after he presented with a complaint of pressure and discomfort with bowel movements along with intermittent rectal bleeding. He had a 3 cm exophytic mass in the rectum and the biopsy reported moderately differentiated adenocarcinoma of the rectum invading submucosa and muscularis propria. CT scan did not reveal distant metastasis. Clinical staging with the aid of transrectal ultrasound was determined to be cT3N1. Due to the patient's personal preference, he refused surgery and wanted only non-surgical options. The patient was given capecitabine along with radiation therapy of 50 Gy in 25 fractions. The patient did not have evidence of local or distant failure on clinical exams and surveillance studies after 36 months post-treatment.

Case 3. A 65-year-old male with no significant past medical history and no family history of colorectal cancer presented to his primary care provider with a complaint of intermittent rectal bleeding and alteration in bowel habits. He underwent colonoscopy and had a 3 cm mid-rectal neoplasm which was hemi-circumferential, lobulated, ulcerated, and adjacent to the 2nd rectal valve. Biopsy demonstrated adenocarcinoma arising in the background of an adenomatous polyp. Staging CT scan of the chest, abdomen, and pelvis was unremarkable for distant metastasis. The tumor was staged as T3N1M0 by transrectal ultrasound. Due to this patient's personal preference, he was treated non-operatively. He received chemotherapy with 5-fluorouracil and leucovorin concurrently with radiation therapy. Thirty months post-treatment, he was without evidence of recurrence.

DISCUSSION

Treatment options for patients with T2-T4 colorectal cancer that lead to complete clinical response after neoadjuvant chemo-radiotherapy remain controversial.[2] The most common type of treatment is neoadjuvant chemotherapy and radiation followed by surgical management.[7] The addition of chemotherapy to the neoadjuvant radiation has been found to improve localized disease control. Combination neoadjuvant treatment results in tumor downstaging, peri-rectal node sterilization, and preparation for surgical treatment. However, the absence of residual tumor cells in the resected surgical specimens after neoadjuvant chemoradiotherapy raised the issue of whether surgical treatment is necessary. This gave rise to a new treatment approach in patients with locally advanced rectal cancer, in which the patient is monitored carefully for any tumor recurrence after the chemo-radiation therapy. This is referred to as the strict surveillance method. This organ preserving strategy was designed to avoid major surgery which typically is associated with significant postoperative morbidity, functional disorders such as urinary, sexual, and anorectal problems, and the need for intestinal stomas.[2] Tumors that recur after the non-surgical approach frequently are amenable to surgical resection.[5]

After a long debate for several years, the wait-and-watch approach for locally advanced rectal cancer is more well-known in the literature.[5] Trials in Europe and United States have supported the management of rectal cancer patients staged at T2-T3 with close surveillance methods using the wait-and-watch approach after receiving neoadjuvant chemoradiation therapy.[5,8,9] These studies demonstrated radiological findings showing complete clinical or pathological response using modalities such as MRI or PET CT scans.

A study conducted by Habr-Gama et al.[2] looked at the wait-and-watch approach. In the study, patients with distal rectal cancer who achieved a complete clinical response with neoadjuvant chemotherapy and radiation were followed without undergoing any surgical management. The patients were followed for approximately 60 months. The results were compared with the control group who underwent total mesorectal excision (TME). The patients in the wait-and-watch category showed impressive results with five-year overall survival of 93% and disease-free survival of 85%.[1,2]

The wait-and-watch approach has been used with selected patients at our cancer center, specifically for patients with locally advanced rectal cancer. The three patients in our case-series have shown optimistic outcomes with no tumor recurrence, at least in the first 24 months after neoadjuvant chemoradiation therapy without any surgical intervention. Our study supported the findings of Maas et al.[4] who conducted a prospective study on their patients using the wait-and-watch approach. Their study included 21 patients with locally advanced rectal cancer with a complete clinical response after chemoradiotherapy. Patients underwent surveillance follow-ups every three to six months using MRI, endoscopy, or CT scans. Mean follow-up was about 25 months. Only one patient developed local recurrence while the other 20 patients were alive without any signs of tumor recurrence. The two-year disease free survival rate for these patients was 89% (95% CI , 43% - 98%), and the cumulative probability for two year overall survival was 100%. In the control group, which included the patients who underwent surgery after the neoadjuvant chemoradiotherapy, the two-year disease free survival was about 93% with an overall survival of 91% respectively. The three patients in our study also showed average overall disease free survival of 24 months with a two-year overall survival of 100%.

