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SHOCK INDEX AS A PREDICTOR OF OUTCOME IN SEPSIS

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ABSTRACT

BACKGROUND: Sepsis screening tools are designed to promote early identification of sepsis. There is wide variation in diagnostic accuracy of these tools in predicting outcome. Clinical tools used for sepsis screening are SIRS criteria, vital signs, qSOFA, SOFA, NEWS and MEWS score. Most of these rely on laboratory information to define treatment strategies causing delays in care. The shock index is a bedside assessment defined as heart rate divided by SBP. Early phase of sepsis demonstrates physiological compensatory mechanism, keeping blood pressure from falling despite presence of decreased circulating blood volume by increasing heart rate. In such events, Shock Index (SI) is useful as an early warning.

AIM OF THE STUDY: To study the disease spectrum of patients with suspected sepsis and assess the usefulness of Shock Index (SI) in predicting the clinical outcome.

METHODS: 75 patients diagnosed with sepsis according to q SOFA Score were included for the study. Vital signs of study participants at the time of admission were used for calculating the SI and qSOFA scores. Blood investigations such as complete blood counts, lactate, creatinine, bilirubin levels, serum electrolytes and ABG analysis were used for calculating the initial SOFA score. Receiver Operating Curve (ROC) comparing SI, SOFA, qSOFA and lactate levels in terms of outcomes such as mortality, inotropic support requirement, ventilatory support and duration of hospital stay of patients was obtained.

RESULTS : Our study showed Shock index is a good predictor of mortality in Sepsis patients after SOFA score. We also found that Shock Index is a better predictor of need for inotropic support in Sepsis patients and is the second best predictor of need for ventilatory support after SOFA score in Sepsis.

CONCLUSION: The urinary tract and lungs are major sites of Sepsis. Shock Index performed as a good indicator of In-Hospital mortality, and its performance was comparable to other established indices like qSOFA score, SOFA score and Lactate levels. Shock index ≥1 was associated with greater rates of inotropic and ventilatory support requirement and longer duration of hospital stay.

CATEGORIES: Emergency Medicine, Internal Medicine, Infectious Disease.

KEYWORDS: Critical Care, Infectious Diseases, Mortality, Ventilator Support, Inotropic Support, Shock Index, Sepsis.

INTRODUCTION

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction can be identified as an acute change in total qSOFA score ≥2 points (or) rise in SOFA score by ≥2 consequent to the infection. qSOFA comprises of parameters such as Respiratory rate ≥22/min, Altered mentation and Systolic blood pressure <100 mm Hg. The baseline qSOFA (or) SOFA score can be assumed to be zero in patients not known to have pre - existing organ dysfunction.

Septic shock is a subset of Sepsis in which underlying circulatory, cellular or metabolic abnormalities are profound enough to substantially increase mortality. Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18mg/dL) despite adequate volume resuscitation.[1] An estimated 49 million cases of sepsis were diagnosed and 11 million sepsis-related deaths took place globally in 2017, accounting for approximately 20% of all-cause deaths worldwide.[2]

The sepsis cases in India alone were estimated to be 11.3 million, with 2.9 million death (297.7 per 100,000 population) in 2017.[3] Gram-negative infections are predominant in India (69%) and Enterobacteriaceae (Klebsiella, Pseudomonas) account for majority of these infections, as opposed to Gram-positive infections in Western countries.[4] Sepsis is the most common cause of admission into Indian Intensive Treatment Units (ITUs) and is a major cause of mortality. The lower respiratory tract and urinary tract are the predominant source of sepsis.[5] However, awareness regarding the same is limited amongst Indian health care professionals and patients.[6]

In the early stages of sepsis, the inflammatory system becomes hyperactive (both humoral and cellular defence mechanisms). However, as the disease progresses, this hyper-inflammatory state is converted to an anti-inflammatory state, which is marked by decreased levels of TNF and increased levels of IL-10. Increased production of IL-10 in the late phase of sepsis contributes to immunosuppression. Depletion of immune cells including lymphocytes compromises the immune system's ability to control.

