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Published in:
Journal of Vascular Surgery

DOI:
10.1016/j.jvs.2018.12.060

Frailty and functional outcomes after open and endovascular procedures for patients with peripheral arterial disease: A systematic review

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ABSTRACT

Background: Frailty has been associated with postoperative complications and mortality across surgical specialties, including vascular surgery. However, the influence of frailty on postoperative functional outcomes is unclear. We sought to determine the influence of frailty on functional outcomes after open or endovascular vascular procedures in patients with peripheral arterial disease.

Methods: This systematic review was conducted according to the PRISMA guidelines. Eligible articles were identified through database searches of Pubmed and EMBASE in April 2017. Studies reporting on frailty and functional outcomes after vascular interventions for peripheral artery disease (PAD) were included. Outcomes of interest were dependency in activities of daily living (ADL), dependent mobility, discharge destination, disability-free survival, and quality of life. Individual studies were assessed for quality and risk of bias using the Quality in Prognosis Studies tool.

Results: Eight studies met the eligibility criteria and were included. The risk of bias was low in two studies, intermediate in three studies, and high in three studies. Methods for frailty assessment were different for each study. Frailty was a predictor for discharge to a higher level of care, dependent mobility, and dependency in ADL after vascular procedures for PAD. Both frailty models and individual frailty characteristics seem to be associated with these adverse functional outcomes.

Conclusions: Despite a limited amount of literature and an overall intermediate quality of the included studies, this systematic review shows an association between frailty and adverse functional outcomes after peripheral arterial procedures for PAD, including discharge to a care facility, dependent mobility, and a decline in ADL functioning. (J Vasc Surg 2020;71:297-306.)

Keywords: Frailty; Frail elderly; Vascular surgery; Peripheral artery disease; Preoperative risk assessment

The worldwide population is aging exponentially.[1] Consequently, there is a growing recognition of frailty, which can be defined as an age-related state of decreased physiological reserve capacity and impaired resistance to (surgical) stressors.[2] The overall reported prevalence rates of frailty in community-dwelling persons aged 65 years or older varies from 11% to 23% and increases with age to greater than 40% in elderly aged 85 years.[3,4] Frailty has been identified as a risk factor for falls, disability in activities of daily living (ADL), hospitalization and death,[5] and is therefore of increasing interest to health care providers.

In surgical patients, frailty is increasingly recognized as a risk factor of adverse postoperative outcomes. It has been associated with postoperative mortality and complications in general,[6] cardiac,[7] gastrointestinal,[8] and emergency surgeries.[9] In vascular surgery, frailty has been identified an independent risk factor for postoperative mortality and morbidity.[10-14] However, the influence of frailty on functional outcomes, such as ADL dependency, discharge to a care facility, mobility, and quality of life is not clear. Because the prevalence of peripheral artery disease (PAD) increases with age[15] and the number of elderly patients is increasing, these outcomes are of interest. Disabling symptoms from limb ischemia can be an indication for surgery or endovascular revascularization; however, frail patients may have a decreased ability to recover from these procedures.

Knowledge about functional outcomes in frail patients undergoing vascular surgery can contribute to preoperative risk assessment and shared decision making between clinicians and their patients. Therefore, the

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Author conflict of interest: none.

Additional material for this article may be found online at www.jvascsurg.org.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2018.12.060

aim of this review was to assess the influence of frailty on functional outcomes after vascular surgery and endovascular procedures for PAD.

METHODS

This systematic review was carried out according to the recommendations of the PRISMA statement.[16] The protocol for this review was registered at PROSPERO international prospective register of systematic reviews (ID: 72057)

Eligibility criteria. Studies were included if they reported on frailty and functional outcomes in patients undergoing vascular surgery or endovascular interventions for PAD. Types of surgery eligible for inclusion were open and endovascular vascular procedures of the lower extremities, including bypass surgery, atherectomy, percutaneous transluminal angioplasty, and amputation. Because there is no consensus on how to measure frailty, studies using different frailty measurements were included. Articles were excluded if a preprocedural frailty assessment was lacking or when frailty was not the study objective. Outcomes of interest were dependent mobility, ADL dependency, discharge destination, disability-free survival, and quality of life. Eligible studies included observational cohort studies, randomized controlled trials, case-control studies, and cross-sectional studies. Unpublished studies and abstracts were excluded.

Literature search. A literature search was conducted in April 2017 in Pubmed and EMBASE. The search strategy, which was designed after consulting a clinical librarian, was composed of search terms for open and endovascular procedures for PAD and terms for frailty. To increase sensitivity, terms for outcome were not added to the search string. No restriction on publication date or language was applied. A full search string adapted for Pubmed is presented in the Supplementary Table (online only).

