PERIOPERATIVE NUTRITIONAL OPTIMIZATION IN PATIENTS UNDERGOING REVASCULARIZATION FOR CRITICAL LIMB ISCHEMIA

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Malnutrition

- Public health issue

- Up to 50% of general and gastrointestinal surgical patients suffered from periop

- Preop nutritional screening and periop supplementation is best practice for general surgery patients

- Nutritional optimization has been shown to improve outcomes in these patients

- Become integrated as a key component of the Enhanced Recovery After Surgery (ERAS) protocol

Malnutrition

- Much progress has been made towards optimizing perioperative nutritional status for general surgery patients in an effort to improve surgical outcomes

- Dearth of information on the association between nutritional status after vascular surgery interventions.

Malnutrition

- Published data in this area has been limited to analyses of existing retrospective datasets

- Data from vascular surgery patients has been limited to an examination of albumin levels in an attempt to find a correlation between these and outcomes

- Serum albumin can be altered in the acute phase due to inflammation

- Represents a single component required for the assessment of nutritional status

Malnutrition

- Approximately 45.5% patients with CLI have been shown to have signs of preoperative malnutrition when undergoing infrainguinal bypass
- Patients with CLI in general are at significantly higher risk for perioperative morbidity and resource utilization when compared to other hospitalized patients
- Unlike many gastrointestinal surgery patients, these patients often do not have a primary gastrointestinal pathology contributing to their malnutrition; more likely, it may be the result of their comorbidities and an overall failure to thrive
- Perioperative nutritional supplementation has the potential to improve the nutritional status of these patients and ultimately improve outcomes. And yet, to date, no prospective trial of nutritional supplementation in CLI patients has been performed

Table I. Demographics and Comorbidities by Preoperative Albumin (<3.5g/dL vs. ≥3.5 g/dL)

Characteristic	Total, No (%)	Hypoalbuminemia, No. (%)	Normal Albumin, No. (%)	P-Value
Total	5110	2327	2783	
Age mean ± SD	67.8±11.7	68.5±11.6	67.2±11.6	<.001
Male	3149 (61.6)	1414 (60.8)	1735 (62.3)	.248
Caucasian	3388 (70.0)	1469 (66.3)	1919 (73.2)	<.001
Body mass index				.016
Underweight	237 (4.6)	121 (5.2)	116 (4.2)	
Normal	1814 (35.5)	863 (37.1)	951 (34.2)	
Overweight	1703 (33.3)	733 (31.5)	970 (34.9)	
Obese	1356 (26.5)	610 (26.2)	746 (26.8)	
Preoperative functional status				<.001
Independent	3831 (75.0)	1500 (64.5)	2331 (83.8)	
Partial dependence	1153 (22.6)	740 (31.8)	413 (14.9)	
Total dependence	122 (2.4)	85 (3.7)	37 (1.3)	
Smoking	2145 (42.0)	886 (38.1)	1259 (45.2)	<.001
Diabetes	2620 (51.3)	1355 (58.2)	1265 (45.5)	<.001
Dyspnea, none	4112 (80.5)	1840 (79.1)	2272 (81.6)	<.001
Dyspnea on exertion	857 (16.8)	394 (16.9)	463 (16.6)	
Dyspnea at rest	141 (2.8)	93 (4.0)	48 (1.7)	
Prior revascularization or amputation	3163 (61.9)	1480 (63.6)	1683 (60.5)	.022
Renal failure	115 (2.3)	88 (3.8)	27 (1.0)	<.001
Dialysis	644 (12.6)	472 (20.3)	172 (6.2)	<.001
Prior TIA/CVA	1133 (22.2)	557 (23.9)	576 (20.7)	.005
Steroid use	278 (5.4)	152 (6.5)	126 (4.5)	.002
Weight loss	125 (2.4)	85 (3.7)	40 (1.4)	<.001
COPD	745 (14.6)	373 (16.0)	372 (13.4)	.007
CHF	219 (4.3)	149 (6.4)	70 (2.5)	<.001
Recent MI	162 (3.2)	109 (4.7)	53 (1.9)	<.001
Hypertension	4409 (86.3)	2039 (87.6)	2370 (85.2)	.011
DNR status	69 (1.4)	41 (1.8)	28 (1.0)	.020
Recent operation	460 (9.5)	337 (15.2)	123 (4.7)	<.001
Wound or infection	2477 (48.5)	1453 (62.4)	1024 (36.8)	<.001
Anemia	930 (18.3)	665 (28.7)	265 (9.6)	<.001
Emergent Operation	292 (5.7)	145 (6.2)	147 (5.3)	.145
General anesthesia	4519 (88.4)	2053 (88.2)	2466 (88.6)	.669
Vein bypass	3531 (69.1)	1617 (69.5)	1914 (68.8)	.798
Tibial bypass	2553 (50)	1256 (54)	1297 (46.6)	<.001

