

# Comparison of MPI and APACHE II in the Prognosis of Perforating Peritonitis

HIMANSHU AGRAWAL<sup>1</sup>, ARUN K GUPTA<sup>2</sup>, NIKHIL GUPTA<sup>3</sup>, MANU VATS<sup>4</sup>, SUMIT PATHANIA<sup>5</sup>, CK DURGA<sup>6</sup>

## ABSTRACT

**Introduction:** Peritonitis is an important surgical emergency that a surgeon has to face. Reproducible scoring systems that allow a surgeon to determine the severity of peritonitis are essential to prognosticate the patient.

**Aim:** To evaluate effectiveness of Mannheim Peritonitis Index (MPI) in comparison to Acute Physiology and Chronic Health Evaluation (APACHE) II in assessing prognosis of patients with perforation Peritonitis.

**Materials and Methods:** In this prospective observational study from November 2015 till March 2017, 63 patients above 18 years of age presenting with perforation peritonitis were included. APACHE II and MPI scoring systems were calculated in all the patients in order to assess their individual risk of morbidity and mortality. The outcome variables studied were: Postoperative wound infection, wound dehiscence, anastomotic leak, respiratory complications, duration of hospital stay, need of ventilator support and mortality. The inferences were drawn with the use of statistical software package SPSS v22.0. The

tests used were ANOVA, Chi-square analysis and t-test. The p value <0.05 was taken as significant.

**Results:** Out of total subjects of 63, Mean age of male subjects was 37.4 years and female subjects was 38.5 years. The mean APACHE II score of 63 patients was  $11.2 \pm 8.1$  with range of 0 to 35 and the mean MPI score was  $26.9 \pm 7.2$  with range of 6 to 39. APACHE II was able to predict postoperative respiratory complications ( $p < 0.001$ ), postoperative need for ventilatory support ( $p < 0.001$ ), hospital stay duration (p-value <0.05) level and mortality (p-value 0.003) while MPI was able to predict postoperative respiratory complications ( $p < 0.001$ ), postoperative need for ventilatory support ( $p < 0.001$ ) and mortality (p-value 0.025). Neither APACHE II nor MPI could predict postoperative anastomotic leak, postoperative wound infection, and postoperative wound dehiscence.

**Conclusion:** MPI is a useful and simple method to determine outcome in patients with peritonitis and is comparable to APACHE II in assessing the prognosis in perforation peritonitis. It can be used in place of APACHE II score in prognosticating patients of perforation peritonitis.

**Keywords:** Acute Physiology and Chronic Health Evaluation, Mannheim Peritonitis Index, Outcome variables

## INTRODUCTION

Peritonitis is one of the most commonly encountered acute surgical problems that a surgeon has to face. Peritonitis due to hollow viscus perforation has a high mortality rate in spite of advances in the surgical treatment. Early prognostic evaluation of peritonitis is important to select patients who will require an aggressive management for optimum outcome [1,2].

Various scoring systems have been used to indicate prognosis of patients with peritonitis [3-5]:

- Disease independent e.g., Acute Physiological and Chronic Health Evaluation (APACHE)-II, Simplified Acute Physiology Score II, Multiple Organ Dysfunction Score [Table/Fig-1].
- Disease dependent e.g., MPI, Peritonitis Index of Altona-II score [Table/Fig-2].

The presence of organ failure is assessed as per criterion published by Deitch EA [6] in 1992:

**Renal failure:** Serum creatinine >177 mmol/L (>2 mg/dL) or serum urea >16.7 mmol/L (>46.78 mg/dL) or oliguria <20 mL/hour.

**Shock:** Hypotension is defined as a systolic BP of <90 mmHg or a reduction of >40 mmHg from baseline, in the absence of other causes for the fall in blood pressure.

**Intestinal obstruction (only if profound):** Paralysis >24 hours or complete mechanical ileus.

**Respiratory failure:**  $pO_2$  <50 mmHg or  $pCO_2$  >50 mmHg.

APACHE II is a disease independent scoring system used most commonly in ICU settings. MPI on the other hand is disease specific scoring system. APACHE II has a greater number of variables than MPI which makes it more time consuming and cumbersome calculation when compared to MPI which is relatively simple to

calculate and less time consuming. In emergency settings, time is an important factor. So, we need a scoring system which is easy, less time consuming and also precise in assessing prognosis of the disease. Few studies in the past conducted by Kumar P et al., Fugger R et al., have indicated that MPI may be comparable or even better than APACHE II in emergency setting [7,8]. This study was done to find out efficacy of MPI in comparison to APACHE II to prognosticate perforation peritonitis.

