

Original Article

Predictive value of gamma-glutamyltransferase and neutrophil lymphocyte ratio for postoperative complications following emergency surgery

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Received October 30, 2021; Accepted January 6, 2022; Epub February 15, 2022; Published February 28, 2022

Abstract: The high incidence of postoperative complications and mortality associated with emergency surgery makes it essential to predict the likelihood of these negative outcomes pre-operatively. The need of the hour is of simple, inexpensive and, reliable predictive point of care prognostic markers. This study evaluated the prognostic value of serum GGT and NLR for patients undergoing emergency surgery by correlating them with the grades of postoperative complications according to the Clavien Dindo system. It is an observational longitudinal prospective and retrospective study. The preoperative GGT and NLR, and admission APACHE II scores were measured in patients undergoing emergency surgeries. The patients were monitored for the development of complications in the immediate postoperative period and followed up until the 30th postoperative day. The post-operative complications were recorded in the form of Clavien Dindo grades. The values of GGT, NLR and, APACHE II score were correlated with the Clavien Dindo grades of postoperative complications using Chi-square test, Fischer's exact and, Kruskal Wallis test. Gamma-glutamyltransferase (χ^2 11.282, P 0.127) and NLR (χ^2 8.571, P 0.285) did not show a significant association with Clavien Dindo grades of post-operative complications. APACHE II score correlated significantly with Clavien Dindo grades ($\chi^2=133.080$, P<0.001) and emerged as the best parameter in terms of AUROC, positive predictive value and, diagnostic accuracy. Gamma-glutamyltransferase and Neutrophil Lymphocyte Ratio did not significantly predict post-operative complications following emergency surgery. The APACHE II scoring system showed statistically significant association with postoperative complications, best diagnostic accuracy and, highest predictive value. An existing risk assessment tool proved superior to the novel markers, GGT and NLR, under evaluation.

Keywords: Gamma glutamyl tranferase, neutrophil lymphocyte ratio, emergency surgery, Clavien Dindo classification, APACHE II score, postoperative complications

Introduction

Patients undergoing emergency surgery form an exclusive group. The acute nature of the disease, deranged preoperative physiology, the complexity of the surgery, time-bound need for intervention, all contribute to the higher post-operative complication rates noted in emergency surgery.

Due to the high incidence of postoperative complications and mortality associated with emergency surgery, patients who are at high risk for these complications have to be recognized. Classification of postoperative complications provides a better understanding of the

spectrum of adverse events occurring following surgery. The Clavien Dindo classification system is a simple classification system of post-operative complications that can be readily applied and can help in standardizing the classification of postoperative complications. This classification consists of five grades with the highest being mortality. The strength of this classification system is that it is based on interventions needed to manage specific complications (see **Table 1**) [1]. Hence, we used the Clavien Dindo system to characterize complications in our study population.

Over the years several biochemical parameters, prognostic scores and, risk prediction tools

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Table 1. Clavien Dindo classification system

Grade	Definition
Grade I	Any alteration in the normal postoperative course which does not require pharmacological treatment, surgery, endoscopic or radiological interventions. This grade includes bedside drainage of wound infections
Grade II	Requires pharmacological treatment with medications other than those used for managing grade I complications
Grade III	Requiring surgical, endoscopic or, radiological intervention
III a	Not requiring general anesthesia
III b	Requiring general anesthesia
Grade IV	Life-threatening complication, Needs ICU admission
IV a	Single organ dysfunction
IV b	Multi-organ dysfunction
Grade V	Death
Suffix d	Stands for disability, it is used along with respective complication when the patient has postoperative complication at discharge from the health-care facility

have been formulated for predicting morbidity and mortality in surgical patients. The Acute physiology and chronic health evaluation (APACHE II and APACHE III), Simplified acute physiology score (SAPS II), Mortality probability model (MPM II) are tools used to quantify the severity of physiological derangement in the patient [2, 3]. Scores specific to surgeries include the POSSUM score (Physiological and Operative Severity score for enumeration of mortality and morbidity), P-POSSUM (Portsmouth POSSUM), and, the Surgical Apgar score (SAS). Scoring systems used in trauma include the Denver criteria, the SOFA (Sequential Organ Failure Assessment) score, Revised Trauma Score (RTS) and, TRISS (Trauma and Injury Severity Score). The cumbersome nature of score calculation has prompted the search for simplified prognostic markers that efficiently predict complications.