Table IV. Multivariable Analysis Stratified by Serum Albumin

Serum Albumin	Outcome	Adjusted Odds Ratio	95% CI	P Value
<2.8 vs. ≥3.5 g/dL	30-day Mortality	2.5	1.6-3.8	<.001
	Return to the OR within 30 days	1.6	1.3-2.0	<.001
	Wound complication	0.9	0.7-1.2	0.4
2.8-3.5 vs. ≥3.5 g/dL	30-day Mortality	1.5	1.0-2.3	0.04
	Return to the OR within 30 days	1.3	1.1-1.5	0.003
	Wound complication	1.0	0.8-1.2	0.9

Serum Albumin	Outcome	Adjusted Means Ratio	95% CI	P Value
<2.8 vs. ≥3.5 g/dL	Length of hospital stay	1.2	1.2-1.3	<.001
2.8-3.5 vs. ≥3.5 g/dL	Length of hospital stay	1.1	1.1-1.2	<.001

Covariate	Overall (N=313)	Albumin >3.5 (N=135)	Albumin 2.8-3.5 (N=133)	Albumin ≤2.8 (N=45)	P-value
Demographics					
Age	65.7±10.3	64.2±10.3	67.0±10.2	66.4±10.2	.065
Male Sex	198 (63.3%)	92 (68.1%)	81 (60.9%)	25 (55.6%)	.24
Caucasian Race	127 (40.6%)	57 (42.2%)	53 (39.8%)	17 (37.8%)	.547
Preoperatively at home	266 (85.0%)	117 (86.7%)	116 (87.2%)	33 (73.3%)	.061
Insurance					
Medicare	162 (51.8%)	70 (51.9%)	68 (51.1%)	24 (53.3%)	.868
Medicaid	96 (30.7%)	44 (32.6%)	38 (28.6%)	14 (31.1%)	
Private	52 (16.6%)	19 (14.1%)	26 (19.5%)	7 (15.6%)	
Comorbidities					
Impaired ambulatory status	109 (34.8%)	40 (29.6%)	47 (35.3%)	22 (48.9%)	.063
Obese	89 (30.2%)	38 (29.9%)	42 (32.8%)	9 (22.5%)	.462
Current smoking	120 (38.3%)	65 (48.1%)	43 (32.3%)	12 (26.7%)	.006
Admitted preoperatively	180 (57.7%)	63 (47%)	81 (60.9%)	36 (80%)	<.001
Diabetes	207 (66.1%)	76 (56.3%)	95 (71.4%)	36 (80%)	.003
Hypertension	277 (88.5%)	113 (83.7%)	121 (91%)	43 (95.6%)	.048
Coronary Artery Disease	117 (37.4%)	50 (37.0%)	48 (36.1%)	19 (42.2%)	.759
Congestive Heart Failure	43 (13.7%)	18 (13.3%)	16 (12.0%)	9 (20%)	.4
Chronic Renal failure	84 (26.8%)	29 (21.5%)	37 (27.8%)	18 (40%)	.05
End Stage Renal Disease	42 (13.4%)	12 (8.9%)	17 (12.8%)	13 (28.9%)	.003
Hepatic Insufficiency	9 (2.9%)	3 (2.2%)	3 (2.3%)	3 (6.7%)	.259
Previous stroke	50 (16.0%)	21 (15.6%)	18 (13.5%)	11 (24.4%)	.222
COPD	33 (10.5%)	18 (13.3%)	13 (9.8%)	2 (4.4%)	.226
Active leg infection	62 (19.8%)	12 (8.9%)	38 (28.6%)	12 (26.7%)	<.001
Pre-Op hematocrit <30	78 (25.1%)	11 (8.1%)	41 (31.3%)	26 (57.8%)	<.001
Procedure					
Indication					
Claudication	52 (16.6%)	36 (26.7%)	15 (11.3%)	1 (2.2%)	<.001
Rest pain	55 (17.6%)	32 (23.7%)	19 (14.3%)	4 (8.9%)	
Tissue loss	206 (65.8%)	67 (49.6%)	99 (74.4%)	40 (88.9%)	
Femoral origin	8 (2.6%)	6 (4.4%)	1 (.8%)	1 (2.2%)	.158
Tibial target	168 (53.7%)	64 (47.4%)	74 (55.6%)	30 (66.7%)	.067
Vein conduit					
Autologous GSV	202 (64.5%)	77 (57.0%)	96 (72.2%)	29 (64.4%)	.01
Other vein	45 (14.4%)	30 (22.2%)	11 (8.3%)	4 (8.9%)	
Prosthetic	66 (21.1%)	28 (20.7%)	26 (19.5%)	12 (26.7%)	
Discharged to home	158 (50.5%)	89 (65.9%)	56 (42.1%)	13 (28.9%)	<.001

