The Utility of Lactate as a Biomarker for Sepsis In Cancer Patients

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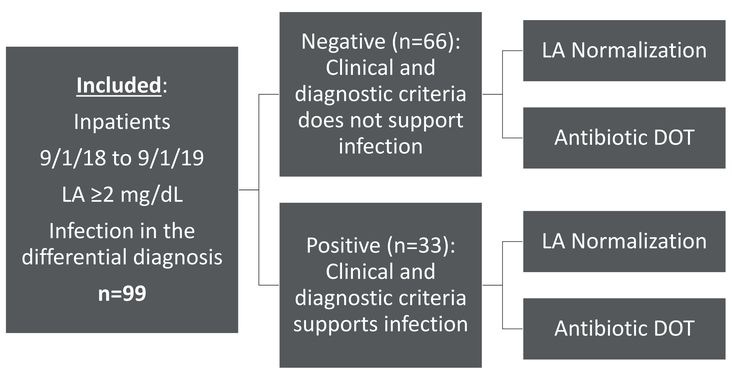
ABSTRACT

- Serum lactate (LA) is included in the initial assessment of patients with sepsis. However, cancer patients develop lactic acidosis for variety of reasons and are underrepresented in most studies. Therefore, elevated LA levels may lead to overdiagnosis of sepsis and excessive antibiotic use. The purpose of this study is to evaluate the utility of LA as a biomarker for sepsis in cancer patients. The primary endpoint is the rate of 24 hour LA clearance between infectious and non-infectious causes of lactic acidosis in cancer patients. Secondary objectives explore the duration of antibiotic therapy (DOT), the impact of liver metastasis on serum LA levels, and the role of procalcitonin (PCT) in distinguishing between infectious and non -infectious causes of lactic acidosis.

OBJECTIVES

- Evaluate if lactic acidosis (serum LA 2 mmol/L) is a reliable marker for infection/sepsis in cancer patients
- Assess the appropriateness of DOT in cancer patients with lactic acidosis
- Explore the value of PCT levels in distinguishing infectious vs non-infectious causes of elevated lactic
- Determine if metastatic liver involvement impacts serum LA and/or PCT

METHODS



RESULTS

Table 1. Analysis of variables between infectious and non-infectious groups

	Infection			No Infection				
	n	Mean	SD	n	Mean	SD	P[a]	Effect[d]
Peak LA (mmol/L)	33	5.32	2.98	66	5.65	3.99	0.98	0.09
Antibiotic DOT	33	14.03	12.42	66	4.26	4.41	**0***	**1.22**
Peak PCT (ng/dL)	20	30.6	37.77	21	4.36	9.32	**0.03***	**0.96**
LA normalization	32	62.5%		62	41.9%		p[c] 0.09	
PCT reduction	18	44%		20	0%		p[c] **0.005**	

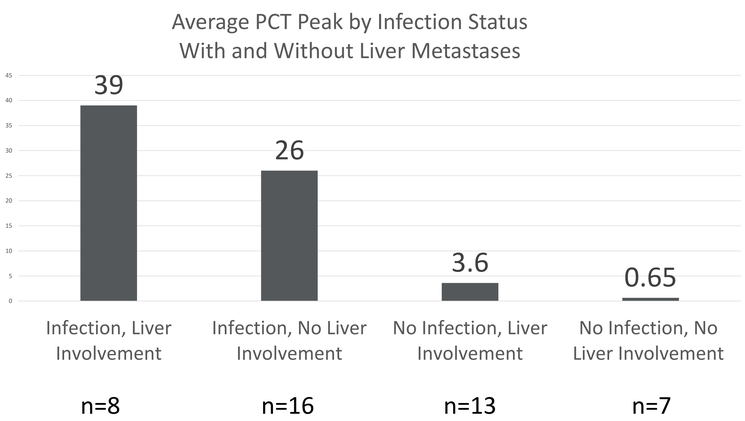
*Indicates significance at .05; a= Wilcoxon p-value; b=Effect size Cohen's d, Moderate and large effect sizes (>0.5) shown in bold; c=chi-square p-value

Table 2. Sub-analysis to assess impact of liver involvement on variables in patients WITHOUT infection

	Liver Involvement			No Liver Involvement				
	n	Mean	SD	n	Mean	SD	p[a]	Effect[d]
Peak Lactate (mmol/L)	38	6.64	4.69	27	4.26	2.24	0.06	0.65
Antibiotic DOT	38	4.87	4.13	27	2.78	3.27	**0.02***	0.56
Peak PCT (ng/dL)	13	3.62	5.49	7	0.65	0.49	**0.005***	**0.76**
LA normalization	36	25%		25	65%		**0.002***	

*Indicates significance at .05; a= Wilcoxon p-value; b=Effect size Cohen's d, Moderate and large effect sizes (>0.5) shown in bold; c=chi-square p-value

Fig1. PCT (ng/dL)



RESULTS

- 99 patients met criteria (infection=33; no infection= 66).
- Table 1. There was no difference in overall mean peak LA between infectious and non-infectious groups (5.32 vs 5.65).
- Table 1. There was a significant difference in:
  - Mean antibiotic DOT (14.03 vs 4.26, p<0.001)
  - Peak PCT levels (30.6 vs 4.36, p=0.03)
  - PCT reduced by at least half after 48 hours (44% vs 0%, p=0.005)
- Table 1. There was a non-significant difference in the rate of 24- hour LA normalization between groups (62.5% vs 41.9, p=0.09).
- Table 2. In patients without infection mean antibiotic DOT and peak PCT were higher in patients with liver metastases. The frequency of LA normalization was lower with liver metastases (p=0. 002).
- Fig 1. Peak PCT was highest in patients with infection and liver metastases, and lowest in patients with no infection and no liver metastases.

DISCUSSION

- Only 33 of patients with lactic acidosis and clinical suspicion for infection were determined to have a true infection. This highlights the challenge in differentiating infectious and non-infectious cases.
- Similar LA levels between infectious and non-infectious groups may be due to the impact of metastatic cancer on serum LA.
- Antibiotic DOT were significantly less in patients without infection likely due to robust antimicrobial stewardship practices
- Peak PCT levels were higher with infection consistent with current literature. However, peak PCT in the non-infectious group was much higher than the accepted normal reference range.
- PCT reduction by half within 48 hours was only seen in infectious patients.
- In patients without infection, mean antibiotic DOT and peak PCT were higher in patients with liver metastases.

CONCLUSIONS

- Lactic acidosis is a poor marker for infection in cancer patients and can lead to inappropriate antibiotic utilization.
- Liver metastases appear to have an impact on LA and PCT clearance. This may also increase inappropriate antibiotic use.
- Relative change in PCT level within 48 hours may be a more useful method for differentiating infectious and non-infectious causes of elevated lactic acidosis in cancer patients.