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## The 5-Factor Modified Frailty Index as a Predictor of Post-operative Complications in Males Undergoing Mastectomy

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## ABSTRACT

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**Background:** The modified five-item frailty index (mFI-5) is a valuable tool for preoperative risk stratification of patients. There is a paucity of literature regarding the use of the mFI-5 in regard to males undergoing mastectomy. The aim of this study was to determine if the mFI-5 can predict negative postoperative outcomes.

**Methods:** The 2005-2016 NSQIP database was queried to identify males aged 60 or older who underwent total mastectomy. Patient demographics, comorbidities, perioperative factors, and postoperative complications were collected. Patients were divided into cohorts based on whether their mFI-5 score was  $<2$  or  $\geq 2$ . Primary outcomes included prolonged postoperative length of stay (LOS), defined as greater than 75<sup>th</sup> percentile of the study population, and postoperative complications.

**Results:** A total of 1,251 patients were identified, of whom 958 patients (76.6%) had mFI-5 scores  $<2$  and 293 patients (23.4%) had mFI-5 scores  $\geq 2$ . A significantly higher prevalence of medical complications occurred in the higher mFI group (6.1% vs. 1.6%,  $p < 0.001$ ). The mFI-5 was an independent risk factor for postoperative medical complications (OR 2.70, 95% CI, 1.28-5.68,  $p = 0.009$ ).

**Conclusion:** This is the first study to evaluate the utility of mFI in predicting postoperative complications in males undergoing total mastectomies. We demonstrate that mFI has utility and is applicable as a risk stratification tool for males undergoing mastectomy.

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### INTRODUCTION

The proportion of the United States population aged 60 and older has continued to rise. As of 2020, the population over the age of 65 grew by one-third since 2010.<sup>1</sup> With life expectancy increasing in the setting of a growing older adult population, surgeons will inevitably encounter more older adult patients

and should increasingly be attentive to the needs of this population to provide safe and specialized treatment.<sup>2</sup>

While the incidence of total mastectomy in women for the treatment of breast cancer is slowly decreasing given the widespread usage of neoadjuvant chemotherapy, mastectomy in males is commonly performed for several indications, including breast cancer, gynecomastia, and gender-affirming surgery. Mastectomy is commonly performed for male breast cancer, which has been increasing in incidence in recent years.<sup>3</sup> It has also been shown to have psychological benefits in those

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who have symptomatic gynecomastia, which is estimated to affect up to 60% of older men.<sup>4,5</sup> Furthermore, there has been a rising demand for mastectomy for gender-affirming surgery (GAS) in recent years, which accounts for approximately 15% of male mastectomies.<sup>6,7</sup> According to the American Society of Plastic Surgeons, there was a 289% increase in GAS among transgender men between 2016 and 2017, and a 15% increase in transgender men pursuing chest surgery between 2019 and 2020.<sup>8,9</sup>

Given the prevalence of gynecomastia in older men, the rise in rates of GAS, and the increasing life expectancy among the United States population, it is likely that the number of mastectomies performed in older males will also increase. Prior to mastectomy, as with any surgical procedure, preoperative risk stratification is essential to determine whether a patient is a suitable candidate for surgery.<sup>10</sup> Frailty is an overall measure of a patient's comorbidity burden and is assessed via a multisystem approach.<sup>11,12</sup> Studies have shown that frailty can effectively predict adverse postoperative outcomes, such as complications and mortality, superior to the predictive value of age alone.<sup>10,13,14</sup> Several frailty indices exist, including the 11-factor modified frailty index (mFI-11), which uses 11 preoperative variables in the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database.<sup>12,15</sup> Lately, the 5-factor modified frailty index (mFI-5) has been increasingly used, with studies demonstrating that the mFI-5 is as efficacious as the mFI-11 in predicting negative outcomes across many surgical subspecialties.<sup>15</sup> The mFI-5 uses a five-point scale that has been shown to positively correlate with a patient's overall frailty.<sup>15</sup> The presence of each variable contributes one point to a patient's overall score: COPD or recent pneumonia, congestive heart failure, non-independent functional status, hypertension requiring medication, and diabetes mellitus. The utility of the newer mFI-5 index versus its 11-factor predecessor comes from its ability to be quickly calculated using patient history alone instead of having trained personnel assess the other variables (i.e., impaired sensorium, ischemic rest pain, functional neurological deficits, etc.).<sup>15</sup>

The mFI-5 has previously been validated as an effective risk stratification tool for females undergoing mastectomy and breast reconstruction.<sup>16-19</sup> However, no studies have evaluated the utility of the mFI-5 in males undergoing mastectomy, and the results of previous studies in female patients may not be reproducible in male patients.<sup>20-22</sup> Therefore, the aim of this study is to determine if the mFI-5 can accurately predict postoperative complications in males undergoing mastectomy, which may impact

clinical decision making, such as the choice to undergo reconstruction.