Renehan et al.[10] conducted a study in the UK of 357 patients with locally advanced rectal cancer; 228 of them underwent surgical treatment after neoadjuvant, and the remaining 129 patients stayed on the wait-and-watch approach. Of these 129 patients, 44 had local tumor regrowth and 36 patients out of 41 received a salvage therapy. In the matched analyses, the study did not find any difference in the three year overall survival (96% in the surgical vs 87% in the wait-and-watch group). Patients managed with wait-and-watch had significantly better three-year colostomy free survival than those who underwent surgical resection (74% vs 47%).

To avoid the extensive procedure of abdominoperineal resection, Appelt et al.[11] studied high dose radiation and chemotherapy in T2-T3, N0-N1 distal rectal adenocarcinomas. About 60 Gy in 30 fractions to tumor and 50 Gy in 30 fractions to the elective lymph nodes were given, along with oral tegafur-uracil 300 mg/m^2 every day for six weeks. Local recurrence rate was 15.5% (95% CI: 3.3-26.3). The most common late toxicity observed in these patients was bleeding from the rectal mucosa, but overall there were no unexpected serious adverse effects. The study concluded that high dose chemo-radiotherapy and watchful waiting might be a safe alternative to abdominoperineal resection in patients with locally advanced distal rectal cancer.

CONCLUSIONS

Findings from several prospective trials have indicated that the approach of watchful waiting for patients with locally advanced distal rectal cancer who have shown complete clinical response with neoadjuvant chemotherapy and radiation might be an effective strategy. Our case series of three patients supported these findings. Our patients showed excellent response with neoadjuvant chemotherapy and radiation with a 100% disease free survival. The major limitation of our study was the small sample size and a short follow-up period. Nevertheless, it is clear from the published prospective trials that the functional results after wait-and-watch treatment are not inferior, but rather superior to outcomes after rectal surgery. In future, we plan to conduct a prospective study regarding the wait-and-watch approach for locally advanced distal rectal cancer..

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Keywords: rectal cancer, treatment, surgery, chemoradiation, wait and watch

CASE REPORT

A Case of Extrapulmonary Tuberculosis Two-Ways

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INTRODUCTION

Tuberculosis (TB) is a widespread epidemic. The World Health Organization estimated 10.4 million cases of tuberculosis in 2016, with 490,000 new cases of multi-drug resistant (MDR) TB.[1] The primary presentation of TB is pulmonary. However, in the United States in 2014, 21% of TB cases were extrapulmonary with the most common sites in descending order of incidence being TB lymphadenitis (38.2%), pleural (16.3%), bone and/or joint (10.4%), peritoneal (5.7%), genitourinary (5%), meningeal (4.5%), and laryngeal (0.2%).[2]

CASE REPORT

A 72-year-old Laotian male presented from an outside facility with altered mental status and fever. His medical history included hypertension, gout, and stage 3 chronic kidney disease. The fever was cyclic in nature for one-month duration, reaching a peak of 103° F and being consistently above 100° F three days prior to presentation. The patient's altered mental status developed over those three days, which consisted of confusion and visual hallucinations. During this time, the patient developed abdominal distension with ascites, which resolved on its own before a paracentesis could be performed. The patient's family reported an unintentional weight loss of 15 pounds over a six-month period.

Prior workup outside of our facility included computerized tomography (CT) of the head, chest, abdomen, and pelvis. The patient's abdomen/pelvis showed omental caking and ascites, suggestive of peritoneal carcinomatosis. CT of the head and magnetic resonance imaging (Figure 1) showed multiple small intra-parenchymal lesions with bilateral cerebral hemispheric involvement and a small brain stem lesion, believed to be either metastases or abscesses.

Upon arrival to our facility, the patient was acutely encephalopathic with persistent visual hallucinations. There was no report of any abdominal pain, nausea, vomiting, or diarrhea. On physical exam, he was febrile and had a soft, non-distended abdomen with no hepatosplenomegaly, fluid wave, shifting dullness, or any signs of residual ascites. He was oriented to person but not to place or time and showed no focal motor or sensory deficits. The patient met sepsis criteria with altered mental status, hypotension, fever, and leukocytosis. Two sets of blood cultures were collected and the patient was started empirically on dexamethasone, vancomycin, and ceftriaxone for suspected central nervous system infection and encephalitis. Lumbar puncture was not performed in light of the intra-parenchymal brain lesions and presumed increased intracranial pressure. Interventional radiology was consulted to assess if any ascitic fluid or omental biopsy could be obtained for analysis, however, neither could be found nor deemed safe for biopsy. Hematology-oncology ordered carcinoembryonic antigen, prostate-specific antigen, and a CA19.9 radioimmunoassay.

On day two of admission, the patient remained febrile and testing was expanded to include a TB QuantiFERON® Gold test, toxoplasma IgG and IgM, histoplasma urine antigen, and human immunodeficiency virus (HIV) 1 and 2 antibodies. The patient continued to be encephalopathic with no change in his physical exam.