## MATERIALS AND METHODS

This prospective observational study from November 2015 till March 2017 was conducted at Department of General Surgery, ABVIMS and Dr. Ram Manohar Lohiya Hospital, New Delhi, India.

**Inclusion criteria:** 63 patients above 18 years of age presenting with perforation peritonitis were included.

**Exclusion criteria:** Patients with perforation peritonitis secondary to abdominal trauma, primary peritonitis and postoperative peritonitis due to anastomosis leak were excluded from the study. Ethical committee clearance was taken. {No.T. P(MD/MS) (42/2015)/IEC/PGIMER/RML/4945} Dt. 26.10.2015. Appropriate patient Consent was taken in each case.

Sample size was calculated and considered according to the previous study with  $p=5\%$  [9] and  $d=$ absolute error of 5%. All the patients in preoperative phase were adequately resuscitated, broad spectrum antibiotic (inj. Ceftriaxone 1gm I.V.) prophylaxis was given, Arterial Blood Gases (ABG) and serum electrolytes were checked and if any abnormality was found, it was corrected, Foley's and Ryles tube catheterisation was done, pulse and BP charting was done, parts preparation done just before induction of anaesthesia and then were subjected to emergency surgery. Outcome of patients was studied in terms of postoperative wound infection;

Physiological variable	High abnormal range					Low abnormal range					
	+4	+3	+2	+1	0	+1	+2	+3	+4	Points	
Temperature-Rectal (°C)	≥41	39 to 40.9		38.5 to 38.9	36 to 38.4	34 to 35.9	32 to 33.9	30 to 31.9	≤29.9		
Mean arterial pressure-mm Hg	≥160	130 to 159	110 to 139		70 to 109		50 to 69		≤49		
Heart rate (ventricular response)	≥180	140 to 179	110 to 139		70 to 109		55 to 69	40 to 54	≤39		
Respiratory rate (non ventilated or ventilated)	≥50	35 to 49		25 to 34	12 to 24	10 to 11	6 to 9		≤5		
Oxygenation: A-aDO <sub>2</sub> or PaO <sub>2</sub> (mm Hg) a. FIO <sub>2</sub> ≥0.5 recorded A-aDO <sub>2</sub> b. FIO <sub>2</sub> <0.5 recorded PaO <sub>2</sub>	≥500	350 to 499	200 to 349		<200  PO <sub>2</sub> >70	PO <sub>2</sub> 61 to 70		PO <sub>2</sub> 55 to 60	PO <sub>2</sub> <55		
Arterial pH (preferred)	≥7.7	7.6 to 7.69		7.5 to 7.59	7.33 to 7.49		7.25 to 7.32	7.15 to 7.32	<7.15		
Serum HCO <sub>3</sub> (venous mEq/l) (not preferred)	≥52	41 to 51.9		32 to 40.9	22 to 40.9		18 to 21.9	15 to 17.9	<15		
Serum sodium (mEq/mL)	≥180	160 to 179	155 to 159	150 to 154	130 to 149		120 to 129	111 to 119	≤110		
Serum potassium (mEq/mL)	≥7	6 to 6.9		5.5 to 5.9	3.5 to 5.4	3 to 3.4	2.5 to 2.9		<2.5		
Serum creatinine (mg/dL)	≥3.5	2 to 3.4	1.5 to 1.9		0.6 to 1.4		<0.6				
Haematocrit (%)	≥60		50 to 59.9	46 to 49.9	30 to 45.9		20 to 29.9		<20		
White blood cell count (per mm <sup>3</sup> ) (in 1000)	≥40		20 to 39.9	15 to 19.9	3 to 14.9		1 to 2.9		<1		
Glasgow coma score Score=15 minus actual GCS											
A. Total physiology score (Sum of 12 above points)											
B. Age points (Years) ≤45=0; 45 to 54=2; 55 to 64=3; 65 to 74=5; >75=6											
C. Chronic health points: If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follow a. For non-operative or emergency postoperative patients- 5 points b. For elective postoperative patients- 2 points											
Total APACHE II Score (add together points from A+B+C)											

[Table/Fig-1]: APACHE II Scoresheet.