## METHODS

The 2005 to 2016 ACS NSQIP database was queried to identify male patients aged 60 years and older who underwent total mastectomy. NSQIP is a risk-adjusted data collection mechanism designed to enable hospitals to benchmark quality initiatives by capturing uniform preoperative risk factors and intraoperative variables for surgical patients and tracks 30-day postoperative complications.<sup>23</sup> Because of the inherent limitations of the NSQIP database, it is not possible to infer the sex of the patient during a mastectomy for GAS, and thus all patients listed as male in the database were included in this study.

Men who underwent mastectomy were identified using year-appropriate Current Procedural terminology (CPT) codes: simple mastectomy (CPT 19303); skin-sparing mastectomy (CPT 19304); radical mastectomy (CPT 19305); mastectomy, radical, urban type (CPT 19306); mastectomy, modified radical (CPT 19307). While there has been previous misreporting of CPT code 19304 as a subcutaneous mastectomy, when it was intended to have been coded as skin-sparing mastectomy, we include this code in our analysis to be inclusive of all males who underwent any type of mastectomy.<sup>24,25</sup> Patients who underwent any other concurrent procedure unrelated to their breast surgery were excluded. Patients who underwent partial mastectomy were also excluded.

Data regarding patient demographics, medical comorbidities, perioperative factors, and postoperative complications was collected. Of note, while race was a captured data point, only White, Black, and Asians were analyzed statistically either due to the low number of individuals in other races (e.g., American-Indian/Alaskan, Native Hawaiiin/Pacific Island) or due to lack of data on race for certain patients. Additionally, due to the limitations of the NSQIP database, specific details on the timing of post-operative reconstruction (e.g., immediate, delayed-immediate, delayed) after mastectomy are lacking. Surgical complications were defined as superficial surgical site infections, deep wound infections, organ space infections, wound dehiscence, and return to the operating room. Medical complications were defined as pneumonia, unplanned reintubation, failure to wean off ventilation, progressive renal insufficiency, acute renal failure, venous thromboembolism, urinary tract infection, stroke, bleeding requiring transfusion, myocardial infarction, sepsis, and cardiac arrest. A mFI-5 score was calculated for each patient based on the presence



of diabetes, hypertension, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD) or pneumonia within 30 days of surgery, and dependent functional status, with scores ranging from 0 to 5. Patients were stratified into cohorts based on whether their mFI-5 score was  $<2$  or  $\geq 2$ . We used a threshold mFI-5 score of  $\geq 2$  based on the precedent set in previous studies that evaluated the predictive value of mFI-5 for postoperative morbidity in various surgical specialties.<sup>12,26-29</sup> Primary outcomes included postoperative length of stay, and postoperative complications (medical and surgical). Prolonged postoperative LOS was defined as greater than 75<sup>th</sup> percentile of the entire study population.

Statistical analysis was performed with STATA version 17.0 software (StataCorp, College Station, TX). Univariate analyses were performed using Pearson Chi-square test or Fisher's Exact test, as applicable, for categorical variables, and Student's *t*-test for continuous variables. Potential confounders were controlled for using multivariate regression analysis. Statistical significance was defined at values of  $P \leq 0.05$ .