Gamma-glutamyltransferase, formerly known as gamma-glutamyl transpeptidase is an enzyme involved in transferring “gamma-glutamyl groups” from one compound to another molecule. Elevated GGT levels were found to be associated with all forms of liver disease including alcoholic liver disease, porphyria cutanea tarda (PCT), Non-alcoholic steatohepatitis (NASH), fatty liver, obesity and, metabolic syndrome [4-6]. Hannigan et al. detected raised GGT levels in 451 human tumors [7]. Abnormal GGT levels were associated with acute cardiac events, hypertension, smoking and, cerebrovascular accidents, both ischemic and hemorrhagic stroke [8-10]. Elevated GGT levels were also shown to predict all-cause mortality. The prognostic role of GGT in post-operative complications following emergency surgery has not been explored to our best knowledge.

The neutrophil-lymphocyte ratio (NLR) is derived from the ratio of neutrophils to that of lymphocytes. Persistent lymphopenia adversely affects the patient outcome and concomitantly yields a high NLR ratio. High NLR correlated with mortality and postoperative complications after emergency laparotomies for benign and malignant conditions. The prognostic value of NLR in all emergency surgeries needs further exploration.

This study is an attempt to have a better understanding of the prognostic value of serum GGT and NLR for patients undergoing emergency surgery by correlating them with the grades of postoperative complications according to the Clavien Dindo system.

Materials and methods

Study design and duration

This is an observational, longitudinal prospective and, retrospective study. The retrospective part of the study was conducted over 18 months from 2019, April to 2020, September. The prospective part of the study was done over 6 months from 2020, October to 2021, March.

Inclusion and exclusion criteria

Inclusion criteria: Males and females of age 18-80 years undergoing emergency surgery for: 1. Hollow viscus perforation; 2. Acute intestinal obstruction; 3. Strangulated hernia; 4. Blunt and penetrating abdominal trauma; 5. Diabetic foot; 6. Necrotizing soft tissue infection; 7. Wet gangrene; 8. Traumatic amputation.

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Exclusion criteria: Patients with chronic liver disease, viral hepatitis, alcoholics, chronic kidney disease (CKD) and, malignancy.

A total of 189 emergency surgery patients were included in the study, of which 139 (73.5%) were males and 50 (26.5%) were females.

Methodology

The pre-operative GGT and NLR values were recorded meticulously and the APACHE II score was calculated for all the patients enrolled in the study. The GGT values were obtained from the preoperative liver function panel. NLR value was obtained by dividing the neutrophil by the lymphocyte count obtained from the complete blood count. APACHE II score was calculated using laboratory and clinical parameters in the preoperative period using online calculation software system. The patients were diligently monitored in the post-operative period and followed up till the 30th post-operative day. All complications that occurred during this period were recorded according to the Clavien Dindo grading system. Data regarding the pre-operative complete blood counts, liver, renal function parameters and, relevant history of the patient were also carefully recorded after duly obtaining written informed consent from the patients.

Statistical analysis

Chi-square tests and Fischer exact tests were used to correlate the parameters with Clavien Dindo's grade of postoperative complications. Kruskal Wallis test was used to correlate data with a non-parametric distribution. Fisher's exact test was used when more than 20% of the total number of cells had an expected count of less than 5. No group comparisons were done in this study. A *p*-value <0.5 was considered statistically significant.

Results

A total of 189 patients, 18 years and above, satisfying the inclusion criteria were enrolled in the study, the mean age of patients being 43.33±15.77 years. Demographic parameters of patients, relevant history, pulse rate, blood pressure, pre-operative complete blood counts, renal and liver function tests, primary disease pathology, surgical procedure and, postopera-

tive complications were correlated with Clavien Dindo grades. A statistically significant association of Clavien Dindo grades was also noted with APACHE II score, pre-operative pulse rate, diastolic blood pressure, hemoglobin, serum albumin, SGPT, blood urea, serum creatinine and, serum calcium (see **Table 2**).

Correlation of neutrophil lymphocyte ratio (NLR) with Clavien Dindo

The median NLR of the study population was 10 (mean: 11.52), mean NLR in patients without any complications was 10.72 (7.65), the highest mean NLR (15.06) was noted in patients with Grade I complications while the lowest mean NLR of 9.35 was observed with Grade IVa complications. The association with various grades of Clavien Dindo however was not statistically significant (χ^2 8.571, *P* 0.285) (see **Table 3**).