If sepsis is identified early and aggressively treated, then mortality benefits are highest. There is evidence suggesting less hospital mortality in patients assigned to early goal directed therapy. Early identification results in early therapeutic intervention to restore balance between oxygen delivery and oxygen demand.[7] Delay in recognition of those in sepsis causes ongoing volume depletion and microcirculatory inflammation, resulting in severe and irreversible organ dysfunction,[8] thereby contributing to increased morbidity in sepsis.[9] However no rapid diagnostic tests are currently available to accurately identify the patients with sepsis or those at high risk of developing sepsis. This is unlike certain other life-threatening conditions (eg: myocardial infarction), for which highly accurate diagnostic tests are available. Moreover, diagnostic tests for sepsis like culture will take at least 48 hours to become positive and that delay in antibiotics while waiting for a culture will be associated with poorer outcomes. Thus in the meantime, clinicians must rely on their clinical judgment to identify sepsis among patients with infection. Some of the commonly used outcome predictors are SOFA score, q SOFA score and Lactate level. The scores are calculated 24 hours after admission to the ICU and every 48 hours thereafter (thus, the term "Sequential" Organ Failure Assessment).The aggregate score represents the risk of death from sepsis and indicates the urgency of the response. The qSOFA score is a modified version of the Sequential (Sepsis-related) Organ Failure Assessment score (SOFA) score. A score ≥2 is associated with poor outcomes due to sepsis. It describes an assessment score for patients outside the intensive care unit to facilitate the identification of patients potentially at risk of dying from sepsis.[10] In Patients with sepsis increased serum lactate level is thought to be due[11] to tissue hypoxia leading to increased anaerobic glycolysis resulting in overproduction of lactate, decreased lactate clearance as a result of liver dysfunction and

acute kidney injury.

Shock index (SI) is defined as the heart rate divided by systolic blood pressure. It derived using two simple physiological measures as a simple bedside assessment.

In patients with sepsis, peripheral vasodilatation results in decrease in systemic vascular resistance (SVR). Heart rate increases as a compensatory mechanism, in an attempt to maintain the blood pressure. Thus in the early stages of sepsis, the blood pressure may be normal. Hence blood pressure alone may not be a reliable marker in identifying patients with early sepsis. However shock index would be increased, owing to the tachycardia, and thus can predict early sepsis. The normal range for this unitless measure is currently accepted as 0.5-0.7, though some evidence suggests that up to 0.9 is acceptable[12] Values approaching 1.0 are indicative of worsening hemodynamic status and shock. It may also be used as a means to track progress of resuscitation.[13]

MATERIALS AND METHODS

A Hospital based prospective observational study was conducted for a period of 2 years, from February 2021 to January 2023 in M S Ramaiah Hospitals. 75 inpatients admitted in the Department of General Medicine were included in the study. Septic patients with suspected infection, after fulfilment of two or more points of qSOFA score were included in the study. Patients aged less than 18 years and pregnant females were excluded from the study as their physiological responses to an acute illness may differ from an average adult.

Age, sex, demographic data and clinical history were recorded for all study participants. Initial vital signs recorded at the time of admission and blood investigation reports including haemoglobin, WBC counts, platelet counts, blood lactate levels, serum creatinine, bilirubin, sodium and potassium levels, arterial blood gas analysis were used for calculating the Shock Index (SI) and q SOFA scores. The results of blood cultures and serology reports will also be obtained from the hospital records. PaO2/FiO2, Mean Arterial Blood Pressure (MAP), Respiratory Rate (RR), Glasgow Coma Scale (GCS) score and Urine output are also noted for all patients.

Statistical Methods

Data was entered into Microsoft Excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data.

Continuous data was represented as mean and standard deviation. Independent t test was used as a test of significance to identify the mean difference between two quantitative variables. Receiver Operating Characteristic curves (ROCs) were constructed for Shock Index and mortality. ROCs and optimal cut-off points were chosen for the calculation of sensitivity, specificity, positive and negative predictive values of Shock Index. A test that predicts an outcome no better than chance has an area under the ROC curve of 0.5. An area under the ROC curve above 0.8 indicated fairly good prediction. MS Excel and MS word were used for graphical representation of data in the form of graphs such as bar diagram, Pie diagram. P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical softwares such as MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) were used to analyze data.