## RESULTS

A total of 1,251 male patients were identified. Average age and body mass index (BMI) for the entire cohort was 71.8 years and 29.3 kg/m<sup>2</sup>. There

were 958 patients (76.6%) with mFI-5 scores  $<2$ , and 293 patients (23.4%) with mFI-5 scores  $\geq 2$ . BMI was significantly higher in the higher mFI group (31.1 vs. 28.7 kg/m<sup>2</sup>,  $P < 0.001$ ). There was no significant difference in racial distributions between cohorts ( $P = 0.387$ ). There was a higher prevalence of comorbidities in the group with increased frailty including diabetes mellitus (83.3% vs. 4.4%,  $P < 0.001$ ), CHF (3.4% vs. 0.1%,  $P < 0.001$ ), COPD/pneumonia (20.5% vs. 2.6%,  $P < 0.001$ ), and preoperative steroid use (5.1% vs. 2.5%,  $P = 0.024$ ). American Society of Anesthesiologists (ASA) Classes 3 and 4 were more prevalent in the patients with higher frailty scores (Class 3: 69.3% vs. 47.6%; Class 4: 11.9% vs. 2.6%,  $P < 0.001$ ), and ASA Classes 1 and 2 were more prevalent in those with lower frailty scores (Class 1: 3.4% vs. 1.4%; Class 2: 46.3% vs 17.4%,  $P < 0.001$ ). There were no differences in smoking or end-stage renal disease between cohorts. Operative duration did not differ between frailty cohorts ( $P = 0.327$ ), with an overall average operative time of 81.8 minutes. The rate of post-mastectomy reconstruction was low (3.0%) in the entire study population and did not differ when stratified by frailty groups (3.3% vs. 1.7%,  $P = 0.171$ ). The presence of concurrent axillary procedures during total mastectomy, such as sentinel lymph node biopsy or lymph node dissection, was similar between cohorts (36.1% vs. 35.5%,  $P = 0.846$ ).

**Table 1.** Demographics and patient comorbidities stratified by modified frailty index cohort

Variable	Total (n=1,251)	mFI-5<2 (n=958)	mFI-5≥2 (n=293)	P-value
Age (yr)	71.8 ± 8.0	71.6 ± 8.0	72.4 ± 7.9	0.117
BMI (kg/m <sup>2</sup> )	29.3 ± 5.9	28.7 ± 5.7	31.1 ± 6.2	<0.001
Race				0.387
Caucasian	960 (76.7%)	743 (77.6%)	217 (74.1%)	
African American	114 (9.1%)	80 (8.4%)	34 (11.6%)	
Asian	26 (2.1%)	20 (2.1%)	6 (2.0%)	
Diabetes mellitus	286 (22.9%)	42 (4.4%)	244 (83.3%)	<0.001
Smoking	116 (9.3%)	93 (9.7%)	23 (7.8%)	0.360
Congestive Heart Failure	11 (0.9%)	1 (0.1%)	10 (3.4%)	<0.001
COPD/Pneumonia	85 (6.8%)	25 (2.6%)	60 (20.5%)	<0.001
End-Stage Renal Disease	2 (0.2%)	2 (0.2%)	0 (0%)	1.000
Steroids	39 (3.1%)	24 (2.5%)	15 (5.1%)	0.024
ASA Class				<0.001
1	37 (3.0%)	33 (3.4%)	4 (1.4%)	
2	495 (39.6%)	444 (46.3%)	51 (17.4%)	
3	659 (52.9%)	456 (47.6%)	203 (69.3%)	
4	60 (4.8%)	25 (2.6%)	35 (11.9%)	
Operative duration (min)	81.8 ± 56.0	82.8 ± 58.2	78.7 ± 48.1	0.327
Post-mastectomy reconstruction	37 (3.0%)	32 (3.3%)	5 (1.7%)	0.171
Axillary procedure	450 (36.0%)	346 (36.1%)	104 (35.5%)	0.846

ASA: American Society of Anesthesiologists; BMI: body mass index; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease





Table 1 summarizes patient demographics, comorbidities, and perioperative factors stratified by mFI cohorts. Postoperative length of stay (LOS) was significantly greater in the mFI $\geq$ 2 group (1.2 vs. 0.9 days, P=0.029). A greater proportion of patients with mFI $\geq$ 2 had a prolonged postoperative LOS (>1 day) compared to mFI<2 patients (15.4% vs. 9.3%, P=0.003). A significantly higher prevalence of medical complications occurred in the higher mFI group (6.1% vs. 1.6%, P<0.001). Among the medical complications, pneumonia (1.7% vs. 0%, P=0.001), urinary tract infection (1.4% vs. 0.1%, P=0.012),

unplanned reintubation (1.0% vs. 0%, P=0.013), and sepsis (2.0% vs. 0.1%, P=0.001) occurred significantly more often in the higher mFI cohort. Postoperative surgical complications and readmissions occurred at similar rates between mFI groups.