Study variable	Adverse factor	Points
1. Age	>50 years	5
2. Sex	Female	5
3. Organ failure	Present	7
4. Malignancy	Present	4
5. Evolution time	>24 hours	4
6.. Origin of sepsis	Noncolonic	4
7. Extension of peritonitis	Generalised	6

[Table/Fig-2]: MPI Scoresheet.

MPI score ranges from 0-47

wound dehiscence assessed clinically, anastomotic leak, respiratory complications, duration of hospital stay, need of ventilator support and mortality. MPI score [Table/Fig-2] was calculated in all the patients and compared with APACHE II score (as a standard).

According to MPI score, patients were divided into Low risk 0-21, Moderate risk >21-29 and High risk >29. Patients were divided into Low risk <10, Moderate risk >11-20 and High risk >20 as per APACHE II score.

## STATISTICAL ANALYSIS

Statistical analysis was done using statistical software package SPSS v22.0. Data were represented as mean±SD. Continuous variables were compared using t-test and ROC plotting was done to predict the critical value. Correlation between two continuous variables was established using Pearson's correlation coefficient. The p-value <0.05 was taken as significant.

## RESULTS

Of the 63 patients, 50 were males and 13 were females. Mean age of male subjects (37.4 years) and female subjects (38.5 years). Total of 69.8% (44 patients) had wound infection, 42.9% (27 patients) had respiratory complications, 33% (21 patients) had wound dehiscence,

30% (19 patients) required ventilatory support, 7.9% (5 patients) had anastomotic leak and 19% (12 patients) died in the postoperative period [Table/Fig-3].

Serial number	Postoperative consequences	Frequency (%)
1	Wound infection	44 (69.8%)
2	Wound dehiscence	21 (33.3%)
3	Respiratory complications	27 (42.9%)
4	Ventilatory support	19 (30.2%)
5	Anastomotic leakage	5 (7.9%)
6	Death	12 (19%)

[Table/Fig-3]: Frequency of all outcome variables.

The mean APACHE II score was 11.2±8.1 with range of 0 to 35. The mean MPI score was 26.9±7.2 with range of 6 to 39 [Table/Fig-4].

APACHE II score	No. of patients	MPI score	No. of patients
<10	34	<21	10
>10-20	21	>21-29	31
>20	8	>29	22

[Table/Fig-4]: Frequency distribution of patients according to APACHE II and MPI score.

The postoperative morbidity and mortality were calculated according to APACHE II scoring [Table/Fig-5a,b] and MPI scoring [Table/Fig-6a,b]. APACHE II was able to predict postoperative respiratory complications, postoperative need for ventilatory support, hospital stay duration and mortality; while MPI was able to predict postoperative respiratory complications, postoperative need for ventilatory support and mortality. Neither APACHE II nor MPI could predict postoperative anastomotic leak, postoperative wound infection, and postoperative wound dehiscence.

Chi-square analysis of MPI as well as APACHE II score severity grading showed that there is increased risk of respiratory complications,

Postoperative complications		APACHE II score			Total	Pearson's chi-square	p-value
		0-10	11-20	21 or more			
Postoperative Wound Infection	No	10	7	2	19	1.347	0.510
	Yes	28	10	6	44		
Total		38	17	8	63		
Wound dehiscence	No	28	10	4	42	2.313	0.315
	Yes	10	7	4	21		
Total		38	17	8	63		
Respiratory complication	No	29	6	1	36	15.528	<0.001***
	Yes	9	11	7	27		
Total		38	17	8	63		
Ventilatory support	No	34	8	2	44	18.780	<0.001***
	Yes	4	9	6	19		
Total		38	17	8	63		
Anastomotic leak	No	35	15	8	58	1.031	0.597
	Yes	3	2	0	5		
Total		38	17	8	63		
Mortality	No	34	14	3	51	11.607	0.003**
	Yes	4	3	5	12		
Total		38	17	8	63		

**[Table/Fig-5a]:** Comparison of postoperative morbidity according to APACHE II scoring.  
\*\*Moderately significant; \*\*\*Highly significant

		APACHE II score	Duration of hospital stay
APACHE II score	Pearson correlation	1	0.249
	Sig. (2-tailed)		0.049
	N	63	63

**[Table/Fig-5b]:** Correlation of APACHE II with hospital stay duration.  
The mean post hospital duration was 9.4 days with range of 1 to 30 days; Correlation is significant at the 0.05 level (2-tailed)

need of ventilator support and mortality with increase in both the scores [Table/Fig-5,6].