Sample size was estimated based on the sensitivity of 77% for shock index above or equal to 1 in predicting mortality in sepsis patents as reported by study done by Lombard et al.

RESULTS

In our study, total subjects were 75 in number, among these 44 (58.7%) were males and 31 (41.3%) were females. In our study population, the most common etiology for sepsis was Urinary tract infection at 34.7% (26 patients) and second most common cause was Pneumonia at 24.0% (18 patients) of the study population.

	Frequency (n)	Percentage (%)
Acute cholecystitis	5	6.7
Acute gastroenteritis	4	5.3
Diabetic foot	4	5.3
Bed sore	1	1.3
Meningitis	1	1.3
Meningoencephalitis	6	8
Necrotizing fasciitis	6	8
Neutropenic sepsis secondary to SJS	1	1.3
Parapharyngeal abscess	2	2.6
Perianal abscess	1	1.3
Pneumonia	18	24.0
Urosepsis	26	34.7
Total	75	100.0

Table 1: Distribution of Etiologies of Sepsis

	Minimum	Maximum	Mean	SD
Age	18	92	55.19	14.667
Pulse Rate	77	178	111.81	16.696
SBP	60	160	93.71	19.501
DBP	40	590	67.91	62.575
MBP	47	120	72.36	14.971
HCO3	6.5000	31.6000	18.613600	5.9626025
P/F RATIO	6.5000	455.000	253.48852	128.470289
Sodium	106	154	132.60	7.519
Potassium	1.8000	7.1000	4.335333	1.2496663
CREAT	0.2100	8.2400	2.246800	1.7839769
Bilirubin	0.2000	17.7700	2.146800	2.8417149
HB%	6.0000	15.9000	10.096000	2.4622249
WBC	500	159000	17519.87	19203.317
Platlet	0.1800	15.0000	2.237427	2.3448570
Lactate	0.5000	13.4000	3.139200	2.7350289
SOFA	4	19.0	8.508	4.0819
QSOFA	2	3	2.08	0.673
Shock Index	0.5000	2.5000	1.286347	0.3752031

Table 2: Descriptive statistics of Various parameters

Among 75 subjects, 27 were culture positive sepsis patients, out of which 14 (18.65%) patients showed positive blood cultures, 10 (13.33%) patients showed urine culture positive results and 3 patients (4.0%) showed in growth in body fluids. Among culture positive sepsis patients, most common organism isolated was Escherichia Coli in 10 patients of the total 27 culture positive patients. In clinical profile at presentation to the Emergency Department, 13 (17.3%) subjects were febrile, 55(73.3%) were hypotensive, 61(81.3%) subjects were tachypnoeic and 52 (69.3%) subjects were found to have GCS less than or equal to 13. Creatinine of less than 1.2mg/dl was present in 26 (34.7%) patients. 22 (29.3 %) had creatinine between 1.2 and 1.9, and 12 (16.0 %) patients had values between 2.0 and 3.4. The number of patients with serum creatinine between 3.5 - 4.9 and greater than 5mg/dl were 6(8.0%) and 9 (12 %) respectively. 44(58.7 %) patients had bilirubin less than 1.2 mg/dl, and 6 (8 %) had values between 1.2 to 1.9 mg/dl. Bilirubin values between 2.0- 5.9 mg/dl was present in 19 (25.3 %). Platelet counts of more than 1.5 lakh was present in 41 (54.7%) patients. Of 75 study subjects, 21 subjects (28 %) had P/F ratio between 300- 400, 12 (16 %) had P/F ratio between 200-300. WBC counts at admission were also noted. 27 (36.0 %) patients had WBC counts between 4000-

12,000 cells/cumm, which was within normal limits. Whereas, 6 (8 %) patients had WBC counts less than 4000 and in 42 (56.0%) patients the WBC counts were more than 12,000 cells/cumm.
Mean age in our study was 55.19 with SD of 14.667. Mean Shock index was 1.29 with SD of 0.36. Maximum shock index value was 2.5 and minimum shock 0.5. Mean SOFA score was 8.5 with SD of 4.08. Maximum shock index value was 19 and minimum shock 4. Mean Serum lactate was 3.14 with SD of 2.73. Maximum shock index value was13.4 and minimum shock 0.5.
Among 75 subjects, Shock index calculated at presentation to emergency department was less than 0.7 in 3 (4.0 %) patients , between 0.7-1 in 13 (17.3 %) patients and more than one in 59 (78.7%) patients.