Correlation of gamma glutamyl transferase (GGT) with Clavien Dindo

The median overall GGT of the study population was 26.6 U/L (mean: 39.02). The mean GGT in patients without any complications was 39.66 U/L (SD 37.31), highest mean GGT (76.70 U/L) was observed in patients with Grade III b complications while the lowest mean GGT of 26.97 U/L was observed with Grade IV a complication. A mean GGT value of 37.24 U/L was associated with Grade V complication (mortality). The association with different grades of Clavien Dindo (**Table 4**) was not statistically significant (χ^2 11.282, *P* 0.127).

APACHE II score correlation with Clavien Dindo

The mean APACHE II score in patients without any complications was 4.25 (SD 3.29). The highest score (20.73) was observed in patients with Grade V complications while the lowest score of 5.17 was observed with Grade I complications. APACHE II score varied significantly with various grades of Clavien Dindo (**Table 5**). The study observed that an APACHE II score ≥ 7 predicts complications with 78% sensitivity and 83% specificity with an odds ratio and relative risk of 13.2 (6.06-28.74) and 2.24 (1.76-2.97) respectively. APACHE II score emerged as the best parameter in terms of AUROC, positive predictive value and, diagnostic accuracy.

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Table 2. Association between Clavien Dindo grades and study parameters