Duplicates were removed using Mendeley Reference Manager. Subsequently, two reviewers (F.A., L.V.) independently screened all articles for eligibility based on title and abstract. Of all titles matching the inclusion criteria, the full text was read for a final selection by the same two reviewers. Reference lists of all identified articles were manually searched for additional studies. In case of doubt about eligibility, a third reviewer (P.N.) was consulted. Disagreement was resolved by consensus.

Data extraction and quality assessment. A data extraction sheet was used to derive the following information from each study: publication data, study design, patient characteristics (sample size, age, gender), type of intervention, used frailty measurement, incidence of frailty, length of follow-up, and reported outcome. When available, odds ratios (OR) were reported, with corresponding 95% confidence intervals (CIs). When unavailable, the incidence of the reported outcome was given in percentages for frail and nonfrail patients, with corresponding significance level of the difference. When logistic regression analysis was performed and regression coefficients were reported without corresponding OR, ORs were calculated as the exponential function of the regression coefficient.[17] Corresponding 95% CIs were calculated using the reported standard error. When prognostic model performance was tested, values for the area under the curve in a receiver operating characteristic analysis were reported.

Quality of the individual studies was assessed by two reviewers (F.A., L.V.) independently using the Quality in Prognosis Studies tool.[18] Disagreements were resolved by consulting a third reviewer (P.N.).

Data synthesis. Results of the included studies were not pooled using meta-analysis, because of the heterogeneity in methods used to screen for frailty and in reported outcomes.

RESULTS

Study selection

The search strategy identified 1633 unique articles, of which 1583 were excluded based on title and abstract. The full texts of the remaining 50 articles were read, of which eight met eligibility criteria and were included in the systematic review (Fig 1). A manual search did not yield any additional results. The literature search was performed a second time in December 2017 using the same databases. No additional results were found.

Study characteristics

Table I summarizes study characteristics. Out of eight articles, three were prospective observational cohort studies[22-24] and five were retrospective observational cohort studies.[19-21,25,26] Articles were published between 2004 and 2016. Patients were included between 2006 and 2013, with the exception of one study that included patients from 1996 to 2001. The number of study participants varied from 100 to 15,843. Three studies were conducted in the United States, three in the United Kingdom, one in Australia, and one in Hong Kong. In five studies, the cohort consisted of patients who had various types of vascular surgery (ie, peripheral, aorta or carotid artery surgery).[19,20,22-24] Two articles reported on lower extremity amputation[21,26] and one on open and endovascular lower extremity revascularization.[25] In the studies on lower extremity amputation, the indication for amputation was PAD. In one study, only 66% of patients underwent surgery.[22]

Frailty measurements

Different frailty measurements were used in the individual studies (Tables I and II). Ambler et al[19] retrospectively recorded 15 frailty characteristics, covering six domains of

