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RESEARCH ARTICLE

Screening Colonoscopy Adverse Events in Aging Adults: Does Frailty Matter?

Toosizadeh N[1,2,3], Ehsani H[1,3], Taleban S[1,4], Golden T[1,5], Tirambulo C[1] and Mohler J[1,2,3]*

[1]*Arizona Center on Aging, College of Medicine, University of Arizona, Tucson, Arizona, USA*

[2]*Division of Geriatrics, General Internal Medicine and Palliative Medicine, College of Medicine, University of Arizona, Tucson, Arizona, USA*

[3]*Division of Biomedical Engineering, College of Engineering, University of Arizona, Tucson, Arizona, USA*

[4]*Division of Gastroenterology & Hepatology, College of Medicine, University of Arizona, Tucson, Arizona, USA*

[5]*Department of Medicine, College of Medicine, University of Arizona, Tucson, Arizona, USA*

***Corresponding author:** *Jane Mohler, MPH, PhD, Arizona Center on Aging, College of Medicine, University of Arizona, 1821 E. Elm Street, Tucson, AZ 85719, USA, Tel: 520-626-5800, Fax: 520-626-5801*

Abstract

Screening colonoscopy is beneficial in screening for colorectal cancer, though it is not without risks, which increase with increasing age. The objectives of this prospective feasibility and outcomes study was to assess the effectiveness of the upper-extremity frailty (UEF) test to risk stratify adults ≥ 50 years of age undergoing routine screening colonoscopy.

Socio-demographic data, the Charlson Comorbidity Index (CCI), and UEF clinical frailty syndrome classification (non-frail versus pre-frail/frail) were assessed prior to colonoscopy, and acute colonoscopy outcomes were stratified into three severity categories. Logistic regression and ANOVA/ANCOVA were employed.

41% of non-frail had one or more complications, versus 70% of pre-frail/frail group. Those in the pre-frail/frail group had nearly three times the number of acute colonoscopy complications (OR 2.84, p = 0.01) when compared to the non-frail. Chronological age, and comorbidity score (CCI) failed to predict complication outcomes. UEF frailty was useful in predicting acute complications in screening colonoscopy.

Keywords

Colonoscopy, Screening, Frailty, UEF, Outcomes

Introduction

Screening recommendations become more complex with increasing age. Colorectal cancer (CRC) is second in cancer deaths in the United States (US cancer stats), and lifetime risk of CRC is 1/22 [1]. Screening and early treatment prevent an estimated 10,000 additional deaths each year in comparison with late-stage diagnosis [2]. The United States Preventive Services Task Force recommends screening for colorectal cancer starting at age 50 years and continuing until age 75 years, with those 76 to 85 years screened based on overall health and prior screening history [3]. However, screening colonoscopy is associated with risks, including complications from testing, over-diagnosis and treatment [4]. Screening colonoscopy is not without serious adverse events in asymptomatic persons including hypotensive events, perforations and major bleeds; and these increase with age [5]. Frailty syndrome has been demonstrated to be a robust predictor of falls, incident disability, hospitalization, surgical complications and mortality [6], and the integration of frailty measures in clinical practice is crucial to inform the recommendation regarding geriatric screening and intervention [7]. The purpose of this feasibility/outcome study was to assess the effectiveness of the validated upper-extremity frailty (UEF) test [8,9] as a risk stratification tool in routine screening colonoscopy in adults.

Methods

Participants included adults undergoing routine CRC screening colonoscopy (June 2016 to July 2017) from a major integrated Academic Medical Center. Inclusion

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criteria included: 1) ≥ 50 years; and 2) Capacity to understand instructions. Exclusion criteria included: 1) Mobility impairment preventing performance of UEF; non-English speaking. The study was approved by the University of Arizona Institutional Review Board, and informed written consent was obtained by trained coordinators according to the principles expressed in the Declaration of Helsinki from all participants [10].

Socio-demographic data, and the Charlson Comorbidity Index (CCI) [11] were assessed before the UEF assessment, just prior to undergoing colonoscopy [8,9]. The Anesthesia Society of America's "ASA Physical Status Classification System a I (normal healthy patient) to VI (declared brain dead) Anesthesia risk classification system was assigned prior to anesthesia.

Upper Extremity Frailty (UEF) test

The validated UEF test was used to assess frailty using wearable motion sensors (BioSensics LLC, Cambridge, MA) during a 20-second trial of rapid elbow flexion and extension while in a seated position. Several outcomes representing kinematics and kinetics of elbow flexion were derived, based on physical frailty features including: slowness (speed of elbow flexion), weakness (strength of upper-extremity muscles), exhaustion (muscle fatigue), and flexibility (upper-extremity range of motion). Standard frailty categories (non-frail, pre-frail, and frail) were derived. UEF model development and validation processes have been explained comprehensively within our previous work, and demonstrate a 99% sensitivity and 97% specificity when compared to the Fried Frailty Index [12].