Parameters	Clavien Dindo Grade								P-value
	None (n=64)	Grade I (n=18)	Grade II (n=19)	Grade III a (n=14)	Grade III b (n=1)	Grade IV a (n=18)	Grade IV b (n=9)	Grade V (n=45)	
Age (Years)	44.66±15.10	38.39±14.58	38.79±14.27	49.07±17.89	30.00±0	41.67±14.07	42.56±13.46	44.96±17.96	0.5001
Gender									0.4963
Male	48 (75.0%)	14 (77.8%)	15 (78.9%)	13 (92.9%)	1 (100.0%)	11 (61.1%)	6 (66.7%)	30 (66.7%)	
Female	16 (25.0%)	4 (22.2%)	4 (21.1%)	1 (7.1%)	0 (0.0%)	7 (38.9%)	3 (33.3%)	15 (33.3%)	
Any comorbidity	19 (29.7%)	2 (11.1%)	1 (5.3%)	2 (14.3%)	0 (0.0%)	1 (5.6%)	1 (11.1%)	16 (35.6%)	0.0293
Diabetes mellitus	11 (17.2%)	2 (11.1%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (13.3%)	0.3373
Hypertension	4 (6.2%)	1 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (11.1%)	0.6243
Chronic medications	11 (17.2%)	2 (11.1%)	2 (10.5%)	2 (14.3%)	0 (0.0%)	1 (5.6%)	1 (11.1%)	13 (28.9%)	0.4513
Presence of addictions	25 (39.1%)	9 (50.0%)	8 (42.1%)	4 (28.6%)	0 (0.0%)	2 (11.1%)	2 (22.2%)	13 (28.9%)	0.2063
Smoking/Tobacco Use (Present)	22 (34.4%)	9 (50.0%)	7 (36.8%)	4 (28.6%)	0 (0.0%)	2 (11.1%)	2 (22.2%)	12 (26.7%)	0.3033
Analgesic abuse	1 (1.6%)	2 (11.1%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0.3703
H/o Past Surgery (Present)	16 (25.0%)	3 (16.7%)	4 (21.1%)	1 (7.1%)	0 (0.0%)	6 (33.3%)	2 (22.2%)	9 (20.0%)	0.7743
Pulse Rate (BPM)	97.56±13.25	100.83±16.47	103.81±12.46	105.85±14.59	108.00±0	99.41±12.66	114.75±14.14	109.61±18.07	0.0081
Systolic BP (mmHg)	109.95±17.98	109.78±24.60	108.06±15.75	112.62±22.10	96.00±0	118.29±24.46	103.50±17.10	101.98±23.76	0.1321
Diastolic BP (mmHg)	71.74±10.97	70.33±13.45	69.50±9.22	69.08±9.75	62.00±0	72.47±11.91	70.75±10.14	63.29±11.53	0.0301
Hemoglobin (g/dL)	11.62±2.53	12.63±2.15	10.79±3.16	10.94±3.67	16.79±0	12.18±3.53	12.16±3.47	9.91±2.31	0.0031
TLC (/cu.mm)	13361.88±8471.57	15356.33±5536.89	14074.79±8603.89	14759.29±7003.98	21030.00±0	11895.33±9549.00	11606.88±5866.51	11926.77±6951.20	0.2991
Neutrophils (%)	79.84±11.85	85.76±5.27	80.70±9.09	84.60±4.61	85.95±0	82.61±5.34	78.15±16.00	82.84±12.20	0.4951
Platelet Count (Lacs/cu.mm)	2.38±1.11	2.69±1.41	3.13±1.70	2.60±1.11	3.07±0	1.84±0.80	2.77±2.89	2.56±1.66	0.2171
Total Bilirubin (mg/dL)	0.79±0.70	1.15±1.59	1.68±2.23	0.52±0.26	4.24±0	1.57±2.97	1.16±1.87	1.07±1.51	0.1061
Direct Bilirubin (mg/dL)	0.46±0.43	0.53±0.51	1.01±1.56	0.31±0.16	1.82±0	0.92±1.94	0.72±1.19	0.65±0.85	0.1551
SGOT (U/L)	38.83±42.17	53.57±33.38	46.99±64.37	41.14±45.45	91.00±0	44.72±29.84	71.91±78.37	68.04±87.54	0.1681
SGPT (U/L)	41.18±40.08	91.03±80.77	70.02±87.00	57.65±58.18	99.00±0	68.52±75.86	111.54±115.63	89.86±111.26	0.0181
ALP (U/L)	235.89±139.06	240.49±180.79	332.95±405.24	213.51±226.34	156.40±0	199.00±91.30	274.04±193.40	218.00±111.68	0.9401
Total Protein (g/dL)	6.15±1.17	6.36±1.12	6.02±1.35	5.57±1.48	7.64±0	5.73±0.77	5.74±1.33	5.62±0.98	0.0631
S. Albumin (g/dL)	3.55±0.67	3.67±0.54	2.99±0.66	3.37±0.77	4.53±0	3.41±0.49	3.10±0.77	3.06±0.70	0.0011
Blood Urea (mg/dL)	47.64±42.83	56.77±51.19	62.44±51.43	47.24±27.30	73.00±0	79.72±59.28	50.99±30.31	76.30±53.31	0.0251
S. Creatinine (mg/dL)	1.08±0.98	1.17±0.76	1.37±1.04	1.05±0.38	3.83±0	1.74±0.82	1.06±0.55	1.59±0.90	0.0011
S. Sodium (mEq/L)	134.86±6.44	136.18±4.46	135.58±5.47	135.74±6.95	149.00±0	139.78±7.59	138.39±4.36	137.26±10.13	0.1011
S. Potassium (mEq/L)	4.29±0.80	4.38±0.76	4.49±0.77	4.34±0.61	5.80±0	4.49±0.89	4.48±0.86	4.42±1.07	0.8001
S. Calcium (mg/dL)	8.18±0.92	8.27±0.46	8.05±0.86	8.26±0.56	10.18±0	8.23±0.99	7.74±0.59	7.71±0.95	0.0141
Neutrophil Lymphocyte Ratio	10.72±7.65	15.06±7.71	10.63±5.72	10.43±3.57	11.00±0	9.35±4.24	9.50±8.05	13.38±10.10	0.2851
GGT (U/L)	39.66±37.31	44.37±47.38	46.26±62.38	28.39±30.52	76.70±0	26.97±24.79	55.56±50.97	37.24±32.59	0.1271
APACHE II Score	4.25±3.29	5.17±2.94	6.53±3.66	7.50±4.33	13.00±0	14.67±4.54	15.44±2.83	20.73±4.31	<0.0011

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Table 3. Comparison of the 8 subgroups of the variable Clavien Dindo grade in terms of NLR (n=186)

NLR	Clavien Dindo Grade								Kruskal Wallis Test	
	None	I	II	III a	III b	IV a	IV b	V	χ^2	P-value
Mean (SD)	10.72 (7.65)	15.06 (7.71)	10.63 (5.72)	10.43 (3.57)	11.00 (NA)	9.35 (4.24)	9.50 (8.05)	13.38 (10.10)	8.571	0.285
Median (IQR)	8 (4.75-15)	13 (9-19.5)	11 (6-15)	11 (7.25-13)	11 (11-11)	8 (7-11)	6 (4.5-14.25)	11 (6-17)		
Range	1-31	6-31	2-20	5-16	11-11	4-20	1-22	1-45		