Table 2 describes surgical and medical postoperative complications. Sub-analysis of males who underwent post-mastectomy reconstruction revealed similar rates of surgical complications amongst mFI cohorts.

**Table 2.** Post-operative complications stratified by modified frailty index cohort

Variable	Total (n=1,251)	mFI-5<2 (n=958)	mFI-5 $\geq$ 2 (n=293)	P-value
Hospital LOS (days)	0.9 $\pm$ 2.1	0.8 $\pm$ 1.8	1.2 $\pm$ 2.8	0.046
Postoperative LOS (days)	0.9 $\pm$ 2.0	0.9 $\pm$ 1.8	1.2 $\pm$ 2.6	0.029
Prolonged Postoperative LOS (>1 day)	134 (10.7%)	89 (9.3%)	45 (15.4%)	0.003
Any Surgical Complication	76 (6.1%)	55 (5.7%)	21 (7.2%)	0.371
Superficial Surgical site infection	28 (2.2%)	21 (2.2%)	7 (2.4%)	0.842
Deep wound infection	7 (0.6%)	5 (0.5%)	2 (0.7%)	0.669
Organ space infection	2 (0.2%)	1 (0.1%)	1 (0.3%)	0.414
Wound dehiscence	4 (0.3%)	2 (0.2%)	2 (0.7%)	0.235
Return to operating room	41 (3.3%)	31 (3.2%)	10 (3.4%)	0.852
Any Medical Complication	33 (2.6%)	15 (1.6%)	18 (6.1%)	<0.001
Pneumonia	5 (0.4%)	0 (0%)	5 (1.7%)	0.001
Venous thromboembolism	8 (0.6%)	7 (0.7%)	1 (0.3%)	0.689
Urinary tract infection	5 (0.4%)	1 (0.1%)	4 (1.4%)	0.012
Reintubation	3 (0.2%)	0 (0%)	3 (1.0%)	0.013
Bleeding requiring transfusion	10 (0.8%)	7 (0.7%)	3 (1.0%)	0.707
Myocardial infarction	3 (0.2%)	1 (0.1%)	2 (0.7%)	0.139
Sepsis	7 (0.6%)	1 (0.1%)	6 (2.0%)	0.001
Septic Shock	3 (0.2%)	1 (0.1%)	2 (0.7%)	0.139
Cardiac arrest	2 (0.2%)	1 (0.1%)	1 (0.3%)	0.414
Readmission	40 (3.2%)	27 (2.8%)	13 (4.4%)	0.168

LOS: length of stay

Multivariate regression analysis demonstrated that mFI was an independent risk factor for postoperative medical complications (OR 2.70, 95% CI, 1.28-5.68, P=0.009) when controlling for potential confounding variables. Additionally, higher

BMI and ASA class were also independent risk factors for postoperative medical complications.

Frailty was not an independent risk factor for prolonged postoperative length of stay, while ASA class was an independent risk factor for prolonged postoperative LOS (Tables 3 and 4).

**Table 3.** Multivariate Regression Analysis for Postoperative Medical Complications

Variable	Odds Ratio	95% CI	P-value
mFI Score	2.70	1.28-5.68	0.009
Body mass index	1.05	1.00-1.11	0.046
Steroids	2.49	0.70-8.88	0.160
Race	1.01	1.05-3.74	0.945
ASA Class	2.0	1.05-3.74	0.036

ASA: American Society of Anesthesiologists; CI: confidence interval; mFI: modified frailty index

**Table 4.** Multivariate Regression Analysis for Prolonged Postoperative Length of Stay

Variable	Odds Ratio	95% CI	P-value
mFI Score	1.23	0.97-1.57	0.091
Body mass index	1.02	0.99-1.05	0.228
Steroids	1.04	0.39-2.75	0.936
Race	1.03	0.86-1.24	0.736
ASA Class	1.59	1.16-2.18	0.004

ASA: American Society of Anesthesiologists; CI: confidence interval; mFI: modified frailty index