	Frequency (n)	**Percentage (%)**
<0.7	3	4.0
0.7-1	13	17.3
>1	59	78.7

Table 3: Distribution of subjects according to Shock INDEX

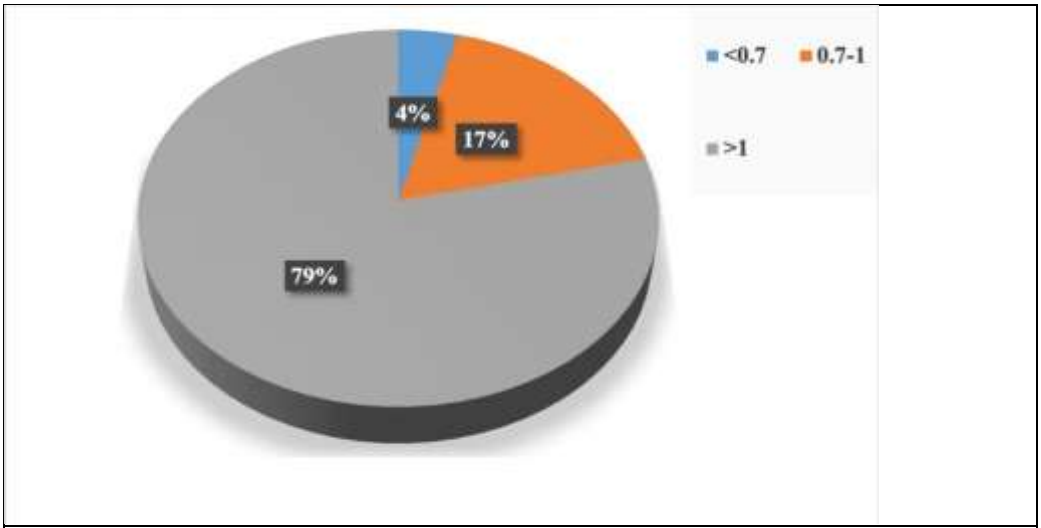

Figure 1: Graph showing Distribution of subjects according to Shock INDEX

Duration of hospital stay was between 1-7 days in 34 patients and 8- 14 days in 25 patients (33.3%). It was 15 - 21 days and more than 21 days among 10 (13.3%) patients and 6 (8%) patients respectively. In our study, out of 75 patients, 56 (74.7 %) patients required inotropic support and 19 (25.3%) patients did not require inotropic support. 35 (46.7%) patients required ventilatory support which includes both Non- invasive and Invasive ventilatory support. In our study of 75 patients, 32(42.7%) died during during hospital stay.

SOFA score is the best among four parameters in predicting Ventilator support, next best is Shock index. Similarly higher SOFA scores at presentation was also associated with higher mortality (26.4% mortality with <10 vs 81.8% with >10) with significant P value of <0.001. qSOFA scores of 3 were associated with higher mortality than qSOFA score of 2 (68.4% versus 33.9%) with significance (P value of 0.015). Mortality rate is higher (55.0% vs 28.6%) with higher lactate levels (greater than 2mmol/L) with P value of 0.035.

However in patients with SOFA score less than 11, only 34% required support (P value <0.001). Lactate levels of greater than or equal to 2 was associated a higher need for ventilator support than the group with lower lactate levels (60% versus 31.4%). This relation was also found to be statistically significant with p value less than 0.002. 45.8% of patients with shock index more than 1 had a hospital stay of 1-7 days, compared to 66.7% of patients with shock index less than 0.7.