By hospital day three, mental status began to improve with the patient being alert, awake, and oriented to person, place, and time. The patient's TB QuantiFERON® Gold test was positive, with the patient's family denying any history of or exposure to TB. HIV antibodies were negative. Chest x-ray was performed in light of the positive Quantiferon test and showed no signs of active TB or cavitary lesions. Urine histoplasma antigen was negative, as well as the full oncology workup. Blood cultures at that time showed no growth. Toxoplasma IgG was positive, while his IgM was negative. Infectious diseases assessed the need to treat for TB in light of a positive Quantiferon test but a negative chest x-ray, and whether to treat toxoplasma with brain lesions but a negative IgM.

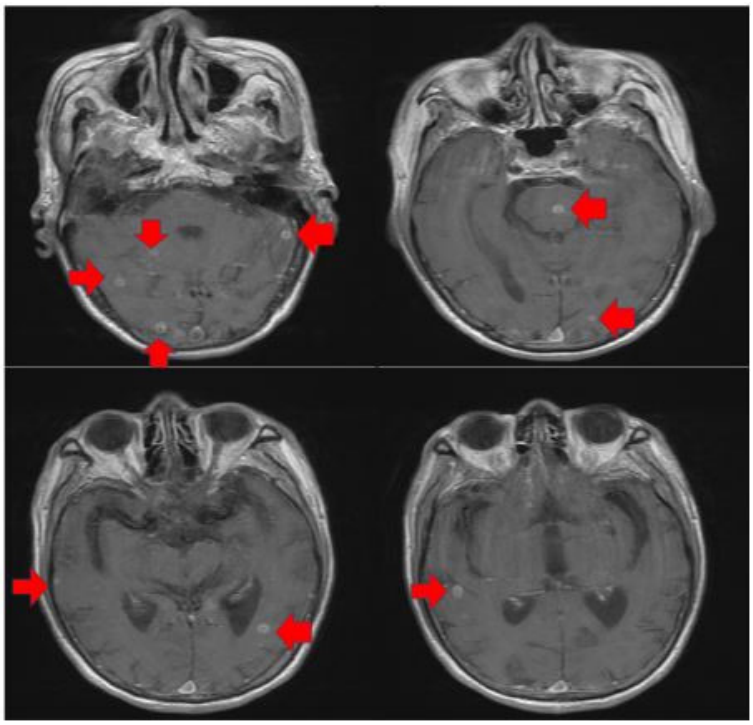

Figure 1. Magnetic resonance imaging showed multiple small intra-parenchymal lesions with bilateral cerebral hemispheric involvement and a small brain stem lesion.

On day six, the patient underwent brain biopsy procedure to assess whether the lesions represented underlying malignancy or infection. The initial pathology results showed caseating granuloma within the brain lesions, most likely representing TB. Cultures of the lesions were taken with mycobacterial cultures. The patient underwent a repeat TB QuantiFERON® Gold test which came back negative, but in spite of this, the patient was started on quadruple therapy for TB empirically due to the pathology from his brain biopsy.

One month after the biopsy, Mycobacterium cultures returned positive for Mycobacterium tuberculosis, confirming the diagnosis of Mycobacterium tuberculosis encephalitis.

DISCUSSION

This case exhibited two different presentations of extrapulmonary TB: presumed abdominal/peritoneal TB followed by TB meningitis/encephalitis. The most common pathogenesis of both abdominal/peritoneal TB and TB meningitis/encephalitis is from hematogenous spread from primary pulmonary TB, each being a form of disseminated TB; however, only 15 - 25% of abdominal TB patients and 40% of TB meningitis patients have concomitant pulmonary TB.[3] Extrapulmonary TB most often occurs months after pulmonary TB.

Risk factors for extrapulmonary TB in the general population include HIV infection, young age, old age, especially if age is greater than or equal to 65, Asian or African origin, and female sex.[4] Risk factors for abdominal/peritoneal TB specifically include alcoholic liver disease and cirrhosis, continuous ambulatory peritoneal dialysis for chronic renal failure, diabetes mellitus, and Bacillus Calmette-Guérin therapy for superficial bladder carcinoma.[5,6] Our patient had two risk factors for TB meningitis, age greater than 65 and coming from southeastern Asia, but denied any of the abdominal TB specific risk factors.