Tables 2: Outcomes

Covariate	Overall (N=313)	Albumin >3.5 (N=135)	Albumin >2.8 - 3.5 (N=133)	Albumin ≤2.8 (N=45)	P-value
Wound Complication	17 (5.4%)	8 (5.9%)	7 (5.3%)	2 (4.4%)	.925
Urinary Tract Infection	7 (2.2%)	4 (3.0%)	3 (2.3%)	0 (0.0%)	.508
Myocardial infarction	7 (2.2%)	2 (1.5%)	4 (3%)	1 (2.2%)	.700
Bleeding complication	10 (3.2%)	3 (2.2%)	6 (4.5%)	1 (2.2%)	.523
Pulmonary complication	11 (3.5%)	2 (1.5%)	7 (5.3%)	2 (4.4%)	.228
Perioperative graft occlusion	6 (1.9%)	3 (2.2%)	2 (1.5%)	1 (2.2%)	.9
30 day mortality	310 (99.0%)	134 (99.3%)	132 (99.2%)	44 (97.8%)	
90 day mortality	12 (3.8%)	2 (1.5%)	6 (4.5%)	4 (8.9%)	.07
One year mortality	29 (9.3%)	10 (7.4%)	13 (9.8%)	6 (13.3%)	.477
30 days ED presentation	69 (22.0%)	24 (17.8%)	30 (22.6%)	15 (33.3%)	.091
90 days ED presentation	110 (35.1%)	40 (29.6%)	45 (33.8%)	25 (55.6%)	.006
30 day Readmission	83 (26.5%)	24 (17.8%)	41 (30.8%)	18 (40.0%)	.005
90 day Readmission	143 (45.7%)	48 (35.6%)	65 (48.9%)	30 (66.7%)	.001

30-day Readmission

	OR	95% CI	P-value
Albumin: ≤2.8	1.9	.86 – 4.22	.113
Albumin: >2.8-3.5	1.72	.95 – 3.12	.073
End staged renal disease	*2.09*	*1.03 – 4.22*	*.041*
Tibial target	*1.74*	*1.004 - 3*	*.048*
Hypertension	2.71	.91 – 8.08	.075
Admitted preoperatively	1.63	.92 – 2.88	.092

90-day Readmission

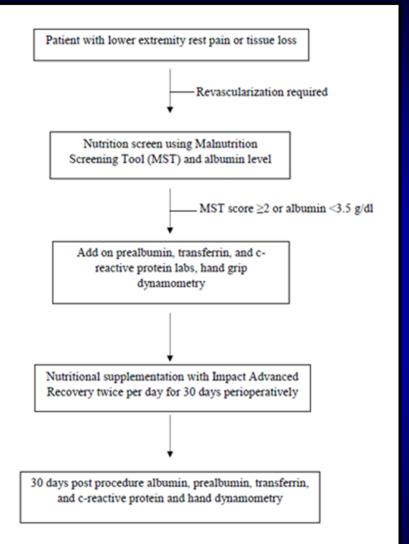|	OR	95% CI	P-value
Albumin: <2.8	*2.63*	*1.21 – 5.71*	*.015*
Albumin: >2.8-3.5	1.4	.82 – 2.4	.222
Chronic renal failure	*3.16*	*1.77 – 5.64*	*<.001*
Active leg infection	*1.92*	*1.02 – 3.6*	*.043*
Current smoking	1.69	.99 – 2.88	.054
Hypertension	1.85	.83 – 4.14	.134
Discharged to home	.67	.41 – 1.11	.121

