

# The dilemma of poor diagnosis of concurrent chronic venous disease (CVD) in the setting of lower limb (LL) cellulitis



Torda A<sup>1,2</sup>, Perera M<sup>1</sup>

<sup>1</sup>Faculty of Medicine, University of New South Wales, Randwick, NSW; <sup>2</sup>Department of Infectious Diseases, Prince of Wales Hospital, Randwick, NSW

## Introduction

Lower limb (LLC) cellulitis is a common bacterial infection responsible for 2-3% of hospital admissions, with an increasing incidence. According to the Australia Refined Disease Related Groups (AR-DRG) data, cellulitis without or with catastrophic or severe complications, the number of episodes in Australia between 2013-14 were respectively, 60,634 and 13,881 (AIHW, 2014). The presence of concurrent Chronic Venous Disease (CVD) has been reported as a factor influencing clinical outcome with regards to treatment failure (relapse or recurrence). Despite this, assessment, documentation and management of CVD in patients presenting with LLC and concurrent CVD, is incredibly variable. This is despite the fact that targeting predisposing factors such as CVD, along with prompt antibiotic therapy is the most effective means of preventing complications and recurrence of cellulitis<sup>1</sup>. The aim of this study was to investigate the impact of recognition and active management of CVD via compression therapy, on the clinical outcomes of LLC.

## Methods

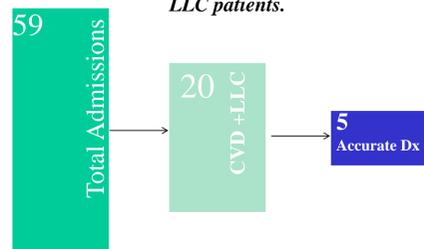
The study was conducted in a large tertiary teaching hospital in two parts. The first part consisted of a qualitative prospective diagnostic accuracy study to assess the accuracy of diagnosis of concurrent CVD in LLC admissions over a 3 month period in 2015 was conducted. Patients admitted with LLC underwent an independent secondary assessment by experts, within 96 hours of admission to determine the presence of concurrent CVD. A review was undertaken of the admitting diagnosis, documentation and subsequent management.

A retrospective cohort study was also conducted to assess the impact of active CVD management on outcome of cellulitis. This examined the records of 200 patients with documented CVD and a primary episode of LLC, admitted between January 1<sup>st</sup> 2006 and September 30<sup>th</sup> 2014. Data was collected on variables including demographics, co-morbidities, features of the clinical presentation, hospital CVD classification (CEAP<sup>2</sup>), antibiotics, management of CVD and follow up. The primary outcome measure was treatment failure – relapse (<4 weeks) or recurrence (>4 weeks), or treatment success at 1 year after initial event. A univariate analysis for each clinical outcome was undertaken using binary logistic regression models, forcing the variables. A multivariate analysis via backward stepwise likelihood ratio binary logistic regression was conducted for univariate factors with *p* value <0.2. For the comparative analysis, an independent samples t-Test was performed.

## Results

During the small prospective diagnostic accuracy study, there were 59 LLC admissions. Of these, 20 patients (34%) were found to have concurrent CVD by expert assessment (Figure 1). In only 5 patients was this actually documented prior to expert review and in no cases was classification according to the commonly used CEAP<sup>2</sup> classification documented. In the 5 patients with CVD documented at the time of admission, 80% had compression commenced.

Figure 1. Diagnostic accuracy of concurrent CVD in LLC patients.



It was also found that in 95% of CVD +LLC cases, the CVD was class 4 or higher according to the CEAP classification (Table 2).

Table 1. CEAP classification of concurrent CVD in LLC patients.

Characteristic	Total Cohort n=20	Accurate Diagnosis Cohort n=5
CEAP Class		
C1	1 (5%)	NF
C4a	8 (40%)	1 (20%)
C4b	6 (30%)	2 (40%)
C5	1 (5%)	NF
C6	4 (20%)	2 (40%)

In the retrospective component of this research, of the 200 cases identified for the case control study, the median age of patients was 78 years (27 - 98), which included 101 males (50.5%). They had other common co-morbidities as shown in Table 2.

Table 2. Frequency of Co-Morbidities in LLC

Co-morbidity/Risk Factor	n (%)
Diabetes mellitus/Insulin Intolerance	59 (29.5%)
Obese/overweight	46 (23%)
Ex-Smoker	38 (19%)
Current Smoker	18 (9%)
CABG (venous graft)	17 (8.5%)
Peripheral Arterial Disease +/- Peripheral Neuropathy	40 (20%)
History of ipsilateral DVT	23 (11.5%)
Total Knee Replacement/Knee Surgery	16 (8%)
Local Surgery	16 (8%)
Tinea Pedis	19 (9.5%)
Lower Leg Oedema	67 (33.5%)
Saphenectomy	18 (9%)
Ulcer	99 (49.5%)
Local Trauma to Skin	29 (14.5%)

### Clinical outcome of LLC

Relapse occurred in 20% of patients overall. Univariate and multivariate analysis of factors was performed to determine association of CVD management with relapse. (Table 3)

Table 3. Factors associated with relapse of LLC.