## DISCUSSION

This is the first study to evaluate the utility of mFI in predicting postoperative complications in males undergoing total mastectomies. Males undergoing mastectomy are much less studied than their female counterparts, and tools that may aid physician decision making and mitigate complications in at-risk patients are imperative. Our results demonstrate that an mFI score  $\geq 2$  is associated with a higher rate of postoperative medical complications in males undergoing mastectomy. Patients with increased frailty also had significantly higher BMI and a higher prevalence of patients on chronic steroid medication, both of which could potentially confound the results observed. Additionally, patients with a higher ASA classification (class 3 and 4), a preoperative factor that has been shown to be associated with higher perioperative risk,<sup>30</sup> were more likely to have mFI scores  $\geq 2$ , while those with lower ASA classes (class 1 and 2) tended to have mFI scores  $\leq 2$ . The mFI-5 was found to be an independent risk factor for postoperative medical complications (OR 2.70,  $P=0.009$ ) when multivariate regression analysis was performed to account for BMI, steroid use, ASA class and race in males undergoing mastectomy. This finding provides further evidence that the mFI tool is a better predictive tool for morbidity than using age alone in the male mastectomy population. While BMI and ASA class were also independent risk factors for postoperative medical complications, the frailty index provides the strongest odds ratio of 2.70.

Dammeyer *et al.* investigated the use of the mFI-5 in females undergoing mastectomy using the NSQIP database and found that an mFI-5  $\geq 2$  was associated with increased postoperative complications.<sup>19</sup> However, we found that mFI-5 was not independently predictive of postoperative surgical complications, a finding which contradicts the findings of the aforementioned study.<sup>19</sup> While this non-concordant finding between males and females is not entirely clear, the mFI-5 remains an important risk stratification tool to help predict postoperative complications and to aid in shared decision-making between patients and physicians.<sup>31</sup> The data in this study present an important discussion point on the usage of risk stratification tools for predictive postoperative complications. Because frailty is associated with higher postoperative medical complications, physicians can recognize that performing total mastectomy in males with breast cancer presents with the same risks of performing surgery on any frail population. Thus, when facing the choice of performing total mastectomy in this population, surgeons can focus on medical optimization in their patients rather than other specific risk factors.

Moreover, a patient's frailty was not associated with postoperative surgical complications, which further provides evidence that a patient with higher frailty is inherently at higher risk of medical complications after surgery, an unsurprising fact. While the mFI-5 is helpful in determining the risk of complications, it should be noted that its use is not uniquely tied to the male breast cancer population, but further provides data supporting the use of frailty as a quick tool to assess the risk of surgery in high-risk patients.

Of note, there was no difference in rates of postoperative complications following breast reconstruction between mFI-5 groups. Male breast reconstruction after mastectomy is rare, and data is scarce on this subject.<sup>32</sup> Despite federal law mandating that physicians discuss breast reconstruction with all patients undergoing mastectomy, this is rarely done with males compared to females.<sup>33</sup> Given that postoperative complications following reconstruction was similar between frailty cohorts, we advocate that surgeons should offer breast reconstruction to all males undergoing mastectomy as post-mastectomy reconstruction is associated with increased quality of life in both males and females.<sup>34-38</sup>

While the NSQIP database provides insightful information, our study is not without limitations. The NSQIP database only provides data on 30-day morbidity, and thus our values are likely an underreported representation of the real population. Other limitations of the database include previously cited pitfalls of NSQIP, such as the lack of specific surgical indications, outcomes of a given procedure, and disproportionate inclusion of data from large teaching hospitals.<sup>39</sup> Additionally, there are likely more factors that influence morbidity, such as insurance and socioeconomic status, that are not captured in the NSQIP database. Also, as stated in our methods, we could not determine the sex of the patient during a mastectomy for gender-affirming surgery, and thus all patients listed as male in the database were included in the study.

## CONCLUSION

As mastectomy in males is commonly performed, perioperative risk stratification is an effective tool to predict postoperative morbidity in this population. We demonstrated that mFI-5 is a useful predictor of 30-day postoperative medical complications in males undergoing total mastectomy. It should be used with the understanding that medically high-risk patients overall are inherently at risk of surgical complications and that this specific population is not an exception.



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## CONFLICTS OF INTEREST

There are no conflicts of interest to report for any of the authors.

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