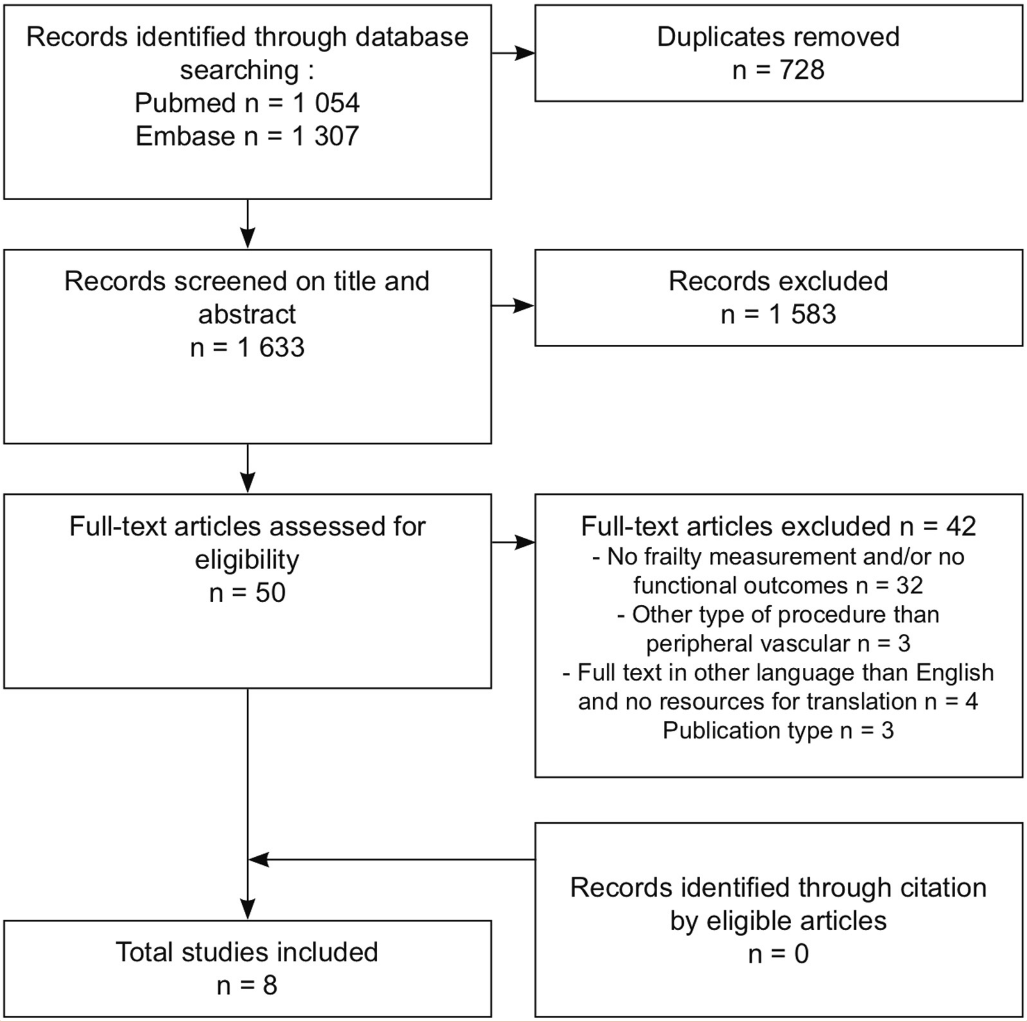

Fig 1. Flow chart of literature search and study selection.

frailty: comorbidity (the Charlson Comorbidity Index (CCI), polypharmacy, and anemia), physical function (ADL dependency and mobility), nutrition, cognition and mood, geriatric syndromes, and social vulnerability. Additionally, based on multivariable analysis, two frailty models were developed. The first consisted of anemia, dependent mobility, polypharmacy, risk of pressure ulcers, depression, and emergency admission. The second consisted of ADL dependency, depression, polypharmacy, a history of falls, and emergency admission. Arya et al[20] used the modified Frailty Index,[27] an 11-point screening tool for frailty that has been validated for the American College of Surgeons National Surgical Quality Improvement Program database, from which the cohort of this study was assembled. The modified Frailty Index covers the domains of comorbidity, ADL dependency, and impaired sensorium. Leung et al[21] tested for frailty using the Barthel score, a 10-point measurement for ADL dependency and mobility.[28] McRae et al[22] defined frailty as presence of one or more of the following parameters: baseline ADL dependency, cognitive impairment, and evidence of malnutrition. In the 2015 article from Partridge et al,[23] frailty was assessed by the Edmonton Frail Scale,[29] which assesses nine domains of frailty: cognition, general health status, ADL dependency, social support system, polypharmacy, nutrition, depression, incontinence, and timed get up and go (TGUG). Additionally, grip strength and gait speed were tested. In their 2014 study, with the same patient cohort, Partridge et al[24] used the Montreal Cognitive Assessment (MoCA).[30] Vogel et al[25,26] assessed ADL performance, cognitive impairment, and the CCI in both their studies.

Quality and risk of bias

Quality assessment is presented in Table III. The risk of bias was categorized as low in two studies,[20,22] intermediate in three studies,[19,23,24] and high in three studies.[21,25,26] Owing to a retrospective study design, five studies were at risk of selection bias and misclassification of study participants as frail or nonfrail. These studies all excluded patients with incomplete data. In one study, the number of patients with incomplete

Table I. Study characteristics

Author	Study design	Sample size	Age, years[a]	Type of surgery or endovascular intervention (% of n)	Frailty measurement	Functional outcomes	Follow-up duration
Ambler et al, 2015[19]	Retrospective observational cohort	N = 413	77 [65-95]	Lower limb revascularization n.s. (42%) AAA repair n.s. (33%) Carotid artery n.s. (13%); other (13%)	Individual characteristics Two self-composed frailty models	Discharge to care facility	Mean, 18 months (range, 12-24 months)
Arya et al, 2016[20]	Retrospective cohort from ACS-NSQIP database	N = 15 843	69.7 ± 10.4	Lower limb revascularization: open bypass (28%), endovascular (14%) AAA repair: open (5%), EVAR (15%) Carotid artery: CEA (37%), stenting (1%)	MFI	Discharge to care facility	30 days
Leung et al, 2004[21]	Retrospective observational cohort	N = 100	77.9 [65-97]	Lower limb amputation at or above ankle (100%)	Barthel score	Independent ambulation	6 months
McRae et al, 2016[22]	Prospective observational cohort	N = 110	75.0 ± 7.0	Lower limb revascularization n.s. (15%). Lower limb amputation (15%) AAA repair: open (7%) Carotid artery: CEA (10%) Other vascular, eg, embolectomy (8%), other nonvascular, eg, split skin graft (11%), conservatively (34%)	≥1 of: dependency in ADL, cognitive impairment (AMT <7), malnutrition (MST ≥2)	Geriatric syndrome (increase in number of ADL for which human assistance is required, delirium, falls, and/or pressure ulcer) Discharge to higher level of care	Until hospital discharge
Partridge et al, 2015[23,b]	Prospective observational cohort	N = 125	76.3 ± 7.3	Lower limb revascularization: bypass graft (17%), endovascular (23%) Lower limb amputation (5%) AAA repair: open (4%), EVAR (35%) Imaging (10%), other (6%)	EFS, gait speed, grip strength	Composite adverse functional outcomes (falls on ward and dependent transfers at day 3 postoperatively)	Until hospital discharge
Partridge et al, 2014[24,b]	Prospective observational cohort	N = 114	76.3 ± 7.4	Lower limb revascularization: bypass graft (16%), endovascular (22%) Lower limb amputation (5%) AAA repair: open (3.5%), EVAR (35%) Imaging (10.5%), other (8%)	MoCA	Composite adverse functional outcomes (falls on ward and dependent transfers at day 3 postoperatively)	Until hospital discharge