The clinical presentation of abdominal TB is very non-specific, with the most common presenting symptoms being fever, weight loss, abdominal pain, diarrhea, and abdominal distension.[7] Peritoneal TB presents in one of three forms: wet type with ascites, fibrotic type with localized abdominal swelling, or dry-plastic type with the typical "doughy" abdomen, often with omental caking. Typically, patients presenting with peritoneal TB move through the three types in successive fashion, starting with wet type then moving onto fibrotic type to dry plastic types, and this succession occurs in a subacute fashion over a time period of weeks. Definitive diagnosis of peritoneal TB comes from fluid cultures or biopsy from the abdomen.[5,8] Our patient's initial presentation was typical of wet type with ascites which resolved on its own and progressed to dry plastic type with omental caking.

TB meningitis is a more common presentation of extrapulmonary TB with the typical clinical presentation being similar to that of other forms of meningitis: stiff neck, headache, fever, vomiting, altered consciousness occurring in greater than 50% of patients, and anorexia, personality changes, weight loss, night sweats, coma, and plegia or paresis being less common.[9] Our patient initially presented with headache, fever, altered level of consciousness, anorexia, personality changes, and weight loss. Definitive diagnosis of TB meningitis typically is achieved with detection of Mycobacterium tuberculosis in the cerebrospinal fluid via lumbar puncture, either via smear microscopy, mycobacterial culture, or nucleic acid amplification test. Our patient instead underwent brain biopsy with caseating granuloma being found on biopsy.

Of note, our patient's initial TB QuantiFERON® Gold was reactive. However, when the test was repeated, it was non-reactive. The ultimate diagnosis came from culture from the patient's brain lesions which grew on mycobacterial culture 30 days after the initial biopsy. TB QuantiFERON® Gold has shown a specificity ranging from 96 - 98.1%, and a sensitivity ranging from 67 - 89%.[10] The U.S. Centers for Disease Control and Prevention caution against using a negative QuantiFERON® Gold result as a method of ruling out TB in particular populations, especially if there is a high clinical suspicion of TB as there was in this case.[2]

CONCLUSION

This case highlighted the need for a high level of clinical suspicion with regards to diagnosing TB in a patient who is at high risk for developing extrapulmonary TB due to coming from an endemic region for TB. Our patient had quite the typical presentation for abdominal TB that had progressed from wet to dry type. Abdominal ascites and intra-parenchymal brain lesions cast a wide differential, including more common liver pathologies and malignancy. Still, TB should be included in that differential and investigated when risk factors are present, as they were in this case.

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Keywords: tuberculous, Mycobacterium tuberculosis, encephalitis

CASE REPORT

Cerebellar Atrophy and Neurocognitive Disorder as Primary Presentation of Antiphospholipid Syndrome in a Young Male

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INTRODUCTION

Antiphospholipid syndrome (APS) is a multisystem autoimmune disorder characterized by arterial or venous thrombosis and pregnancy morbidity in the presence of antiphospholipid antibodies (aPL).[1] It can be primary or secondary. Primary antiphospholipid syndrome occurs in the absence of any other related disease. Secondary antiphospholipid syndrome occurs with other autoimmune diseases, such as systemic lupus erythematosus.

The presence of aPL can be demonstrated in one of three ways: the presence of anticardiolipin antibodies (aCL), β 2-glycoprotein I antibodies (GPI), or lupus anticoagulant antibodies (LA).[1] To meet classification criteria for antiphospholipid syndrome, patients should have one clinical criterion, either vascular thrombosis (venous or arterial) or pregnancy morbidity (at least one fetal death or preterm delivery or three or more unexplained, consecutive, spontaneous pregnancy losses) and one laboratory criterion, the presence of aPL antibodies need to be seen twice and at least 12 weeks apart for confirmation. Neurological manifestations are common in APS and are attributed mainly to vascular thrombosis and aPL-induced neuronal tissue injury. The most common neurological presentation is an ischemic cerebrovascular accident (CVA) or transient ischemic attack (TIA). However, clinical presentations including cognitive dysfunction, headaches, seizures, and psychosis may be atypical in some cases, which makes diagnosis more difficult.[2]

In our case, a male patient initially presented with a neurocognitive disorder, dementia, cerebral atrophy, and seizure of unknown etiology. A diagnosis of APS was made after a brain biopsy revealed microinfarcts and intimal fibrosis and an aPL antibody test was positive.

CASE REPORT

A 37-year-old male presented to the clinic with an abnormal gait, chronic fatigue, muscle stiffness, and cutaneous bruises. He had suffered these symptoms for many years and initially was diagnosed with a cerebellar neurodegenerative disease of unknown cause. He had seizures and neuropsychiatric symptoms that primarily was represented with mild cognitive impairment and frequent headaches with nonspecific anxiety. Initial brain images revealed atrophy of the brain without a clear explanation.

