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Gender and frailty predict poor outcomes in infrainguinal vascular surgery

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ABSTRACT

Background: Women have poorer outcomes after vascular surgery as compared to men as shown by studies recently. Frailty is also an independent risk factor for postoperative morbidity and mortality. This study examines the interplay of gender and frailty on outcomes after infrainguinal vascular procedures.

Materials and methods: The American College of Surgeons National Surgical Quality Improvement Program database was used to identify all patients who underwent infrainguinal vascular procedures from 2005–2012. Frailty was measured using a modified frailty index (mFI; derived from the Canadian Study of Health and Aging). Univariate and multivariate analysis were performed to investigate the association of preoperative frailty and gender, on postoperative outcomes.

Results: Of 24,645 patients (92% open, 8% endovascular), there were 533 deaths (2.2%) and 6198 (25.1%) major complications within 30 d postoperatively. Women were more frail (mean mFI = 0.269) than men (mean mFI = 0.259; $P < 0.001$). Women and frail patients (mFI>0.25) were more likely to have a major morbidity ($P < 0.001$) or mortality ($P < 0.001$) with the highest risk in frail women. On multivariate logistic regression analysis, female gender and increasing mFI were independently significantly associated with mortality ($P < 0.05$) as well as major complications. The interaction of gender and frailty in multivariate analysis showed the highest adjusted 30-d mortality and morbidity in frail females at 2.8% and 30.1%, respectively and that was significantly higher ($P < 0.001$) than nonfrail males, nonfrail females and frail males.

Conclusions: Female gender and frailty are both associated with increased risk of complications and death following infrainguinal vascular procedures with the highest risk in frail females. Further studies are needed to explore the mechanisms of interaction of gender and frailty and its effect on long-term outcomes for peripheral vascular disease.

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1. Introduction

Over the last 2 decades, the management of lower extremity peripheral arterial disease (PAD) has changed drastically. With the introduction of new technologies and endovascular techniques, vascular surgeons can offer a wide array of interventions for patients, even those who would have been considered poor candidates for open repair. Despite recent advances, women undergoing vascular surgical procedures have been found to have a greater risk for poor outcomes, including increased mortality and worse functional status compared to their male counterparts [1–4]. In studies specific to lower extremity revascularization, female gender has been found to be an independent risk factor for morbidity and mortality [5–11]. Various explanations for this observation include the finding that women often present with more severe disease and at later stages of disease [6,8,12,13]. Women have also been found to be more likely to have emergency surgery compared to men [5]. Other hypotheses include limitations in access due to smaller vessel size in women, postmenopausal hormonal effects on vasculature, and misunderstanding of PAD symptoms as osteoporosis or arthritis [4,13,14].

Frailty has also been shown in recent literature as an independent risk factor for poor outcomes after surgery [15–25]. Although there is no consensus definition for frailty, definitions include "a decreased physiological reserve to respond to stressors"; "a precursor and etiologic factor in disability, but is not synonymous with either disability or comorbidity" and "a grouping of problems and losses of capability which make the individual more vulnerable to environmental challenge" [26,27]. Different methods to quantify frailty have been described, including multiple frailty indices, sarcopenia, questionnaire-based scales, and combination methods. One of the most commonly used scales is the frailty index (FI) as described in the Canadian Study on Health and Aging [28]. Although there are 70 possible deficits described by the Canadian Study on Health and Aging, an FI with as few as 10 deficits has been shown to be a reliable tool [29].

Gender and frailty have both been described as risk factors for poor outcomes after vascular procedures, but there is no clear data on the interplay between the two factors. Frailty may be a measure through which gender differences are mediated. Both are important predictors of outcomes, but how they interact with each other remains a question. The purpose of this study was to evaluate the effect of gender and frailty on outcomes after infrainguinal vascular procedures and the interplay between gender and frailty. Our hypothesis was that gender and frailty both mediate poor postoperative outcomes in infrainguinal vascular procedures, with particular compounding of these effects in frail women.

2. Materials and methods

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database was queried for all patients who underwent infrainguinal vascular procedures (CPT codes 35556, 35566, 35570, 35571, 35583, 35585, 35587, 35656, 35666, 35671, 37224–37,235) from 2005–2012. This database consists of prospectively collected clinical information for major inpatient and outpatient surgical procedures performed at more than 200 participating hospitals throughout the United States and Canada. This database represents de-identified data and does not contain any protected health information. Patient data, including demographics, comorbidities, intraoperative data, and 30-day surgical outcomes were reviewed. In accordance with the ACS NSQIP database, patients under age 16 y were excluded and patients over age 89 y were coded as 90+ to protect patient confidentiality [30]. Additionally, endovascular procedures were recorded in the database only after 2010. Studies have shown the ACS NSQIP data collection and auditing process to be highly reliable, with strong inter-rater reliability [31]. After consultation with the Emory institutional review board, institutional review board approval and need for patient informed consent was waived given the lack of protected health information and de-identified nature of the ACS NSQIP database.

Our primary outcomes were 30-d mortality and 30-d morbidity. Morbidity was divided into major morbidity as well as less severe complications. Major morbidity was defined as occurrence of Clavien-Dindo class IV complications (life threatening or requiring intensive care management: unplanned intubation, failure to wean from ventilator >48 h, acute renal insufficiency requiring dialysis, new onset neurologic deficit or coma, myocardial infarction, cardiac arrest, pulmonary embolism, postoperative bleeding requiring transfusion, graft failure), whereas less severe complications included surgical site infection, pneumonia, deep vein thrombosis, urinary tract infection, peripheral nerve injury that are recorded in the ACS NSQIP database [32]. These variables are defined and recorded per the ACS NSQIP database.

2.1. *Modified frailty index (mFI)*

Preoperative frailty was quantitatively measured using an 11-point modified frailty index (mFI), derived from the Canadian Study of Health and Aging (Appendix A) [28]. The mFI has previously been validated in the ACS NSQIP database and has been used as a marker of frailty in other vascular surgical studies [24,33]. The mFI is calculated by adding one point for the presence of each variable then dividing the sum by 11. Frailty was defined as mFI $\geq$0.25. The mFI was used both as a scale (values, 0–1) and as an indicator for the presence of frailty (mFI <0.25 or mFI $\geq$0.25).

2.2. *Statistical analysis*

Discrete categorical variables were expressed as counts or percentages and analyzed with chi-square or Fisher exact test where applicable. Continuous variables were expressed as means (±standard deviations, std) or as medians (±interquartile ranges) if they were not normally distributed. Continuous variables between groups were assessed by independent Student *t* test. As the ACS NSQIP database records all patients over 90 y of age as "90+," age calculations were performed using 90 y as the presumed age for all patients in