Table I. Continued.

Author	Study design	Sample size	Age, years[a]	Type of surgery or endovascular intervention (% of n)	Frailty measurement	Functional outcomes	Follow-up duration
Vogel et al, 2014[25]	Retrospective observational cohort	N = 702	≥67	Lower limb revascularization: open (50%), endovascular (50%)	ADL performance score, MDS CPS, CCI	Level of independency in ADL	6 months
Vogel et al, 2014[26]	Retrospective observational cohort	N = 4965	81 [67-≥86]	Lower limb amputation (10% transmetatarsal, 32% below-knee, 58% above-knee)	ADL performance score, MDS CPS, CCI	Level of independency in ADL	6 months

AAA, Abdominal aortic aneurysm; *ACS-NSQIP,* American College of Surgeons National Surgical Quality Improvement Program; *ADL,* activities of daily living; *AMT,* Abbreviated Mental Test; *CCI,* Charlson Comorbidity Index; *CEA,* carotid endarterectomy; *EFS,* Edmonton Frail Scale; *EVAR,* endovascular aneurysm repair; *MDS CPS,* Minimum Data Set Cognitive Performance Scale; *mFI,* modified Frailty Index; *MoCA,* Montreal Cognitive Assessment; *MST,* Malnutrition Screening Tool; *n.s.,* not specified.
[a]Age is given as mean ± standard deviation or as median [interquartile range].
[b]Same cohort.

data was relatively large (n = 88/702).[25] Two studies had a relatively small number of patients with incomplete data (n = 3/413[19] and n = 76/4965[26]). In two studies, the number of patients with incomplete data was not reported.[20,21] Risk of confounding was common owing to the retrospective recording of data,[19-21,25,26] incomplete measurement of known risk factors for adverse functional outcome,[21] or not including risk factors in multivariate statistical analyses.[23,24] In five studies, patients underwent various types of vascular interventions (ie, peripheral [open and endovascular], aorta, or carotid artery surgery).[19,20,22-24] Only one of these studies performed subgroup analysis per type of procedure.[20] In one study, only 66% of the population underwent surgery or endovascular revascularization and no subgroup analysis was performed; however, correction for surgical severity was performed in statistical analysis.[22]

Association between frailty models and postoperative functional outcomes

Four studies used a model to screen for preoperative frailty and assessed the association with functional outcomes after open or endovascular interventions for PAD (Table II).

Frailty was a predictor for discharge to a care facility in three studies. One study reported an OR of 1.6 (95% CI, 1.3-1.8) for nonhome discharge after open and endovascular lower limb, aortic, and carotid artery interventions, for frail vs nonfrail home-dwelling patients. This model was adjusted for age, comorbidity, and perioperative factors.[20] In subgroup analysis per type of procedure, the unadjusted OR for nonhome discharge for frail vs nonfrail patients was 2.3 (95% CI, 1.9-2.8) after infrainguinal bypass surgery, 2.7 (95% CI, 1.9-3.8) after suprainguinal bypass surgery, and 2.0 (95% 1.3-3.3) after peripheral endovascular interventions. A second study found an OR of 4.2 (95% CI, 1.3-13.8; $P = .02$) for discharge to a higher level of care for frail vs nonfrail patients after admission for PAD, adjusted for age, sex, comorbidity, and surgical severity.[22] The third study developed two frailty models (Table II) and found that frailty was a moderate to good predictor for discharge to a care facility after lower limb revascularization, and aortic and carotid artery surgery (area under the curve of 0.78 and 0.84 in receiver operating characteristic analysis, for the first and second models, respectively).[19]