A physical exam showed significant abnormal gait and muscle strength of 4/5 in both the upper and lower extremities. Primary lab results revealed acute kidney injury and thrombocytopenia. Hypercoagulable panel studies (e.g., protein C, protein S, prothrombin gene mutation, and Factor V Leiden) were collected and results were unremarkable. A follow-up MRI showed worsening brain atrophy secondary to chronic cerebral ischemia, and a brain biopsy showed microinfarcts and intimal fibrosis (Figure 1). An underlying autoimmune disease was suspected, and the patient's work-up came back with the following results: cardiolipin IgG >100 GPL U/ml (negative <10 GPL U/ml, strongly positive ≥80 GPL U/ml), β 2-GP1 IgG >100 U/ml (positive ≥15 U/ml), aPTT 63 S (normal <40 S), and an aPTT-LA mix that remained high.

The patient met the criteria for antiphospholipid syndrome according to the presence of antiphospholipid antibodies in addition to the vascular thrombosis, which led to microinfarctions of the brain microcirculation that eventually resulted in cerebral and cerebellar atrophy and neurocognitive disorder. Treatment was started with aspirin 81 mg daily, hydroxychloroquine 200 mg twice daily, and warfarin with targeted INR (2 - 3). On subsequent visits, the patient reported improvement in his headaches, muscle stiffness, and overall general condition. Most importantly, since starting treatment, surveillance brain imaging has remained stable, and the patient's renal function has improved.

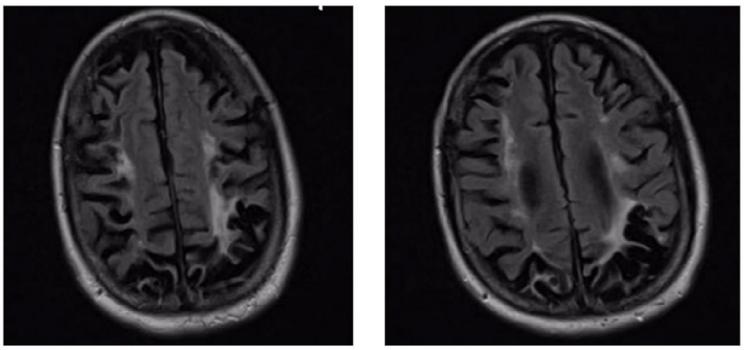

Figure 1. An MRI of the brain showed an increased white matter signal in the centrum semiovale representing encephalomalacia. There was generalized prominence of the cortical sulci representing diffuse cerebral volume loss.

DISCUSSION

The incidence of cerebellar CVA is approximately 1.5% with an average age of 62 years.[3] The main causes are atherosclerosis and cardiac emboli. CVA is relatively rare in younger age groups, and a thorough evaluation to rule out thromboembolic disease should be considered for younger patients. The prevalence of APS with ischemic CVA is as high as 22%, and patients with CVAs are 5.48 times more likely to have the aPL antibodies than the patients without CVAs (95% CI 4.42-6.79).

Neurological manifestations have been reported due to thrombosis, cerebral ischemia, and direct neuronal cell injury by anticardiolipin antibodies, which also can lead to neuropsychiatric symptoms including headache, migraines, chorea, anxiety, and cognitive disorders.[4,5] These neurological manifestations may be confused with other neurological syndromes. The presence of aPL has strong correlations with ischemic CVA, cognitive deficits, and white matter lesions;[6] furthermore, patients who are β 2-GPI-positive have a twofold increased risk of CVA within 15 years of follow-up compared with aCL-negative individuals.[7]

The guidelines recommend anticoagulation for secondary prevention.[8] Warfarin is the standard of care with INR of 2 - 3. Ongoing studies examine the efficacy and safety of direct oral anticoagulants in thrombotic APS, especially rivaroxaban, which potentially provides an additional benefit to the anticoagulant effect, by limiting complement activation in APS patients with thrombotic events while they are on warfarin. On the other hand, hydroxychloroquine (HCQ) has been used in SLE patients, but some studies report that HCQ has a very important role in APS patients by decreasing the aPL antibody titers, preventing recurrent arterial thrombosis, and inhibiting platelet aggregation by inhibiting aPL-induced platelet GPIIb/IIIa receptor expression.[9,10]

Early treatment with anticoagulants and aspirin in those patients are crucial to prevent recurrent CVAs and TIAs.[9] HCQ has an important role to decrease the antibody titers and anti-inflammatory effect. Several experimental measures are addressing the immunomodulatory mechanism in treatment of anti-phospholipid syndrome, through inhibition tissue factor upregulation, which is an important mechanism that explains the pro-thrombotic effects of aPL. These measures include tissue factor inhibition, p38 mitogen-activated protein kinase inhibition, nuclear factor-kB inhibition, platelet glycoprotein receptor inhibition, hydroxychloroquine, statins, inhibition of b2GPI and/or anti-b2GPI binding to target cells, complement inhibition, and B cell inhibition. Further studies are required for the role of HCQ in secondary thrombosis prevention.