Colonoscopy procedure and complications

Acute complications during and immediately following the colonoscopy were recorded. Blood pressure, heart rate, and oxygenation status were measured every two minutes during the procedure, and every five minutes following the procedure until discharge. Complications were stratified into three categories according to severity. Major complications required hospitalization or blood transfusion. Minor complications, included changes in cardiovascular status included systolic ≤ 90 or ≥ 180 mmHg, heart rate < 40 or > 100), and desaturation (SpO_2 < 90). Medication reversal agents (e.g., atropine and metoprolol) and increased oxygen, changes in cardiac rhythm, myocardial infarction, colon perforation, rectal hemorrhage, and colonoscopy completion rates were recorded, as well as post-procedure difficult arousal or ongoing pain.

Statistical analysis

Pre-frail and frail participants were combined due to our small sample size (frail subjects n = 5). The association between frailty and colonoscopy complication occurrence was assessed using multinomial logistic regression, considering complication occurrence (yes or no) as the dichotomous dependent variable. Frailty group and the covariate of age were considered as independent variables. Sociodemographic and clinical variable group comparisons were performed with chi^2 (proportions) and t-tests (means), and CCI score among frailty groups were assessed using one-way analysis of variance (ANOVA) model. Differences in number of complications between the frailty groups were assessed using analyses of covariates (ANCOVA), considering age as a covariate. The above analyses were repeated separately by assigning either major complications, minor complications requiring intervention, or minor complication requiring no intervention as the dependent variable. Similarly, we assessed the association between CCI score and colonoscopy complication (or the number of complications) as the dependent variable. All analyses were done using JMP (Version 11, SAS Institute Inc., Cary, NC), and statistical significance was concluded when $p < 0.05$.

Results

Participants

Ninety-nine participants were enrolled: 49 were non-frail (mean age: 60.8 ± 7.8 years) and 50 were pre-frail/frail (mean age: 64.8 ± 9.2 years) (Table 1). Pre-frail/frail participants differed from non-frail participants, as they were older (6%, p = 0.02); and male sex (63% compared to 34%) in the non-frail group (p < 0.01). Ninety-four percent of pre-frail/frail and 92% of non-frail participants received propofol (Diprivan) during the colonoscopy; the remainder received fentanyl (Fenilate) and midazolam (Versed).

Clinical measures

Charlson Comorbidity Index measure did not differ between frailty groups (Table 1).

Table 1: Demographic data, complications, comorbidity and ASA scores for non-frail and pre-frail/frail groups.

Variable	Non-frail Group	Pre-frail/Frail Group	p-value	CI	Effect Size
Number, n (% of total)	49 (49%)	50 (51%)	-	-	-
Male, n (% of the group)	31 (63%)	17 (34%)	< 0.01*	(-1.07) - (-0.24)	-
Mean age, years (SD)	60.82 (7.81)	64.76 (9.17)	0.02*	(-3.67) - (-0.27)	0.23
Mean stature, cm (SD)	173.18 (8.29)	167.36 (10.32)	< 0.01*	(1.04) - (4.78)	0.31
Mean body mass, kg (SD)	82.38 (16.83)	81.39 (19.35)	0.79	(-3.13) - (4.11)	0.03
Mean BMI, kg/m^2 (SD)	27.49 (5.77)	28.99 (6.00)	0.21	(-1.92) - (0.43)	0.13
Adverse outcomes, n (SD)†	0.72 (0.94)	1.51 (1.72)	0.01*	(-0.69) - (-0.08)	0.30
Comorbidity Score, (0-35) (SD)	3.07 (2.05)	3.80 (2.37)	0.11	(-0.82) - (0.08)	0.17

†p-value is adjusted with age; CI: confidence interval; SD: standard deviation; BMI: body mass index.

Table 2: Complications during and immediately after the colonoscopy procedure.

Complications	Number of Occurrences		
	Non-frail (n = 49)	Pre-frail/Frail (n = 50)	Total (n = 99)
MAJOR[1]			
Myocardial infarction during or immediately after the procedure	0	1	1
Colonic perforation during or immediately after the procedure	0	1	1
Rectal hemorrhage during or immediately after the procedure	0	1	1
MINOR Requiring Intervention			
Hypertension (Systolic > 180 mmHg) during or immediately after the procedure	1	3	4
Hypotension (Systolic < 90 mmHg) during or immediately after the procedure	1	5	6
Tachycardia (HR > 100) during or immediately after the procedure	0	1	1
Desaturation (SpO_2 < 90%) during or immediately after the procedure	0	2	2
MINOR Requiring No Intervention			
Hypertension (Systolic > 180 mmHg) during or immediately after the procedure	2	9	11
Hypotension (Systolic < 90 mmHg) during or immediately after the procedure	16	19	35
Tachycardia (HR > 100) during or immediately after the procedure	3	8	11
Bradycardia (HR < 40) during or immediately after the procedure	1	1	2
Desaturation (SpO_2 < 90%) during or immediately after the procedure	3	3	6
Change in cardiac rhythm during or immediately after the procedure	1	2	3
Difficulty to arouse after the procedure	1	0	1
Procedure aborted due to complication[2]	0	2	2
Total number of complications during and immediately after the procedure (percentage of participants with ≥ 1 complications)	29 (41%)[3]	58 (70%)[4]	87 (56%)[5]

HR: heart rate; SpO_2: peripheral capillary oxygen saturation.