One study found that frailty was an independent predictor for developing geriatric syndromes (defined as a decline in ADL functioning, delirium, falls, and/or pressure ulcers) after admission for PAD, with an OR of 6.7 (95% CI, 2.0-22.1; $P = .002$) for frail vs nonfrail patients, adjusted for age, sex, comorbidity, and surgical severity. Higher surgical severity, defined by the Vascular Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (V-POSSUM) was also associated with developing geriatric syndromes in this study (OR, 4.6; 95% CI, 1.2-17.7; $P = .03$).[22]

One study reported that 54% of frail patients had falls on the ward and dependent transfers at day 3 after open and endovascular lower limb and aortic procedures, compared with 32% of nonfrail patients (adjusted OR, 1.69; 95% CI, 0.51-5.61; $P = .012$).[23]

Association between individual frailty characteristics and functional outcomes

All included studies reported associations between individual frailty characteristics and adverse functional outcomes after vascular procedures for PAD (Table II). Fig 2 shows these individual frailty characteristics and the number of associations with adverse functional outcomes.

Physical domain

Comorbidity. Five studies reported on the association between comorbidity and functional outcomes after

Table II. Frailty characteristics studied in individual studies

Author	Frailty characteristics										
	Comorbidity	Polypharmacy	Mobility	History of falls	Grip strength	ADL functioning	Anemia	Malnutrition	Cognitive impairment	Depression	Social support system	Hearing or visual impairment
Ambler et al[19]	○	○	○	○		○	○	○	○	○	○	○
		●	●			●	●			●		
		●		●						●		
Arya et al[20]	○											
	●					●						●
Leung et al[21]						○						
McRae et al[22]	○								○			
						●		●	●			
Partridge et al[23,a]			○		○							
	●	●	●			●		●	●	●	●	
Partridge et al[24,a]									○			
Vogel et al[25]	○					○			○			
Vogel et al[26]	○					○			○			

ADL, Activities of daily living.
○ = individual frailty characteristic.
● = frailty characteristic within a model.
[a]Same cohort.

vascular procedures for PAD. The presence of comorbidity was associated with discharge to a care facility after vascular procedures in two studies; one study found that a higher American Society of Anesthesiologists classification was an independent predictor for nonhome discharge (OR, 1.5; 95% CI, 1.3-1.7),[20] and the second study found that a CCI of greater than two was associated with discharge to a care facility ($P < .001$).[19] A third study found no significant relation between a CCI of greater than two and discharge to a higher level of care (OR, 1.3; 95% CI, 0.4-4.5; $P = .68$) or the occurrence of geriatric syndromes (OR, 2.2; 95% CI, 0.7-6.7; $P = .18$). Diabetes was associated with discharge to a higher level of care in this study (OR, 5.5; 95% CI, 1.5-20.7; $P = .01$).[22] Two other studies found that diabetes was associated with an increase in ADL dependency 6 months after open and endovascular procedures for PAD and lower extremity amputations, compared with patients without diabetes.[25,26]

Polypharmacy. The influence of polypharmacy on functional outcomes was assessed in one study. Polypharmacy (using >8 drugs), was independently associated with discharge to a care facility (OR, 1.12; 95% CI, 1.04-1.20; $P = .009$).[19]

Mobility and grip strength. Mobility was assessed in two studies to screen for frailty. In the first study, dependent admission mobility (dependent on walking aid or on others) and a history of two or more falls in the 12 months before arterial vascular intervention, were associated with discharge to a care facility ($P < .001$ for both).[19] In the second study, prolonged TGUG and gait speed were associated with adverse functional outcomes (defined as falls on the ward and dependent transfers at day 3 postoperatively); of patients with a TGUG of 20 seconds or more on admission, 53% had adverse functional outcomes vs 26% of patients with a TGUG of less than 20 seconds ($P = .012$). Of patients with a gait speed of 0.6 m/s or greater on admission, 55% had adverse functional outcomes vs 22% of patients with a gait speed of less than 0.6 m/s ($P = .002$). Additionally, grip strength was tested in this study. In patients with normal grip strength, 31% had adverse functional outcomes compared with 50% of patients with low grip strength ($P = .042$).[23]

ADL dependency. Four studies assessed ADL dependency. One study found that patients who were dependent ambulators after amputation were more ADL-dependent preoperatively compared with patients who were independent ambulators after amputation (mean preoperative Barthel scores of 43.2 vs 83.6, respectively).[21] In two other studies, poor baseline ADL functioning (assessed by using the Minimum Data Set ADL performance score) was associated with worse ADL functioning 6 months after lower limb revascularization ($P < .0001$) and after lower extremity amputation ($P <$