Table 4. Comparison of the 8 subgroups of the variable Clavien Dindo grade in terms of GGT values (U/L) (n=188)

GGT (U/L)	Clavien Dindo Grade								Kruskal Wallis Test	
	None	I	II	III a	III b	IV a	IV b	V	χ^2	P-value
Mean (SD)	39.66 (37.31)	44.37 (47.38)	46.26 (62.38)	28.39 (30.52)	76.70 (NA)	26.97 (24.79)	55.56 (50.97)	37.24 (32.59)	11.282	0.127
Median (IQR)	31.65 (18.75-43)	24.25 (18-43.92)	22 (14.9-48.6)	18.3 (12-32.7)	76.7 (76.7-76.7)	16.4 (14.42-29.72)	33.4 (25.7-44.1)	27.7 (16-44.9)		
Range	6-200	10.8-167	7-216.6	6.5-123.3	76.7-76.7	10.9-110.3	15-167	8.2-175		

Table 5. Comparison of the 8 subgroups of the Variable Clavien Dindo grade in terms of APACHE II score (n=188)

APACHE II Score	Clavien Dindo Grade								Kruskal Wallis Test	
	None	I	II	III a	III b	IV a	IV b	V	χ^2	P-value
Mean (SD)	4.25 (3.29)	5.17 (2.94)	6.53 (3.66)	7.50 (4.33)	13.00 (NA)	14.67 (4.54)	15.44 (2.83)	20.73 (4.31)	133.08	<0.001
Median (IQR)	4 (2-6)	5 (4-7)	7 (4-8.5)	7.5 (4.25-10.75)	13 (13-13)	15 (11.25-17)	15 (14-17)	22 (19-24)		
Range	0-13	0-11	1-13	0-15	13-13	5-25	11-19	9-27		

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Table 6. Association between post-operative complications and disease pathology (n=188)

Diagnosis	Complications			Fisher's Exact Test	
	Present	Absent	Total	χ^2	P Value
Perforation With Peritonitis	81 (74.3%)	28 (25.7%)	109 (100.0%)	17.655	0.015
Acute Intestinal Obstruction	13 (61.9%)	8 (38.1%)	21 (100.0%)		
Blunt Trauma Abdomen	13 (65.0%)	7 (35.0%)	20 (100.0%)		
PVD With Wet Gangrene	5 (38.5%)	8 (61.5%)	13 (100.0%)		
Traumatic Amputation	5 (71.4%)	2 (28.6%)	7 (100.0%)		
Penetrating Trauma Abdomen	4 (66.7%)	2 (33.3%)	6 (100.0%)		
Necrotising soft tissue infection	1 (20.0%)	4 (80.0%)	5 (100.0%)		
Strangulated Hernia	1 (20.0%)	4 (80.0%)	5 (100.0%)		
Diabetic Foot	1 (50.0%)	1 (50.0%)	2 (100.0%)		
Total	124 (66.0%)	64 (34.0%)	188 (100.0%)		

Disease pathology and Clavien Dindo grades

The primary disease pathology was categorized into 9 groups-hollow viscus perforation = with peritonitis, acute intestinal obstruction, PVD with wet gangrene, NSTI, diabetic foot, strangulated hernia, blunt and penetrating trauma abdomen and, traumatic amputation. Fischer's exact test was used to explore the association between disease pathology and the presence of postoperative complications. A statistically significant difference was noted between disease pathology and the presence of postoperative complications (χ^2 17.655, P 0.01). Patients with perforation peritonitis had the largest proportion of post-operative complications (74.3%) (Table 6). A significant correlation could not however be observed between disease pathology and Clavien Dindo grades of post-operative complications (χ^2 49.439, P 0.720).

Discussion

Our study evaluated 189 emergency surgery patients operated on between 1st April 2019 and 31st March 2021. Among the 189 patients included in the study, 139 (73.5%) were males and 50 (26.5%) were females. A higher female preponderance was noted in emergency surgeries by some nationwide studies, while others including extremes of age noted a male predominance [11, 12]. Postoperative complications were noted in 124 (66.0%) patients. This rate is higher than the complication rates ranging from 24.7% to 53.4% observed in studies conducted on emergency surgeries [13, 14]. These studies which evaluated the complication rates in emergency surgery were mainly

focused on a limited number of emergency surgical conditions, including fewer cases of perforation peritonitis and more vascular surgical emergencies [15]. Delayed presentation leading to severe hemodynamic instability coupled with physiological derangements and high morbidity related to the disease pathology could have contributed to the high mortality rates observed in this study [16-19].