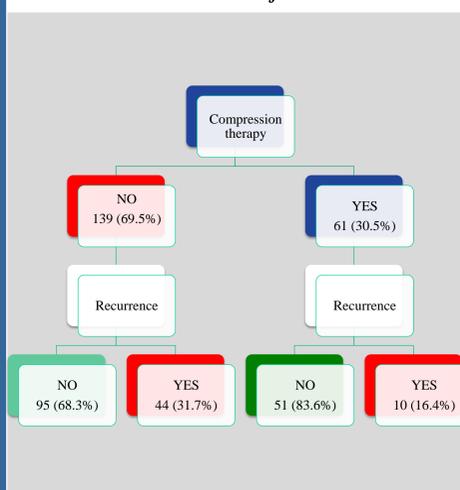
Variable	Univariate		Multivariate	
	P Value	OR (95% CI)	P value	OR (95% CI)
Gender	0.140	0.59 (0.29 – 1.19)	NS	
Current smoker	0.084	2.40 (0.89 – 6.48)	NS	
DVT	0.148	2.05 (0.78 – 5.43)	NS	
Ulcer	0.092	1.84 (0.90 – 3.75)	0.034	2.28 (1.06 – 4.88)
Lymphoedema	0.076	3.44 (0.88 – 13.47)	NS	
LOS (in hospital)	0.191	0.97 (0.92 – 1.02)	NS	
LOS (total)	0.145	0.96 (0.91 – 1.01)	NS	
IV antibiotics	0.189	0.94 (0.86 – 1.03)	NS	
Total antibiotics	0.081	0.94 (0.87 – 1.01)	NS	
Pain	0.181	1.62 (0.80 – 3.23)	NS	
Fever	0.124	0.48 (0.19 – 1.22)	NS	
CVD management	0.132	2.30 (0.78 – 6.83)	0.042	0.25 (0.07 – 0.95)
Previous	0.120	0.37 (0.11 – 1.23)	NS	
Current				
Compression bandage	0.126	0.20 (0.03 – 1.56)	NS	
Initial	0.086	0.34 (0.10 – 1.17)	NS	
Compression	0.111	0.51 (0.22 – 1.17)	NS	

Analysis revealed that the presence of an ulcer is associated with an increased likelihood of having a relapse.

Active CVD management was independently associated with a significantly decreased (OR 0.25, 95% CI 0.07-0.95) likelihood of relapse and recurrence (OR 0.29, 95% CI 0.12-0.71). The use of compression therapy (OR 3.34, 95% CI 1.55-7.20) greatly increased the likelihood of cellulitis treatment success. The proportion of patients with treatment success and compression therapy (73.8%, 45/61) was statistically higher than those without compression therapy (53.2%, 74/139). Multivariate analysis also revealed that presence of pre-morbid LL oedema was highly significant and almost quadrupled the risk of a recurrent event.

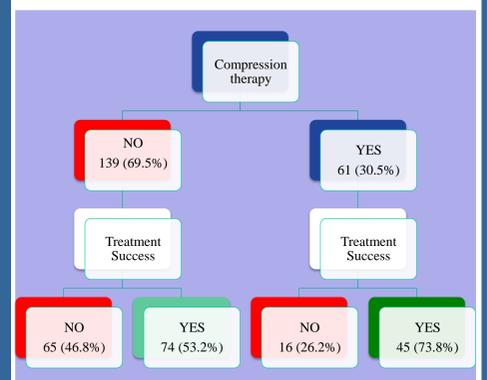
Figure 3 shows that the proportion of individuals with a recurrence was statistically higher in than those who received compression therapy 31.7%, (44/139) versus 16.4% (10/61).

Figure 2. Impact of compression therapy on recurrence of LLC



Treatment success occurred in 119 (59.5%) patients. Multivariate analysis revealed that pre-morbid LL oedema (OR 0.36, 95% CI 0.17-0.73) and previous cellulitis (OR 0.35, 95% CI 0.16-0.75) were negatively associated with treatment success. The use of compression therapy (OR 3.34, 95% CI 1.55-7.20) greatly increased the likelihood of treatment success. The proportion of patients with treatment success and compression therapy (73.8%, 45/61) was statistically higher than those without compression therapy (53.2%, 74/139) (Figure 3).

Figure 3. Impact of compression therapy on treatment success



## Discussion

To our knowledge this is the first study assessing the comparative impact of concurrent active CVD management on cellulitis outcome. This research shows that active management of CVD with compression improves LLC treatment outcomes, independent of other measures. This is consistent with other studies<sup>3,4</sup> which have also found the local factors associated with CVD such as lymphoedema/ulcer to be associated with cellulitis recurrence. The prospective part of this study found however, that we are missing a great number of important management opportunities in these patients. At the time of admission, The LLC is being treated but not the CVD. It is only documented in a small percentage of patients in whom it is present and a contributing factor to the likelihood of LLC relapse or recurrence. This is despite the majority of patients presenting with LLC have advanced clinical signs of CVD. Both LLC and CVD are common conditions and are a huge economic burden on healthcare facilities. So when considering that treatment success is 3x more likely if concurrent CVD is appropriately managed, this study suggests that there is scope for huge financial savings as well as better outcomes for these patients if CVD is assessed for, documented and treated.

## References

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