Table III. Quality assessment

	Study population	Study attrition	Method of frailty measurement	Method of outcome measurement	Measurement of and accounting for confounders	Statistical analysis and reporting
Ambler et al[19]	Unclear	Low	Unclear	Low	Low	Unclear
Arya et al[20]	Unclear	Low	Low	Low	Unclear	Low
Leung et al[21]	Low	High	Unclear	Unclear	High	High
McRae et al[22]	Low	Low	Low	Low	Unclear	Low
Partridge et al[23]	Low	Low	Low	Unclear	Unclear	Unclear
Partridge et al[24]	Low	Low	Low	Unclear	High	Low
Vogel et al[25]	High	Low	Low	High	Low	Unclear
Vogel et al[26]	Unclear	Low	Low	High	Low	Unclear

Low risk of bias; unclear/intermediate risk of bias; high risk of bias.

.001) compared with patients with better baseline ADL function.[25,26] This model was corrected for age, gender, comorbidity, cognitive impairment, and type of procedure. In contrast, a fourth study found that patients who were ADL dependent (defined as a Katz score of <6) had a lesser chance of discharge to a care facility after arterial vascular interventions compared with patients with Katz scores of greater than 6 (OR, 0.72; 95% CI, 0.58-0.86, $P <$ .001).[19]

Anemia. The relationship between anemia and functional outcomes after vascular procedures was assessed in one study. Anemia on admission, defined as a hemoglobin of less than 11.9 g/dL, was not associated with discharge to a care facility ($P = .082$).[19]

Malnutrition. Evidence of malnutrition was associated with discharge to a care facility after vascular procedures in one study ($P < .001$ on univariable regression, corrected for multiple testing).[19]

Mental domain

Cognitive impairment and depression. Cognitive impairment was assessed in five studies. In one study, a documented history of dementia was associated with discharge to a care facility ($P < .001$).[19] A second study found no association between dementia and discharge to a care facility.[22] This study did find an association with increased ADL dependency, delirium, falls, and pressure ulcers ($P = .002$). The number of patients with dementia in this study was small; therefore, only univariate analysis was performed. A third and fourth study showed that patients with impaired preoperative cognitive function, assessed with the CPS, were more dependent in ADL 6 months after lower extremity revascularization ($P < .0001$) and after lower extremity amputation ($P < .001$), compared with patients with normal cognitive function.[25,26] In a fifth study, patients with cognitive impairment, defined as a MoCA score of less than 24, had more dependent transfers and falls on the ward after vascular interventions compared with patients with MoCA scores of 24 or greater. However, this difference was not statistically significant (44.2% vs 35.1%, respectively; $P = .360$).[24] One study assessed the relationship between depression and functional outcomes after vascular interventions, and found that patients with a documented history of depression or current use of antidepressants had a more than three-fold increased odds for discharge to a care facility.[19]

Social domain

Social support system. One study assessed the association between living alone independently and discharge to a care facility after vascular procedures and found no significant association ($P = .281$).[19]

Hearing or visual impairment. The influence of hearing and visual impairment on discharge to a care facility after vascular procedures was investigated in one study. No significant associations were found.[19]

DISCUSSION

This review shows that frailty is associated with adverse functional outcomes, including discharge to a care facility (or a higher level of care), ADL dependency, and dependent mobility after vascular surgery and endovascular interventions for PAD. However, the results of this report should be interpreted with caution for multiple reasons. First, only a limited number of studies was identified that met inclusion criteria. Second, owing to heterogeneity in the measurements for frailty and outcome measurements, comparison of results is difficult. Furthermore, in the majority of studies the study population was diverse and consisted of patients undergoing other types of vascular surgery (ie, aortic or carotid artery surgery) than vascular procedures for PAD. Therefore, it is unclear whether the results are representative