Postoperative complications		MPI score			Total	Pearson's chi-square	p-value
		0-20	21-29	30 or more			
Post operative wound infection	No	5	7	7	19	2.743	0.254
	Yes	5	24	15	44		
Total		10	31	22	63		
Wound dehiscence	No	9	21	12	42	3.921	0.141
	Yes	1	10	10	21		
Total		10	31	22	63		
Respiratory complication	No	9	20	7	36	10.858	0.004**
	Yes	1	11	15	27		
Total		10	31	22	63		
Ventilatory support	No	10	25	9	44	14.779	0.001**
	Yes	0	6	13	19		
Total		10	31	22	63		
Anastomotic leak	No	9	30	19	58	1.978	0.372
	Yes	1	1	3	5		
Total		10	31	22	63		
Mortality	No	10	27	14	51	7.390	0.025*
	Yes	0	4	8	12		
Total		10	31	22	63		

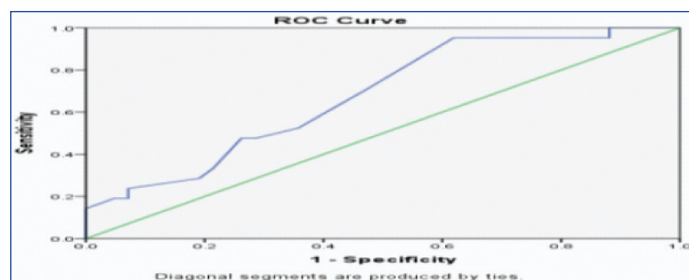
**[Table/Fig-6a]:** Comparison of postoperative morbidity according to MPI scoring.  
\*Significant; \*\*Moderately significant

ROC curve analysis suggests that cut-off value of MPI >26.5 can predict the postoperative wound dehiscence with 71.4% sensitivity and 52.4% specificity [Table/Fig-7].

		Duration of hospital stay	MPI score
Duration of stay	Pearson correlation	1	.211
	Sig. (2-tailed)		.098
	N	63	63

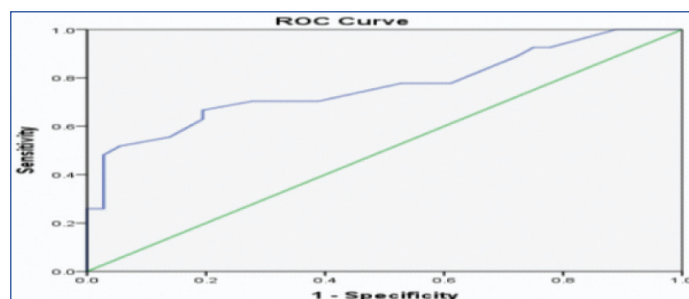
**[Table/Fig-6b]:** Correlations of hospital stay with MPI score.

The mean MPI score has no correlation with hospital stay; (Pearson's correlation coefficient=0.211; p-value >0.05)



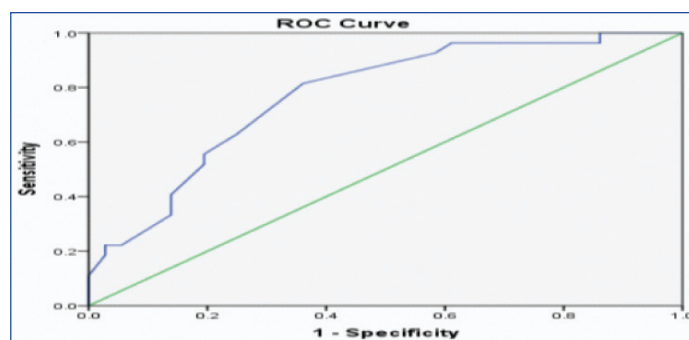
**[Table/Fig-7]:** ROC curve of MPI score for Postoperative wound dehiscence.

ROC curve analysis suggests that cut-off value of APACHE II >9.5 can predict the postoperative respiratory complications with 70.4% sensitivity and 72.8%, specificity [Table/Fig-8a].