[1]All major complications occurred in one patient; [2]There were 6 total procedures aborted, 2 in non-frail and 4 in pre-frail/frail patients; [3]Complications occurred in 20 patients; [4]Complications occurred in 35 patients; [5]Complications occurred in 55 patients.

Colonoscopy complications

Overall, 55 participants experienced at least one complication during or immediately following the colonoscopy procedure, with 87 total adverse events (Table 2). Hypotension occurred most often (41 events). With the exception of bradycardia and difficulty to arouse, the number of complications was higher among pre-frail/frail than non-frail individuals. Only one pre-frail/frail group participant experienced major complications.

Association between frailty and colonoscopy complications

Pre-frail/frail participants had twice as many complications (Table 2); 41% of non-frail participants had one or more complications during or immediately after colonoscopy, versus 70% of pre-frail/frail group. When examining the association between frailty, age, comorbidity, and ASA with colonoscopy complications, those in the non-frail group had nearly three times fewer colonoscopy complications (OR 2.84, p = 0.01, CI 0.11-0.95).

Events occurred more often in the pre-frail/frail versus the non-frail group regardless of age including those aged 50-64 (n = 33, 21, 3 non-frail/pre-frail/frail respectively); in those aged 65-74 (n = 15, 18, 2 non-frail/pre-frail/frail respectively); and in those ages 75 and above (n = 1, 6, 0 non-frail/pre-frail/frail respectively).

Comorbidity score (OR 0.87 p = 0.19, CI -0.36-0.07) was not statistically significant (not shown). No significant association was observed between age or CCI score and number of complications. Of note, pre-frailty/frailty group assignment was the only measure to predict adverse outcomes both during and immediately after the procedure (data not shown).

When stratifying minor complications, frailty spectrum was significantly associated with occurrence of minor complications that required intervention (p < 0.01); however, frailty was not significantly associated with minor complications requiring no intervention (p = 0.15). All three major complications and the two aborted colonoscopies occurred in the pre-frail/frail group.

Discussion

In our prospective feasibility and outcomes study of patients undergoing routine screening colonoscopy, we found the UEF assessment a simple and time efficient (one to two minutes) tool allowing implementation in a busy academic medical center setting. Where chronological age and comorbidity score (CCI) failed to predict acute colonoscopy outcomes. Our results indicate that when compared to age or comorbidity index, frailty more accurately reflects acute complications during and immediately following colonoscopy. Despite guidelines, neither patient chronological age nor comorbidities

proved sufficient in predicting colonoscopy outcomes. Our results were consistent in predicting outcomes throughout the procedure, as pre-frailty/frailty was the only measure to predict adverse outcomes both during and immediately after the procedure.

Our study has several strengths. The UEF proved easily performed and feasible and is a useful instrument in assessing risk of patients undergoing screening colonoscopy, and importantly does not require gait. Our analysis reveals that UEF frailty screening performs better than patient age or comorbidity status in predicting acute screening colonoscopy outcomes. Additional prospective studies evaluating various frailty measurements in endoscopy will be helpful in clarifying its role in forecasting endoscopic outcomes.

Limitations include our younger cohort, small sample size and our single institution. Our study was designed to examine the effectiveness of frailty in predicting acute complications of screening colonoscopy in aging adults; further studies are needed to evaluate longer-term outcomes, and in patients undergoing colonoscopy for non-screening purposes. We grouped frail and pre-frail patients in our analyses due to the small sample (n = 5) of frail individuals. Despite our small sample of pre-frail/frail subjects, and despite our relatively young age of participants within this study, we still found statistical significance in the primarily pre-frail group, indicating that even they are at significantly increased risk of complication, thereby strengthening the clinical relevance of our findings.

Conclusions and Clinical Recommendations

Older adult screening recommendations become increasingly complex with increasing age. Despite colorectal cancer screening guidelines, patient age and comorbidities do not adequately account for older adult heterogeneity, and proved insufficient in predicting poor colonoscopy outcomes in this study. These measures should not be relied upon to fully inform CRC screening decisions. The prospective nature of this study allowed for more accurate and precise assessment of outcomes. Providers should risk stratify with frailty measurement when making colorectal cancer screening recommendations in older patients.

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