	Total Death	**<0.7**	**0.7-1**	**>1**
Gram Negative	7	0	0	5
Gram Positive	4	0	0	3

Table 4: Comparing shock index in Gram Positive and Gram negative sepsis patients with Mortality

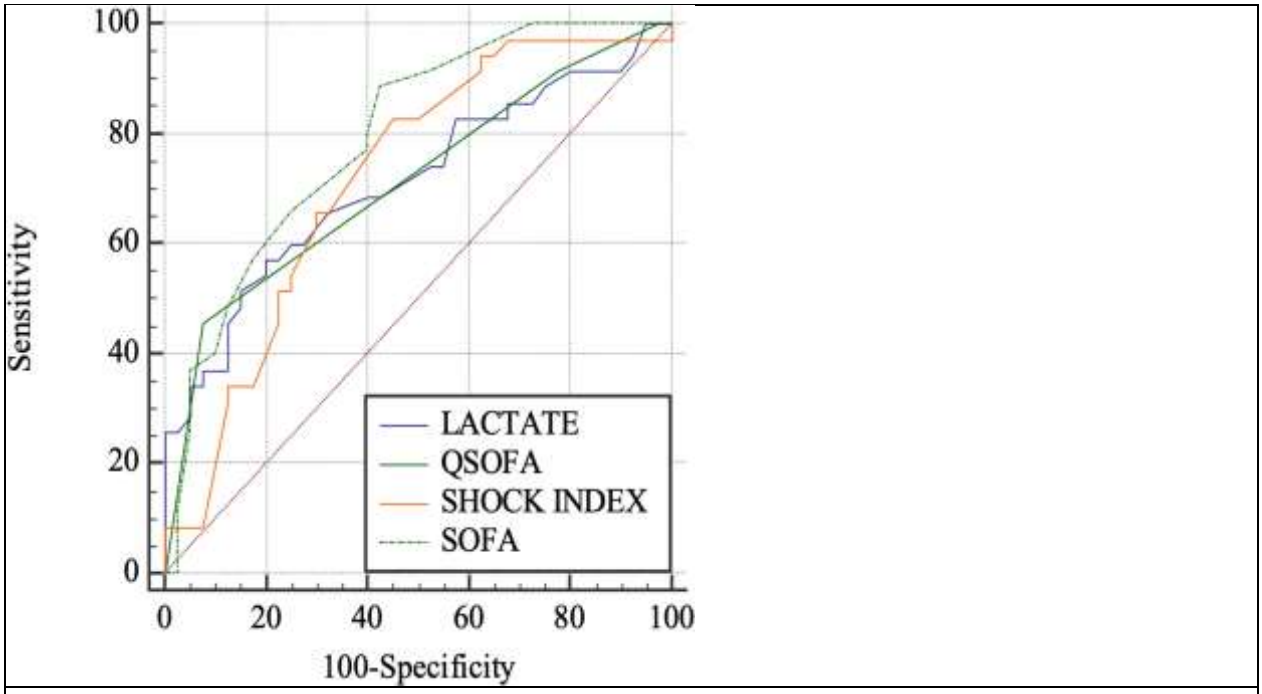

Figure 2: ROC curve for lactate, SOFA, QSOFA, shock index in predicting Ventilator support

	AUC	**95% CI**
Lactate	0.713	0.596 to 0.811
QSOFA	0.714	0.598 to 0.812
Shock index	0.719	0.603 to 0.816
SOFA	0.792	0.683 to 0.877

Table 5: AUC for lactate, SOFA, QSOFA, shock index in predicting Ventilator support

Cut off of Shock index in predicting mortality in our study is 1.22 with sensitivity of 71.9% and specificity of 72.1%. Similarly cut off of SOFA score in predicting mortality is 6, however it was more sensitive (93.7%) and less specific (58.1%) when compared with Shock Index.

Clinically significant association (p values 0.004) was identified between Shock Index at presentation and in-hospital mortality in our study. Patients with higher Shock Index at the time of admission (shock index greater than or equal to 1.0), had higher in-hospital deaths (52.5%) than patients with Shock Index between 0.7 to 1 (7.7%), with an absolute difference of 29.99%. This effect of Shock Index on mortality was irrespective of the aetiology of infection. All deaths caused by gram negative bacilli and gram positive cocci occurred in the group with Shock Index value greater than 1.0.