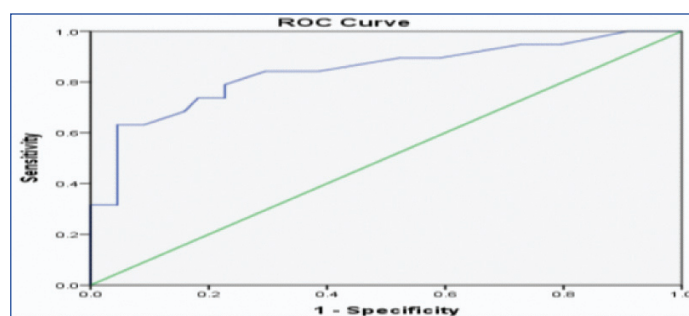
**[Table/Fig-8a]:** ROC curve of APACHE II score for Postoperative respiratory complications.

ROC curve analysis suggests that cut-off value of MPI >26.5 can predict the postoperative respiratory complications with 81.5% sensitivity and 64.0% specificity [Table/Fig-8b].



**[Table/Fig-8b]:** ROC curve of MPI score for postoperative respiratory complications.

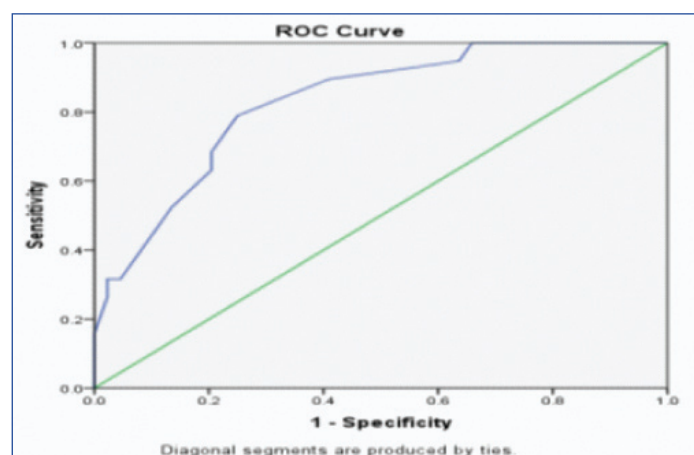
ROC curve analysis suggests that cut-off value of APACHE II >9.5 can predict the postoperative need of ventilation support with 84.2% sensitivity and 70.5% specificity [Table/Fig-9a].



**[Table/Fig-9a]:** ROC curve of APACHE II score for postoperative ventilator support.

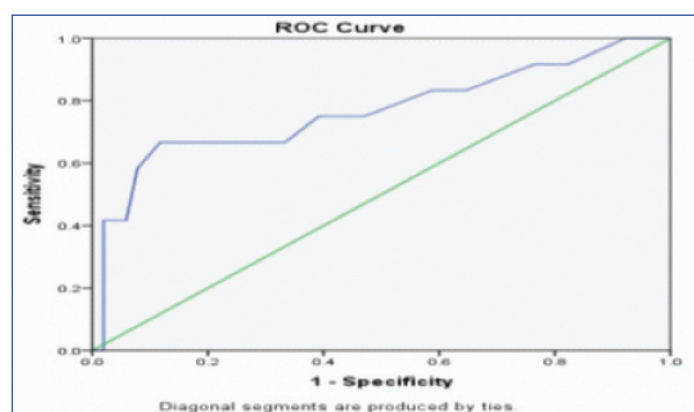


ROC curve analysis suggests that cut-off value of MPI >28.0 can predict the postoperative need of ventilatory support with 78.9% sensitivity and 75.0% specificity [Table/Fig-9b].



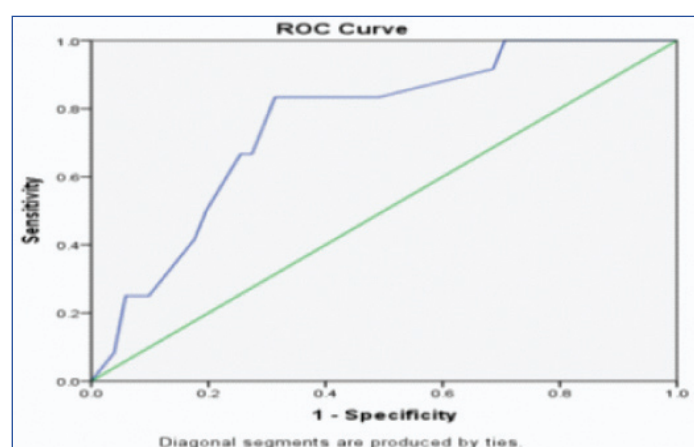
[Table/Fig-9b]: ROC curve of MPI score for postoperative need of ventilatory support.