The treatment of recurrent thrombosis is controversial. However, the available options are targeting high INR, using direct oral anticoagulants, and adding HCQ. The possibility that the INR may not reflect the true anticoagulant intensity in APS patients should be considered. This is due to the variable responsiveness to LA of the reagents used in the INR test, leading to the potential instability of anticoagulation. In our case, the patient started on oral anticoagulants and aspirin to prevent further transient ischemic attacks (TIAs) and CVAs, and that is what kept his brain imaging stable.

CONCLUSIONS

A high suspicion index and a thorough workup for all patients with CVA presenting before the age of 50 are warranted. Data on etiologies and risk factors for young adults with stroke comes from a few single center or population-based cohorts.[11-13] Vasculopathy (such as arterial dissection), cardiac defects, recent pregnancy, other genetic hypercoaguable states, smoking and illicit drug use, premature atherosclerosis, hypertension, low physical activity, metabolic disorders, and possibly migraine should be on the differential list for such presentations. APS should be added and included in the differential list of diagnoses, especially when the patients present with atypical neurological disorders including cerebellar neurodegenerative disease, seizure, and intractable headache.

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Keywords: antiphospholipid syndrome, cerebellar atrophy, neurocognitive disorder, hydroxychloroquine

Abdominal Ultrasound and Abdominal Radiograph to Diagnose Necrotizing Enterocolitis in Extremely Preterm Infants

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INTRODUCTION

Necrotizing enterocolitis (NEC) is an important contributor toward mortality in extremely premature infants and Very Low Birth Weight (VLBW) infants. The incidence of NEC was 9% in VLBW infants (birth weight 401 to 1,500 grams) in the Vermont Oxford Network (VON, 2006 to 2010, n = 188,703).[1] The incidence of NEC was 7% in 1993, increased to 13% in 2008, and decreased to 9% in extremely preterm infants (22 to 28 weeks gestation) in the Neonatal Research Network Centers (1993 to 2012).[2] The incidence of surgically treated NEC varies from 28 to 50% in all infants who develop NEC.[3] Surgical NEC occurred in 52% in the VON cohort.[1] In this cohort, the odds of surgery decreased by 5% for each 100 gram increase in birth.

The incidence of surgical NEC has not decreased in the past decade.[4] The mortality from NEC is significantly higher in infants who need surgery compared to those who did not (35% versus 21%).[1] The case fatality rate among patients with NEC is higher in those surgically treated (23 to 36%) compared to those medically treated (5 to 24%).[3] In addition to surgery, NEC mortality rates are influenced by gestational age, birth weight,[1,2,5] assisted ventilation on the day of diagnosis of NEC, treatment with vasopressors at diagnosis of NEC, and black race.[6,7]

Extremely preterm infants who survive NEC are at risk for severe neurodevelopmental disability and those with surgical NEC have a significantly higher risk of such delays (38% surgical NEC versus 24% medical NEC).[8] Diagnosis of necrotizing enterocolitis is challenging and it is usually suspected based on non-specific clinical signs. Bell's criteria and Vermont-Oxford Network criteria help in the diagnosis of NEC.

Bell's criteria, commonly used for diagnosis, staging, and planning treatment of NEC, were described in 1978 and modified in 1986.[9,10] Bell's stage I signs are non-specific: temperature instability, lethargy, decreased perfusion, emesis or regurgitation of food, abdominal distension, recurrent apnea, and on occasion, increased support with mechanical ventilation. Abdominal distension and emesis are more common than bloody stools in very preterm infants compared to term infants.[7] Abdominal radiographic findings are an integral part of Bell's criteria. Identification of Bell's stage I NEC (early NEC) with abdominal radiograph is challenging, as the features on abdominal radiograph (normal gas pattern or mild ileus) are non-specific. With progression of NEC to Bell Stage IIA, the symptoms (grossly bloody stools, prominent abdominal distension, absent bowel sounds) and features on abdominal radiographs (one or more dilated loops and focal pneumatosis) are more specific.

On the other hand, the Vermont Oxford Network criteria for NEC consist of at least one physical finding (bilious gastric aspirate or emesis, abdominal distension or occult/gross blood in the stool in the absence of anal fissure) and at least one feature on abdominal radiograph (pneumatosis intestinalis, hepatobiliary gas, or pneumoperitoneum).[1] These features correspond to Bell Stage IIA or Stage IIB and are not features of early NEC. Thus relying solely on abdominal radiograph for diagnosis of early NEC, as is practiced currently, has significant drawbacks especially in extremely premature infants.[7] Ultrasound has been suggested to improve the percentage of infants diagnosed with early NEC.[11] However, this imaging modality is not used routinely in the diagnosis or management of NEC.

