Using the Neutrophil:Lymphocyte Ratio as a Biomarker for Sepsis: Which Cutoff is Best?

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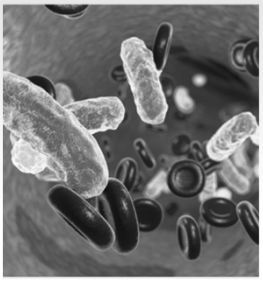
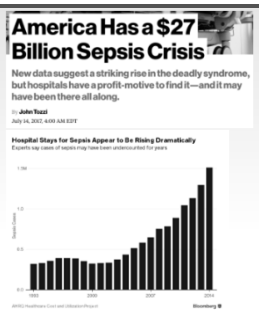
Objectives

1. Define sepsis and describe the impact sepsis has on the United States.
2. Discuss the diagnostic biomarkers for sepsis currently in use.
3. Describe the neutrophil:lymphocyte ratio and its current uses in healthcare.
4. Evaluate the findings of this study regarding the use of the neutrophil:lymphocyte ratio as a biomarker for sepsis.



Sepsis Impact

- Sepsis is a major healthcare crisis facing the United States and the world
- 28-50% mortality rate
- Sepsis doesn't end with infection resolution
- Patient outcomes worsen as diagnosis and treatment are delayed



Sepsis Background

•Sepsis Classifications and Definitions

- Sepsis-2
  - Systemic Inflammatory Response Syndrome (SIRS)
- Sepsis-3

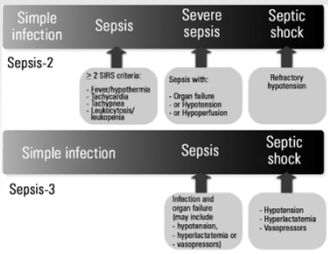
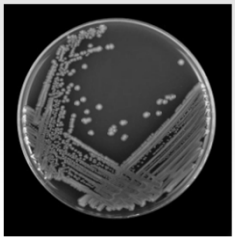


Figure courtesy of Carneiro, A. H., Póvoa, P., & Gomes, J. A. (2017)

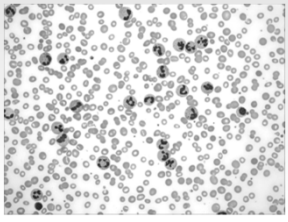
Sepsis Biomarkers

•Cultures
•Procalcitonin
•C-reactive Protein
•Lactate



Neutrophil:Lymphocyte Ratio (NLCR)

•Neutrophilia
•Lymphopenia
•NLCR as a biomarker



Study

- Two Specific Aims
  1. Determine the descriptive statistics of adult septic patients at UTMB Health and determine if a significant difference exists between the NLCR for septic and non-septic patients
  1. Evaluate the clinical utility of alternate NLCR cutoff values (9, 10, 11, 12)

Study Methods

- Study Design
  - Retrospective observational study
  - January 1, 2010 – December 31, 2014
  - Two subject groups
    - 61 subject minimum per group
  - Identified through ICD-9 codes
- Institutional Review Board
  - UTMB IRB approved study in December 2016

Table 2. ICD-9 Codes Used to Identify Study Subjects

ICD-9 Code	Description
995.90	Unspecified SIRS
995.91	Sepsis (SIRS due to infection without organ dysfunction)
995.92	Severe Sepsis (SIRS due to infectious process with organ dysfunction)
995.93	SIRS due to noninfectious process without organ dysfunction
995.94	SIRS due to noninfectious process with organ dysfunction
785.82	Septic Shock

Adapted from Wiedemann (2007)

Results

Table 3. Descriptive Statistics for White Blood Cell Count, Neutrophils, Lymphocytes, and NLCR

	Group	Median	Interquartile Range	Minimum	Maximum	Z Value[a]	p Value[a,b]
WBC Count (cells/mm³)	Study Control	14.1 14.4	10.2 – 19.6 9.5 – 21.9	3.8 1.8	33.7 30.7	-0.355	0.722
Neutrophils (%)	Study Control	87.8 83.5	82.2 – 91.5 74.4 – 88.0	47.1 49.2	97.4 94.1	-3.959	<0.001
Lymphocytes (%)	Study Control	5.9 8.3	3.7 – 8.8 5.5 – 13.65	0.8 2.2	22.7 42.1	-3.517	<0.001
NLCR	Study Control	15.2 9.9	10.0 – 24.2 5.4 – 16.4	2.1 1.2	121.8 42.0	-3.609	<0.001

a. Z value and *p* value calculated using Mann-Whitney U Test
b. Significant *p* value <0.05

Results

Table 4. Performance Characteristics for Proposed Cutoff Values

NLCR Cutoff Value	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	+ LR (95% CI)	- LR (95% CI)
9.0	81.0 (72.4 – 89.7)	47.8 (39.8 – 59.7)	64.6 (55.2 – 74.1)	68.1 (54.8 – 81.4)	1.55 (1.21 – 1.99)	0.40 (0.24 – 0.67)
10.0	75.9 (66.5 – 85.3)	50.7 (38.8 – 62.7)	64.5 (54.8 – 74.2)	64.2 (51.2 – 77.1)	1.54 (1.17 – 2.03)	0.47 (0.30 – 0.75)
11.0	67.1 (56.7 – 77.5)	58.2 (46.4– 70.0)	65.4 (55.1 – 75.8)	60.0 (48.1 – 71.9)	1.61 (1.16 – 2.21)	0.57 (0.39 – 0.82)
12.0	63.6 (53.0 – 74.4)	61.2 (49.5 – 72.9)	65.3 (54.6 – 76.1)	59.4 (47.8 – 71.0)	1.64 (1.13 – 2.26)	0.59 (0.41 – 0.83)

Results

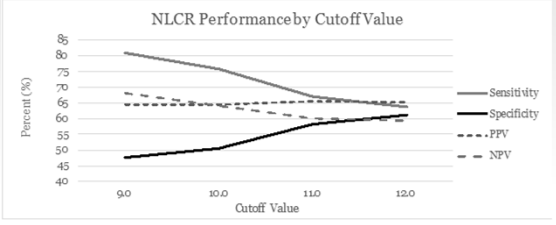


Figure 1. NLCR Performance by Cutoff Value

Discussion

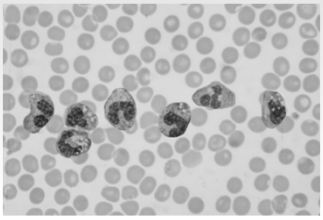
Table 5. Comparison of NLCR Performance Against Other Sepsis Biomarkers

Analyte	Cutoff Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Procalcitonin[a]	2.0 ng/mL	26.4	**88.6**	64.0	61.0
CRP[a]	20 mg/L	**88.1**	14.5	44.1	61.4
Lactate[a]	2.5 mmol/L	24.9	82.7	52.6	58.7
NLCR[b]	9.0	81.0	47.8	64.6	**68.1**
NLCR[b]	10.0	75.9	50.7	64.5	64.2
NLCR[b]	11.0	67.1	58.2	**65.4**	60.0
NLCR[b]	12.0	63.6	61.2	65.3	59.4

a. Adapted from Ljungstrom et al. (2017)
b. Results from the current study

Conclusion

The results of this study do not indicate that the NLCR is an acceptable independent biomarker for the identification of sepsis in the emergency department.



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Questions?