	Cut off	**Sensitivity**	**Specificity**	**NPV**	**PPV**
Lactate	>2.9	56.2%	76.7%	64.3%	70.2%
QSOFA	>2	40.6%	86%	68.4%	66.1%
SOFA	>6	93.7%	58.1%	62.5%	92.6%
Shock index	>1.22	71.9%	72.1%	65.7%	77.5%

Table 6: Comparison of Sensitivity, Specificity, NPV, PPV of lactate, SOFA, QSOFA, shock index in predicting mortality at best cut off

DISCUSSION

Mean age of our study population was 55.194.67 +/- 14.667 years which was lower compared to study done by Fengshuo Xu et al,[14] where the mean age was 67 +11 years . In our study gender distribution showed 58.7 % were males and 41.3 % were females. These results were consistent with study conducted by Fengshuo Xu et al.[15] Cultures were positive in 36% of subjects, when compared to Clinicomicrobiological profile study of 400 sepsis patients conducted by Arvind Kumar Anand et al,[16] where blood culture was positive in 28.7%. In our study, urinary tract and lungs were the most common site of sepsis contributing to 26% and 18% respectively, E.coli was the major gram negative (85.2%) bacterial infections identified and it contributed to 29.6% of all cases, is similar to Arvind Kumar Anand et al. majority of the study population (78.7%) had shock index values greater than equal to 1.0 in emergency department which is higher in comparison to study done by Tony Berger et al , where only 22.66% presented to emergency department with shock index values greater than equal to 1.0.[17] A systemic review done by Mohamed Y. Radyet al., showed that Shock index more than one has inadequate oxygen transport and need of more ventilator assistance.[18] The mortality was 42.7% in our study which is lower when compared to prospective observational study conducted by Sharmila Chatterjee et al is 63.6%.[19]

Clinically significant association (p values 0.004) was identified between shock index at presentation and in- hospital mortality in our study, is similar to study done by Berger et al, showed that Subjects with SI index more than or equal to one had mortality rates 3 times higher 84.7% patients with shock index values greater than or equal to 1.0 required inotropes vs 33.3% patients with shock index value of less than 1.0. have statistically significant association (p value <0.001) 54 is like study by Prashanth V N et al, with higher Shock Index of more than 1.2 was associated with poor prognosis and higher rates of vasopressor usage.[20] In a prospective observational study Khie Chen Lie et al on 454 patients, higher SOFA score was associated with prolonged hospital stay. On comparing the predictors of Shock Index with outcome, SOFA is best among four parameters in predicting Ventilator support followed by Shock index. The AUROC of SOFA for predicting Ventilator support in subjects was 0.792 (955 CL; 0.683 - 0.877) in comparison to the AUROC of Shock index which was 0.719(95% CI; 0.603 to 0.816). Shock index is best among four parameters in predicting Inotropic Support followed by SOFA score. The AUROC of shock index for predicting inotrope support in subjects was 0.739 (95% CI; 0.624 - 0.833) in comparison to the AUROC of SOFA which was 0.684(95% CI; 0.567 to 0.787).

SOFA is best among four parameters in predicting mortality followed by Shock index. The AUROC of SOFA for predicting mortality in our study was 0.847 (95% CI; 0.745 - 0.920) with sensitivity 93.7% and specificity 58.1% in comparison to the AUROC of Shock index which was 0.788 (95% CI; 0678 - 0.874) with 71.9% sensitivity, 72.1% specificity and optimum cut-off of >1.22. In retrospective observational study done by Shah Jahan Mohd Yuss of showed that AUROC of Shock index which was 0.847 (95% CI) with 73.1% senstivity, 45.8% specificity and optimum cut-off of >1.20.

CONCLUSION

This study described the spectrum of septic patients presenting to a tertiary care hospital. Gram negative infections still remain the major cause of sepsis, followed by gram positive infections and other miscellaneous infections. The urinary tract and lungs remain the major sites of sepsis. Shock index performed as a good indicator of in-hospital mortality, and its performance was comparable to other established indices like qSOFA score, SOFA score and lactate levels. Shock index greater than or equal to 1.0 at initial assessment is associated with greater rates of requirement of ionotropic and ventilatory support.

Additional Information

Disclosures

Human Subjects: Consent for treatment and open access publication was obtained or waived by all participants in this study. Ramaiah Medical College issued approval ECR/215/Inst/KA/2013-RR-19.

Animal Subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

Conflicts of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Payment/Services Info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial Relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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