As the incidence of surgical NEC and mortality from NEC continues to be high, the literature to demonstrate the shortcomings of abdominal radiographs and promise of abdominal ultrasound in diagnosis of NEC is reviewed.

CHALLENGES OF USING ABDOMINAL RADIOGRAPHY TO DIAGNOSE NEC

Negative abdominal radiographs. Despite developments in the field of imaging, abdominal radiograph continues to be standard of care to diagnose NEC. However, it has been known since the 1980s that premature infants developed significant gangrenous NEC (intestinal gangrene documented at surgery or autopsy) before abdominal radiograph was diagnostic of NEC.[12] The sensitivity of abdominal radiographs was low to diagnose pneumatosis (44%), portal venous gas (13%), and free air (52%), but the specificity ranged from 92 to 100% in a cohort of preterm infants with NEC and some with spontaneous intestinal perforation confirmed at surgery.[13] The authors concluded that negative radiologic findings need to be interpreted with caution in preterm infants suspected to have NEC or spontaneous intestinal perforation.

A higher percent of radiographs were negative for pneumatosis, portal venous gas, pneumoperitoneum in extremely premature infants (birth weight <1,000 grams) compared to term infants.[7] Gasless abdomen as a feature of NEC was absent in term infants but occurred in 42% of extremely premature (EP) infants.

Variability in interpretation of abdominal radiographs in preterm infants with NEC. Significant variation in the interpretation of abdominal radiographs to diagnose NEC, in preterm infants, has been reported.[14] Two studies regarding inter-observer variability in the interpretation of abdominal radiographs in suspected NEC concluded that the management of infants with suspected NEC should not be based solely on radiologic signs and that abdominal radiographs were not sufficient to make a correct and timely diagnosis.[15,16]

More recently, Coursey et al.[17] devised a 10-point scale of abnormal radiographic findings (Duke Abdominal Assessment Scale) and concluded that the inter-observer agreement was superior to earlier studies, but variation in interpretation persisted.

Radiation exposure from multiple abdominal radiographs for NEC in extremely premature infants. Premature infants are exposed to multiple radiographs during their hospital stay and especially those suspected or diagnosed to have NEC. In the study by Iyer et al.,[18] NEC was a significant risk factor associated with radiation exposure.

In summary, abdominal radiographs are not very sensitive to diagnose early NEC with a well-documented problem of inter-observer variability in interpretation. Extremely preterm infants are exposed to increasing doses of radiation from the multiple radiographs done to diagnose and monitor NEC. In addition, there is little evidence regarding the optimal frequency, whether to use one or two views, and how long to continue abdominal radiographs for diagnosis and monitoring progression of NEC.[19] On the other hand, abdominal radiographs can be obtained any time; neonatologists and radiologists are familiar with the features of NEC on abdominal radiograph and a large number of extremely preterm infants have been diagnosed with NEC using abdominal radiographs for decades. Hence, abdominal radiographs continue to be the "gold standard" for diagnosis of NEC at this time.

CHALLENGES OF USING ABDOMINAL ULTRASOUND TO DIAGNOSE NEC

Abdominal ultrasound provides real time images of bowel and fluid in the peritoneal cavity and can depict some features of NEC that cannot be seen with abdominal radiograph such as peristalsis and presence or absence of bowel wall perfusion.[11] Abdominal ultrasound is possibly more sensitive, compared to abdominal radiograph, to detect intramural gas (pneumatosis), portal venous gas, and free gas (pneumoperitoneum).

The technical challenges of using abdominal ultrasound (with Doppler and gray scale) to detect NEC. Efforts to evaluate the role of abdominal ultrasound for diagnosis of NEC date back to the 1980s.[20-22] Recently, Faingold et al.[23] showed that Doppler ultrasound could be used to study bowel viability in infants with NEC. Kim et al.[24] showed the utility of using gray-scale ultrasound to evaluate the bowel wall in infants with NEC.

Three recent reviews detailed the usefulness of abdominal ultrasound in the diagnosis of NEC.[11,25,26] Faingold et al.[23] and Yikilmaz et al.[27] give technical details regarding a thorough ultrasound examination of the abdomen in suspected cases of NEC in preterm infants. These details would help other physicians to develop protocols for use of abdominal ultrasound to diagnose NEC. The initial learning curve regarding the techniques of abdominal ultrasound to detect NEC and the interpretation of images may be steep.