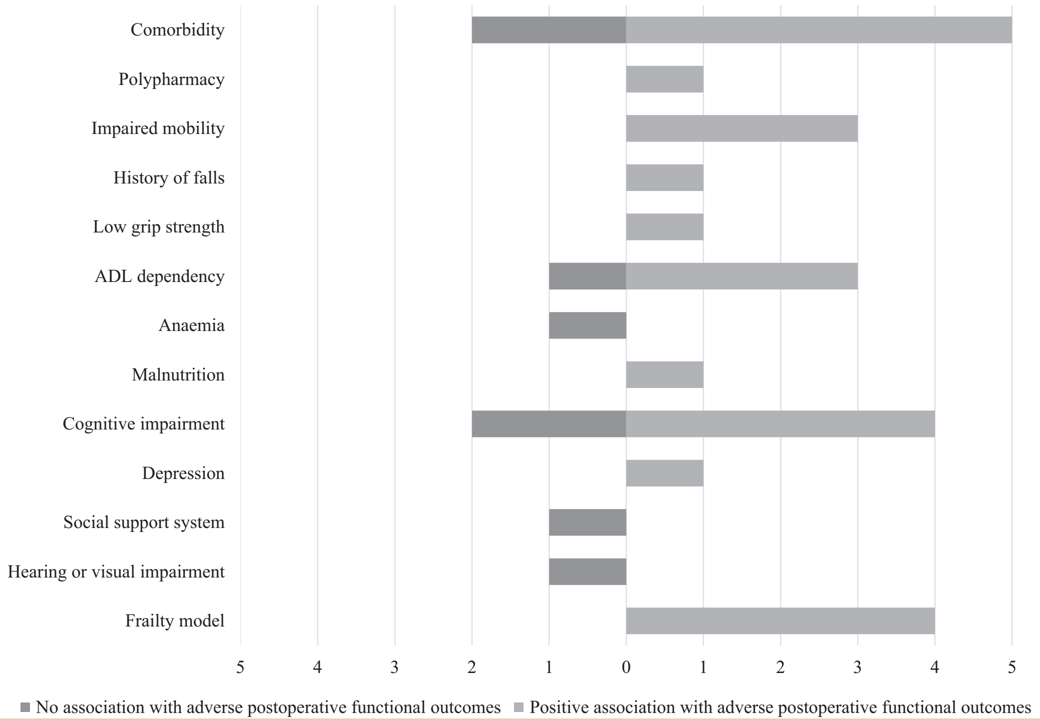

Fig 2. Frailty characteristics and the number of associations with adverse functional outcomes after surgical and endovascular procedures for peripheral artery disease (PAD). The *bars* represent the number of literature reports that present a positive association or no association between a frailty characteristic and adverse functional outcome. *ADL*, Activities of daily living.

for all patients undergoing lower extremity vascular procedures for PAD. Finally, on quality assessment, the risk of bias was estimated to be high in three and intermediate in three out of the eight studies.

Frailty is a multifactorial syndrome and a simple definition or measurement is lacking. It is associated with characteristics such as impaired mobility, weakness, malnutrition, comorbidity, polypharmacy, cognitive impairment, depression, and social isolation.[5,31,32] We assessed not solely the influence of frailty as a syndrome, but also the influence of individual frailty characteristics on functional outcomes after vascular procedures for PAD, to aid vascular surgeons in preoperative risk assessment. For example, in this review, multiple studies reported that preoperative dependent mobility, ADL dependency, and cognitive impairment were associated with adverse functional outcomes, such as discharge to a care facility and a decrease in ADL functioning.

Frailty and functional outcomes in other surgical populations

Although the number of reports on patient-related outcome measures in vascular surgery is limited, studies in other surgical populations support our findings. The association between frailty and discharge to a care facility reported in this review corresponds with results from studies in patients undergoing thoracic aortic surgery,[33] orthopedic surgery,[34] trauma surgery,[35] and urologic surgery.[36] Studies included in this review reported several others factors that were associated with nonhome discharge, including comorbidity, increasing age, and occurrence of postoperative complications.[19,20,22] However, as stated, frailty itself is associated with comorbidity, more advanced age, and a higher rate of postoperative complications. This highlights the complexity of defining individual factors that increase the risk of nonhome discharge. In practice it will often be a multifactorial process. However, frailty was found to be an individual predictor for discharge to a care facility.

Three studies in this review reported an association between frailty (characteristics) and ADL dependency after vascular surgery and endovascular interventions for PAD. Similarly, Schoenenberger et al[37] (2012) studied 106 patients undergoing transcatheter aortic valve implantation, and found that frailty was predictive for a decline in ADL functioning 6 months after transcatheter aortic valve implantation. In contrast, Rønning et al[38] (2014) did not find an association between frailty and decline in ADL functioning after elective colorectal surgery in elderly patients (n = 84). In this study, there was a significant decrease in ADL scores at a mean follow-up of 22 months; however, no predictors for this outcome could be identified.[38] Other frailty-related outcomes in this review included dependent mobility and falls. Unfortunately, no studies reporting on frailty and quality of life after vascular surgery or endovascular interventions could be identified.

Clinical implications. As this review shows, various measurements are used to screen for frailty. Currently, there is no consensus on the best method to detect frailty. Two measurements that are most accepted in literature are the Fried frailty phenotype[5] and the Frailty Index.[39] Because both methods are time consuming, several frailty screening tools have been developed based on the Fried phenotype and the Frailty Index.[29,40-42] However, not all are practical to use in everyday practice, where there is a need for a quick, practical, and effective method to screen for frailty.[43] Several authors suggest using the FRAIL questionnaire, consisting of five self-reported questions, for routine frailty screening during preoperative clinic visits.[42,44] For vascular surgery patients, Mirabelli et al[45] (2018) suggest using a combination of patient-reported frailty (a five-question survey) and clinical judgement (using the Clinical Frailty Scale) to quickly and effectively assess for frailty during routine clinic visits. Further studies support the suggestion that clinical judgement by a trained physician during preoperative assessment is a good method to screen for frailty.[12,40] Hence, a combination of clinical judgement and a self-reported questionnaire could be used in everyday practice.

