Systemic inflammation, wound-related symptoms and biofilm in older adults with chronic venous leg ulcers (CVLU)

Junglyun Kim, PhD[1,2], Joyce Stechmiller, PhD[2], Michael Weaver, PhD[2], Garth James[3], Phill Stewart[3] & Debra Lyon, PhD[2]

1. Chungnam National University College of Nursing; 2. Department of Biobehavioral Nursing Science, University of Florida College of Nursing; 3. Montana state University

Background

- About 8.2 million people are suffering from chronic wounds, and the treatment costs of chronic wounds ranged from $28.1 to 96.8 billion in 2014 in US.
- Since venous leg ulcers(VLUs) tend to be chronic due to their high susceptibility to infection and high recurrence rate, they account for the majority of chronic wounds.
- Patients with venous leg ulcers suffer from diverse symptoms, including pain, fatigue, depression, swelling and exudate, and most patients with VLUs who have delayed healing experience significant symptoms.
- Biofilm is recognized as an important component of wound non-healing and it is believed that the formation of biofilm delays wound healing.
- Therefore, by examining wound-related symptoms corresponding to biofilm and inflammatory markers, such as CRP, during the course of wound treatments, clinicians may predict wound healing trajectories.

Objectives

- To characterize the wound-related symptoms (fatigue, pain, exudate, itching, and edema or swelling) and wound related factors (wound area, the presence of biofilm, total bacteria, the level of serum CRP),
- To explore associations between biofilm and levels of systemic inflammation and the severity of wound-related symptoms in individuals with chronic venous leg ulcers (CVLU) over 8 weeks of wound treatment.

Methods

Study design

- We conducted a prospective, longitudinal, and observational study.
- A total of 117 subjects who received weekly sharp debridement at a wound clinic were enrolled. We collected clinical data every two weeks during the 8 weeks of the study period.

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Methods continued

Study variables

- We characterized patient-host demographic characteristics (age, sex, race/ethnicity, marital status, educational level); general health characteristics (BMI, comorbidities, antibiotics and pain medication) at the baseline.
- Wound factors (wound area, wound days, the presence of biofilm, and total bacteria, ; the wound-related symptoms (fatigue, pain, exudate, itching, and edema or swelling) were characterized overtime and examined their associations.

Measurements

- Host factors, general health information, wound days, wound area were collected from electronic health records.
- Wound symptoms were measured by the Toronto Symptom Assessment System for Wounds.
- The presence of biofilm was determined by a biofilm score of 2 or greater, which was examined using a Leica SP5 confocal scanning laser microscope on stained specimens.
- Total bacteria were measured using minor modifications of the basic technique that was described by Phillips, Yang, and Schultz, 2013.
- Serum CRP was analyzed by ELISA.

Statistical analysis

- Distributions for each variable were examined with descriptive statistics appropriate for measurement level.
- Associations among variables were estimated using a Bayesian approach applied to general linear mixed models.

Discussion& Conclusion

- This study is the first to examine associations among biofilm, inflammatory response, wound-related symptoms, and wound healing in clinical settings. Wound-related symptoms and the level of systemic CRP were associated with biofilm among patients who were receiving weekly sharp debridement.
- Symptom severity associated with CVLU requires clinical assessment and management.
- Symptom severity and level of systemic CRP may be biobehavioral markers for predicting wound healing trajectories.

Results

Table 1. Baseline Sample characteristics (N=117)

Variable		Mean (SD) or Frequency (%)	Range
Age		71.7 (9.6)	55 - 92
Wound Duration (days)		321 (499)	20 - 2944
BMI		34.1 (11.9)	15.4 – 84.1
Charlson Index		5.74 (1.96)	2 - 11
Antibiotic Use	No	46 (39%)	
	Yes	71 (61%)	
Pain Medication Use	No	37 (32%)	
	Yes	80 (68%)	
Sex	Male	64 (55%)	
	Female	53 (45%)	
Marital Status[1]	Married	59 (50%)	
	Divorced	25 (21%)	
	Widowed	18 (15%)	
	Never Married	14 (12%)	
	Unmarried Couple	1 (1%)	
Race	White	94 (80%)	
	African-American	23 (20%)	
Hispanic	No	114 (97%)	
	Yes	3 (3%)	
Smoking History	Never Smoked	58 (50%)	
	Used to Smoke	49 (42%)	
	Current Smoker	10 (8%)	
Education	Elementary School	3 (3%)	
	Some high school	10 (8%)	
	High School Graduate	29 (25%)	
	Some College	37 (31%)	
	College Graduate	36 (31%)	
	Prefer not to answer	2 (2%)	
Wounds at 8 weeks	Healed	47 (40%)	
	Non healed	70 (60%)	

Table 2. Results of Bayes mixed models

Response Variable	Effect	Estimate[a] (95% CrI[b])	PD[c]	BF[d]
Biofilm Presence	Healed	-0.456 (-1.85, 0.83)	75%	2.99
Total Bacteria[1]	Biofilm Presence	1.41 (0.87, 1.94)	100%	>1000
Serum CRP[1]	Biofilm Presence	0.067 (-0.09, 0.22)	81%	4.3
Pain	Biofilm Presence	0.606 (-0.63, 1.82)	84%	5.12
	Pain Med Use	3.73 (1.75, 5.75)	100%	>1000
Fatigue	CCI	0.451 (0.12, 0.79)	100%	249
	Age	-0.106 (-0.17, -0.04)	100%	999
Exudate	Biofilm Presence	0.358 (-0.20, 0.92)	89%	8.49
Edema	CCI	0.356 (0.07, 0.66)	100%	>1000
	Age	-0.010 (-0.16, -0.04)	99%	109

[a] Linear model regression weight. Presented estimates were after controlled other variables.
[b] 95% credibility interval.
[c] Probability of direction.
[d] Bayes factor: >100=Extreme evidence for H1; 30-100=Very strong evidence for H1; 10-30=Strong evidence for H1; 3-10=Moderate evidence for H1; 1-3= Anecdotal evidence for H1; 1= No evidence.

- Based on Bayes Factor (BF) value, there was moderate evidence of a direct association between biofilm presence and levels of C-reactive protein (CRP) (BF 4.3) and moderate evidence of direct associations between biofilm and wound-related symptoms; pain and exudate (BF 5.12, 8.49 respectively).
- There was extremely strong evidence for the association of biofilm with mean total bacteria. .