GGT values were found to vary greatly from region to region and across age groups, making it difficult to formulate a uniform precise range applicable to all [8]. This study was the first attempt to investigate the prognostic role of GGT in postoperative complications following emergency surgery to our knowledge. Serum GGT values, however, did not show a significant correlation (χ^2 11.282, P 0.127) with post-operative complications in this study. Former studies evaluated the predictive value of GGT in negative outcomes after liver resection and surgeries performed for other hepatobiliary pathologies [20, 21]. The results obtained suggest that the elevated GGT levels are found in association with a comorbid illness like liver disease, malignancy and, alcohol intake but do not share any association with negative outcomes following surgery in the absence of these. We believe the inconsistency noted between our findings and previous results point to this. Thus, the role of GGT as an independent prognostic marker of postoperative complications and mortality in emergency surgery needs further characterization.

The optimal NLR values of the healthy adult population were observed to lie between 0.78-3.53 [22]. NLR was found to predict patient

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outcome in resection of hepatic metastasis from colorectal cancer and, pancreatic cancer resection, severe acute appendicitis, gangrenous appendicitis and, mortality in the geriatric population (>80 years age) undergoing emergency laparotomy [23-26]. However, preoperative NLR and postoperative complications did not demonstrate a significant association ($P=0.285$). The lack of correlation in our study probably suggests that the predictive value of NLR is limited to disease states with inflammatory and gross immune dysregulation and not universally applicable to all emergency surgical conditions. Prospective studies with a greater sample size are necessary to arrive at a consensus. The results obtained by various studies in terms of the cut-off NLR value and predictive accuracy for short-term or long-term outcomes were highly variable. The results showed prognostic value only in a subset of the cohort within the study population in some studies, such as that by G. Simpson et al. [27] Deranged inflammatory response and defective immune function are part of many severe illnesses. Elevated NLR values may be the product of interaction between multiple known and unknown factors. The utility of NLR as a predictor of all postoperative complications in emergency surgery hence needs further characterization.

The utility of the APACHE II score in surgical patients has received less attention. Recently researchers have started evaluating APACHE II scores in emergency surgical patients [28]. The advocates against the use in surgical patients argued that the score is primarily based on physiological variables and fails to account for the intra-operative and surgical procedure-related variables and hence is suboptimal for risk stratification of surgical patients. The results of our study say otherwise. APACHE II score correlated significantly with various grades of postoperative complications. Conversely, risk assessment tools tailor-made for surgical patients failed to demonstrate superior risk prediction [29]. The mean APACHE II score ranged from 4.25 (3.29) in the absence of complications to 20.73 (4.31) in Grade V complications in our study. A statistically significant correlation ($\chi^2=133.080$, $P<0.001$) was noted between APACHE II score and Clavien Dindo's grades of complications. These findings agree with the findings of a systematic review conducted by C.M.Oliver et al. evaluating the vari-

ous existing risk prediction tools for emergency laparotomy patients [30]. APACHE II score showed significant predictive value (Hazard Ratio: 6.7) in comparison to the Simplified Acute Physiology Score and surgery-specific scores like Mannheim peritonitis Index. The AUROC curve for APACHE II score in predicting complications was 0.859 (95% CI: 0.808-0.911) in this study. The observed AUROC values were lower than (0.984) those recorded in previous studies on hollow viscus perforation patients [28]. Evaluation of the score on more patients, dynamic changes in the score during the diseased state and, modifying treatment modalities by accounting for patient risk stratification score forms the food for thought for future studies.

The distribution of primary disease pathology was similar to the findings of the global burden of emergency surgery. The primary disease pathology correlated well with the development of complications ($\chi^2 17.655$, $P 0.015$). The observed complication rates were highest in perforation patients. Nearly three quarter (74.3%) of the patients with perforation peritonitis suffered from postoperative complications. The bulk of the perforation patients had peptic ulcer disease-related perforations in our study. The major cause of mortality and complications following emergency surgery worldwide was recorded in peptic ulcer-related disease [31].