ROC curve analysis suggests that cut-off value of APACHE II >9.5 can predict the postoperative mortality with 75.0% sensitivity and 60.8% specificity [Table/Fig-10a].



[Table/Fig-10a]: ROC curve of APACHE II score for postoperative mortality.

ROC curve analysis suggests that cut-off value of MPI >28.0 can predict the postoperative mortality with 83.3% sensitivity and 68.6% specificity [Table/Fig-10b].



[Table/Fig-10b]: ROC curve of MPI score for postoperative mortality.

## DISCUSSION

In this study, MPI score was used to prognosticate patients of perforation peritonitis. APACHE II score was used as a standard score against which the findings of MPI score were compared. APACHE II was able to predict postoperative respiratory complications ( $p<0.001$ ), postoperative need for ventilatory support ( $p<0.001$ ), hospital stay duration and mortality ( $p<0.004$ ) while MPI was able to predict postoperative respiratory complications

( $p<0.001$ ), postoperative need for ventilatory support ( $p<0.001$ ) and mortality ( $p<0.006$ ).

Increase in APACHE II and MPI score did not increase the risk of postoperative wound infection. Inamdar MF and Naresh KL assessed the effectiveness of MPI in predicting the morbidity and mortality in perforation peritonitis and found that 5.8% of patients with MPI score less than 21 developed wound infection while 41.4% of patients had wound infection with MPI score 21 to 27 [10]. They found this outcome to be statistically insignificant.

Postoperative wound dehiscence did not show any correlation with increase in MPI and APACHE II score. Kalra D et al., compared APACHE II with various morbidities and found that postoperative wound dehiscence was statistically insignificant [11]. Muralidhar VA et al., assessed the effectiveness of MPI in Perforation peritonitis and found wound dehiscence was seen in only 4% cases [12]. Postoperative respiratory complications showed statistically significant correlation with increasing MPI and APACHE II score. Patil VA et al., found that high risk group (MPI>29) has more respiratory complications than intermediate (MPI 21 to 29) and low risk group (MPI <21) [13].

Increase in MPI score had no effect on postoperative hospital stay while increase in APACHE II score increased the postoperative hospital stay. Increase in severity of both APACHE II and MPI increased the risk of postoperative ventilatory support requirement. Ahuja A and Pal R found the mean ICU stay of 9.75 days in patients with APACHE II score more than 20 compared to 0.13 days ICU stay in patients having APACHE II score less than 10 (mean hospital stay was 12 days) [14]. Postoperative anastomotic leak did not show any statistical significance with increasing MPI and APACHE II score in the present study.

In this study, twelve out of sixty-three patients died (19%). The high mortality could be attributed to patients presenting late. All patients who presented within 24 hours after onset of symptoms recovered postoperatively and were discharged. However, 12 out of 47 patients who presented >24 hours after onset of symptoms could not survive due to sepsis and Multiple Organ Dysfunction Syndrome. Increase in both APACHE II and MPI increased the risk of postoperative mortality which was statistically significant. Kumar P et al., compared MPI and APACHE II in predicting the outcome in patients of peritonitis and found no significant difference between MPI and APACHE II in predicting the mortality [7].

## Limitation(s)

In this study, there was no case of malignant aetiology and only one patient had chronic obstructive pulmonary disease. The impact on preoperative score and final outcome therefore could not be assessed. Multicentric studies with large sample size may alleviate this issue.

## CONCLUSION(S)

Both APACHE II and MPI scores are equally good in predicting the outcomes of perforation peritonitis. MPI is easy to apply but it does not consider underlying physiological disturbances. It also needs operative findings so in true sense; it cannot be used as a preoperative scoring system. This hampers its use to stratify patients into groups to decide whether definitive surgery or damage control surgery can be carried out safely. On the other hand, APACHE II can be calculated preoperatively to categorise patients but it does not take into account peritoneal contamination which has a huge bearing on the final outcome. It is worthwhile to use combination of both scores for a superior prediction of mortality in patients of perforation peritonitis.

**Declaration:** This article was submitted to Scientific Session of the 16<sup>th</sup> World Congress of Endoscopic Surgery, Jointly Hosted by

Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and Canadian Association of General Surgeons (CAGS), Seattle, Washington, USA, 11-14 April 2018 for poster presentation and was later accepted, but it was never presented.