Intramural gas (pneumotosis) consisting of gas bubbles in the subserosal and submucosal layers of the bowel wall appear as echogenic dots.[25] The foci of dots from pneumatosis may vary from a few dots to multiple dots involving the whole circumference of bowel.

Portal venous gas is seen as echogenic round particles in the parenchyma of the liver (trapped in small branches of portal vein).[25] Free air (pneumoperitoneum) is seen as bright echoes between the abdominal wall and the anterior surface of the liver. Abdominal fluid usually is detected close to the bladder and localized echogenic fluid is suggestive of bowel perforation.

Usefulness of abdominal ultrasound in diagnosing NEC in preterm infants. In the Kim et al.[24] study, detection of pneumatosis using abdominal ultrasound was more accurate than abdominal radiographs in early NEC (Bell stage I). In a prospective study, Dordelmann et al.[28] screened premature infants (796 were routine ultrasound screening without abdominal symptoms and 48 screening for suspected NEC) for portal venous gas using abdominal ultrasound. None of the 796 routine screenings were positive. The study concluded that no other clinical condition other than NEC was associated with visualization of portal venous gas on abdominal ultrasound.

In a retrospective study from the same group of investigators, the use of abdominal ultrasound to detect portal venous to diagnose NEC showed a sensitivity of 82% and specificity of 96%.[29] One infant with volvulus was diagnosed with portal venous gas and was deemed a false positive.

Detection of portal venous gas on abdominal radiographs has been a harbinger of bad outcomes.[30] It is possible that abdominal ultrasound may identify portal venous gas before extensive necrosis of the intestines has occurred.[25] Inadvertent injection of air either during the placement or use of an umbilical venous catheter has been reported as a benign cause of portal venous gas,[31,32] but most often portal venous gas is diagnostic of NEC.

In a recent meta-analysis of abdominal ultrasound studies in infants with suspected NEC (11 studies, n = 748 infants), Cuna et al.[19] have shown that the bowel ultrasound features strongly associated with surgery or death were free air, absent peristalsis, complex ascites, and focal fluid collections. They also found that some bowel ultrasound features were not associated with surgery or death such as portal venous gas, increased bowel perfusion, and simple ascites. Chen et al.[33] found that abdominal ultrasound was significantly superior to abdominal radiograph in the prognostic prediction of NEC.

Limitations of abdominal ultrasound for diagnosis of NEC in preterm infants. The use of abdominal ultrasound for diagnosis of NEC has some technical limitations, especially to assess perfusion of the bowel, and some of these limitations may be overcome in the future with the use of contrast-enhanced ultrasound.[34]

The experience of the radiologist and the sonographer to assess and interpret the abdominal ultrasound for features of NEC is important. In addition, there were no studies to assess the inter-observer and intra-observer variability of interpretation of abdominal ultrasound findings in NEC.[25]

Abdominal radiographs are available round the clock in most neonatal intensive care units. However, abdominal ultrasound may not be available outside of regular hours in most hospitals. Interpretation of abdominal radiographs to diagnose NEC is part of the training for radiology residents and neonatal fellows. It is not clear how many academic programs provide training in interpretation of abdominal ultrasound for diagnosis of NEC to radiology residents and neonatal fellows.

In summary, there is evidence that abdominal ultrasound is useful in diagnosing NEC with a number of limitations as outlined above. There is no evidence for optimal timing and frequency of abdominal ultrasound imaging in suspected cases of NEC. Finally, it is not clear from studies done so far whether the combined imaging (abdominal radiograph plus abdominal ultrasound) would improve outcomes (surgery and/or death) in extremely preterm infants suspected to have NEC.

All studies so far have compared abdominal radiograph with abdominal ultrasound to diagnose NEC. However, a well-designed, randomized, prospective, multi-center clinical trial comparing abdominal ultrasound plus abdominal radiographs to abdominal radiographs alone in extremely preterm infants suspected to have NEC has not been done. This type of study would be important as other efforts toward early identification of NEC in extremely preterm infants, including biomarkers and near-infrared spectroscopy (NIRS), have not yielded clinically significant results.[4]

CONCLUSIONS

Surgical NEC occurs in a high percent of extremely preterm infants with NEC leading to increased mortality and long-term morbidity in these infants.[1,3] Primary prevention of NEC in extremely preterm infants is of utmost important and so are the efforts to decrease surgical NEC. Abdominal radiographs are the current standard for diagnosing NEC but have significant limitations in diagnosing early NEC.[7] Abdominal ultrasound has shown promise in diagnosis and prognosis of NEC.[33] There is an urgent need to decrease surgical NEC and mortality in extremely preterm infants with NEC and a well-designed study comparing abdominal radiograph alone versus simultaneous abdominal radiograph and abdominal ultrasound may help in this regard.

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