Despite the limited amount of literature, this review implies that screening for frailty could be of additional value in preoperative risk assessment and shared decision making. Patients should be informed about the benefits and risks of a procedure, including the risk of functional decline. In patients with PAD, disabling symptoms such as pain, nonhealing ulcers, and necrosis can be clear indications for surgery. In these patients, preoperative frailty assessment can be used to identify possibilities for optimization (eg, physical therapy, nutrition, medication reviews). A recent randomized controlled trial by Partridge et al[46] (2018) with patients aged 65 years or older scheduled for elective vascular surgery, showed that patients receiving preoperative comprehensive geriatric assessment and optimization (n = 85), had a shorter length of hospital stay (3.32 days vs 5.53 days), a lesser incidence of complications, and a lower number of patients discharged to a higher level of care (4 vs 12; $P = .051$) postoperatively, compared with patients receiving standard care (n = 91).[46]

Recommendations for future research. Future research should focus on patient reported quality of life of frail patients before and after vascular surgery and endovascular interventions for PAD, and after conservative treatment, and on the (cost) effectiveness of preoperative frailty assessment and prehabilitation. Furthermore, future research should establish a practical frailty assessment tool that can be used for risk stratification at the outpatient clinic and during postoperative surgical rounds. Finally, research should focus on developing a method for sharing information about frail patients within or between health care systems.

CONCLUSIONS

The amount of literature on functional outcomes after peripheral vascular procedures for PAD in frail patients is limited and consensus on how to measure frailty is lacking. However, this systematic review implicates that frailty is associated with adverse functional outcomes, including discharge to a care facility, dependent mobility, and ADL dependency. Screening for frailty could be of additional value in preoperative risk assessment and optimization, and in shared decision making.

AUTHOR CONTRIBUTIONS

Conception and design: FA, LV, ED, JV, EG, PN
Analysis and interpretation: FA, LV
Data collection: FA, LV
Writing the article: FA
Critical revision of the article: FA, LV, ED, JV, EG, PN
Final approval of the article: FA, LV, ED, JV, EG, PN
Statistical analysis: Not applicable
Obtained funding: Not applicable
Overall responsibility: PN

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Submitted Jul 3, 2018; accepted Dec 22, 2018.

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Supplementary Table (online only). Search strategy adapted for Pubmed

Search string domain	
Vascular surgery and endovascular revascularization procedures of lower extremities for peripheral artery disease	("Vascular Surgical Procedures"[MeSH:noexp] OR "Axillofemoral Bypass Grafting"[MeSH] OR "Embolectomy"[MeSH] OR "Thrombectomy"[MeSH:noexp] OR vascular surg*[tiab] OR bypass graft*[tiab] OR surgical bypass*[tiab] OR vascular graft*[tiab] OR stent*[tiab] OR atherectom*[tiab] OR lower limb amputation*[tiab] OR lower extremity amputation*[tiab] OR leg amputation*[tiab] OR embolectomy*[tiab] OR thrombectom*[tiab] OR revascularizat*[tiab] OR peripheral vascular intervention*[tiab] OR aorto-femoral bypass*[tiab] OR aortofemoral bypass*[tiab] OR aorto-bifemoral bypass*[tiab] OR aortabifemoral bypass*[tiab] OR aorto-iliac bypass*[tiab] OR axillo-femoral bypass*[tiab] OR axillofemoral bypass*[tiab] OR femoro-femoral bypass*[tiab] OR femorofemoral bypass*[tiab] OR femoral bypass*[tiab] OR femoro-popliteal bypass*[tiab] OR femoropopliteal bypass*[tiab] OR femoro-popliteal-tibial bypass*[tiab] OR femoro-tibial bypass*[tiab] OR femorotibial bypass*[tiab] OR distal bypass*[tiab] OR infragenual bypass*[tiab] OR profundoplast*[tiab] OR obturator bypass*[tiab] OR percutaneous transluminal angioplasty[tiab] OR PTA[tiab] OR angioplast*[tiab] OR percutaneous vascular intervention*[tiab] OR endovasc*[tiab])
AND	
Search string determinant	
Frailty	("Frail Elderly"[MeSH] OR frail*[tiab] OR “Geriatric Assessment”[MeSH] OR geriatric assessment*[tiab] OR geriatric syndrome*[tiab] OR “Vulnerable populations”[MeSH] OR vulnerab*[tiab])