## REFERENCES

- [1] Levy MM, Fink MP, Marshall JC. 2001 sccm/esicm/accp/ats/sis international sepsis definitions conference. *Intensive Care Medicine*. 2003;29(4):530-38.
- [2] Nyström PO, Bax R, Dellinger EP. Proposed definitions for diagnosis, severity scoring, stratification, and outcome for trials on intraabdominal infection. *World Journal of Surgery*. 1990;14(2):148-58.
- [3] Jaimes F, Farbiarz J, Alvarez D, Martinez C. Comparison between logistic regression and neural networks to predict death in patients with suspected sepsis in the emergency room. *Critical Care*. 2005;9(2):R150.
- [4] Clermont G. Artificial neural networks as prediction tools in the critically ill. *Critical Care*. 2005;9(2):153-54.
- [5] Kulkarni SV, Naik AS, Subramanian N. APACHE-II scoring system in perforative peritonitis. *Am J Surg*. 2007;194(4):549-52.
- [6] Deitch EA. Multiple organ failure. Pathophysiology and potential future therapy. *Annals of Surgery*. 1992;216(2):117-34.
- [7] Kumar P, Singh K, Kumar A. A comparative study between Mannheim peritonitis index and APACHE II in predicting the outcome in patients of peritonitis due to hollow viscous perforation. *International Surgery Journal*. 2017;4(2):690-96.
- [8] Függer R, Roky M, Herbst F, Schemper M, Schulz F. Validation study of the Mannheim peritonitis index. *Der Chirurg; Zeitschrift für alle Gebiete der operativen Medizen*. 1988;59(9):598-601.
- [9] Malik AA, Wani KA, Dar LA, Wani MA, Wani RA, Parray FQ. Mannheim Peritonitis Index and APACHE II-Prediction of outcome in patients with peritonitis. *Ulus Travma Acil Cerrahi Derg*. 2010;16(1):27-32.
- [10] Inamdar MF, Naresh KL. Effectiveness of Mannheim peritonitis index scoring system in predicting the morbidity and mortality in peritonitis due to hollow viscous perforation. *International Journal of Biomedical Research*. 2014 30;5(12):765-70.
- [11] Kalra D, Gupta S, Yadav BL, Tanwar P, Khan SA, Singh J, et al. Association of clinical outcome and Apache II score in secondary peritonitis (A study of 50 cases). *International Journal of Health Sciences and Research (IJHSR)*. 2016;6(4):107-13.
- [12] Muralidhar VA, Madhu CP, Sudhir S, Srinivasarangan M. Efficacy of Mannheim peritonitis index (MPI) score in patients with secondary peritonitis. *Journal of Clinical and Diagnostic Research: JCDR*. 2014;8(12):NC01-03.
- [13] Patil VA, Mahapatra B, Panchal A, Deolekar S. Effectiveness of Mannheim peritonitis index in predicting the morbidity and mortality of patients with hollow viscous perforation. *International Journal of Research in Medical Sciences*. 2017;5(2):533-36.
- [14] Ahuja A, Pal R. Prognostic scoring indicator in evaluation of clinical outcome in intestinal perforations. *Journal of Clinical and Diagnostic Research: JCDR*. 2013;7(9):1953-55.

### PARTICULARS OF CONTRIBUTORS:

1. Senior Resident, Department of Surgery, PGIMER, Dr. Ram Manohar Lohia Hospital, Delhi, India.
2. Consultant, Department of Surgery, PGIMER, Dr. Ram Manohar Lohia Hospital, Delhi, India.
3. Associate Professor, Department of Surgery, PGIMER, Dr. Ram Manohar Lohia Hospital, Delhi, India.
4. Assistant Professor, Department of Surgery, PGIMER, Dr. Ram Manohar Lohia Hospital, Delhi, India.
5. Senior Resident, Department of Surgery, PGIMER, Dr. Ram Manohar Lohia Hospital, Delhi, India.
6. Consultant, Department of Surgery, PGIMER, Dr. Ram Manohar Lohia Hospital, Delhi, India.

### NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Nikhil Gupta,  
B 406, Panchsheel Apartments, Plot 9, Sector 10, Dwarka, Delhi, India.  
E-mail: nikhilbinita@gmail.com

### PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jul 26, 2019
- Manual Googling: May 01, 2020
- iThenticate Software: May 28, 2020 (13%)

### ETYMOLOGY: Author Origin

### AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jul 25, 2019**  
Date of Peer Review: **Aug 22, 2019**  
Date of Acceptance: **May 06, 2020**  
Date of Publishing: **Jun 01, 2020**