- Serum albumin

- Prealbumin

- Transferrin

- C-reactive protein
  - malnutrition is a catabolic proinflammatory state
  - useful marker of systemic inflammation

- Hand grip
  - Low hand grip dynamometry values are associated with both malnutrition and frailty
  - Independent of ambulatory status
  - Malnutrition Screen Assessment

Malnutrition Screening Tool (MST)

Have you recently lost weight without trying?	Points
No	0
Unsure	2
If yes, how much weight have you lost?	
2-13 lb	1
14-23 lb	2
24-33 lb	3
34 lb or more	4
Unsure	2
Have you been eating poorly because of a decreased appetite?	
No	0
Yes	1

MST score ≥2 then at risk for malnutrition

Patient with lower extremity rest pain or tissue loss

↓ — Revascularization required

Nutrition screen using Malnutrition Screening Tool (MST) and albumin level

↓ — MST score ≥2 or albumin <3.5 g/dl

Add on prealbumin, transferrin, and c-reactive protein labs, hand grip dynamometry

↓

Nutritional supplementation with Impact Advanced Recovery twice per day for 30 days perioperatively

↓

30 days post procedure albumin, prealbumin, transferrin, and c-reactive protein and hand dynamometry

Specific Aim #1

- To assess whether 30 days of perioperative nutritional supplementation, both for bypass and endovascular interventions, improves albumin, pre-albumin, and transferrin, and decreases C-reactive protein levels.

- *We hypothesize that albumin, transferrin, and pre-albumin will improve after 30 days of supplementation.*

Specific Aim #2

- To assess if nutritional supplementation improves hand grip strength at 30 day follow-up using hand dynamometry both for bypass and endovascular interventions

- Grip strength has been used as a marker for malnutrition and to assess functional status and frailty

- We hypothesize that grip strength will improve after 30 days of nutritional supplementation

Specific Aim #3

- To assess correlation between the ERAS Malnutrition Screening Test (MST) and nutritional markers

- The ERAS nutritional screen has been used and validated in general surgery patients

- However, this has not been validated as a screening tool for malnutrition in vascular surgery patients

- *We hypothesize that a high MST score will correlate with low nutritional labs.*

Supplementation

- Impact Advanced Recovery Immunonutrition drink (Nestle, Highland Park, MI) twice per day for 7-10 days
- Boost Optimum drink (Nestle, Highland Park, MI) for the remaining period
- Do not delay procedure for supplementation
- Goal 30 patients
- Pilot study

Patients

- Mean age – 60
- 50% male/female
- All with tissue loss
- Average BMI – 31
- Albumin – 3.14 (2.8-3.4) – 3.37
- Prealbumin – 10.6 - 23
- C-reactive protein - 50.7 - 16
- MST – 3 (204)
- Handgrip – 54.4/51.8 – 51/49

Average Pre/Post Values

- Albumin – 3.14 → 3.37
  - Normal range (3.5 - 5.5)
  - Half-life 20 days
- Prealbumin – 10.6 → 23
  - Normal range (16 - 40)
  - Half-life 2 days
- C-reactive protein – 51 → 16
  - Normal range (<3)
  - Half-life 19 hours
- Handgrip – 54.4/51.8 → 51/49
- MST – 3 (2-4), <2 normal

Challenges

- IRB
- Patient compliance
- Tracking
- Retention

Team

- Jeffrey J Siracuse, M.D. – PI
- Alik Farber M.D. - mentor
- Peter Burke, M.D. – Mentor Chief of trauma and Critical Care
- Lorrie Young, RD – Nutritional research expert
- Myriam Castagne-Charlotin, M.D. – research coordinator
- Gheorghe Doros, Ph.D. – Professor of Biostatistics