The pulse rate, diastolic blood pressure, presence of comorbidity, hemoglobin, SGPT, serum albumin, blood urea, serum creatinine and, serum calcium showed a significant correlation with Clavien Dindo grades of postoperative complications in our study. Further studies incorporating a greater number of patients are essential for validating the predictive value of these parameters. In our study, the APACHE II score showed a significant association with Clavien Dindo grades. APACHE II score was the best parameter in predicting complications in terms of AUROC, highest positive predictive value and, best diagnostic accuracy among all other parameters.

Conclusion

This study was undertaken to find simple and inexpensive, point of care predictors in the form of GGT and NLR for complications among pa-

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tients undergoing emergency surgery. The correlation between GGT and NLR values and Clavien Dindo's grades of complications was not found to be significant. The APACHE II scoring system showed statistically significant association with postoperative complications, best diagnostic accuracy and, highest predictive value. An existing risk assessment tool proved superior to the novel markers under evaluation.

Limitations

The number of patients that could be enrolled in the study was limited to 189 in the wake of the Covid 19 Pandemic, the smaller sample size could have influenced the results obtained. The results obtained reflect complications of the emergency surgery pool of a single tertiary health care institution, hence is suboptimal to multicentric studies. Post-operative complications and mortality were recorded during a 30-day follow-up period, limiting the available data on long-term morbidity and sequelae.

Disclosure of conflict of interest

None.

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References

- [1] Dindo D, Demartines N and Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; 240: 205-13.
- [2] Al-Temimi MH, Griffiee M, Ennis TM, Preston R, Vargo D, Overton S, Kimball E, Barton R and Nirula R. When is death inevitable after emergency laparotomy? Analysis of the American College of Surgeons National Surgical Quality Improvement Program database. *J Am Coll Surg* 2012; 215: 503-11.
- [3] Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL and Ramsay G; SCCM/ESICM/ACCP/ATS/SIS. 2001 SCCM/ESICM/ACCP/ATS/SIS international sepsis definitions conference. *Crit Care Med* 2003; 31: 1250-6.
- [4] Fletcher LM, Kwok-Gain I, Powell EE, Powell LW and Halliday JW. Markers of chronic alcohol ingestion in patients with nonalcoholic steatohepatitis: an aid to diagnosis. *Hepatology* 1991; 13: 455-9.
- [5] Conte D, Bolzoni P, Fraquelli M, Bodini P and Velio P. Non-alcoholic steatohepatitis. Report of five cases and review of the literature. *Ital J Gastroenterol* 1995; 27: 363-5.
- [6] Adjarov D and Ivanov E. Clinical value of serum gamma-glutamyl transferase estimation in porphyria cutanea tarda. *Br J Dermatol* 1980; 102: 541-3.
- [7] Hanigan MH, Gallagher BC, Townsend DM and Gabarra V. Gamma-glutamyl transpeptidase accelerates tumor growth and increases the resistance of tumors to cisplatin in vivo. *Carcinogenesis* 1999; 20: 553-9.
- [8] Whitfield JB. Gamma glutamyl transferase. *Crit Rev Clin Lab Sci* 2001; 38: 263-355.
- [9] Miura K, Nakagawa H, Nakamura H, Tabata M, Nagase H, Yoshida M and Kawano S. Serum gamma-glutamyl transferase level in predicting hypertension among male drinkers. *J Hum Hypertens* 1994; 8: 445-9.
- [10] Pintus F and Mascia P. Distribution and population determinants of gamma-glutamyltransferase in a random sample of Sardinian inhabitants. "ATS-SARDEGNA" research group. *Eur J Epidemiol* 1996; 12: 71-6.
- [11] Armenia SJ, Pentakota SR and Merchant AM. Socioeconomic factors and mortality in emergency general surgery: trends over a 20-year period. *J Surg Res* 2017; 212: 178-86.
- [12] Schwartz DA, Hui X, Schneider EB, Ali MT, Canner JK, Leeper WR, Efron DT, Haut E, Velopulos CG, Pawlik TM and Haider AH. Worse outcomes among uninsured general surgery patients: does the need for an emergency operation explain these disparities? *Surgery* 2014; 156: 345-51.
- [13] Akinbami F, Askari R, Steinberg J, Panizales M and Rogers SO Jr. Factors affecting morbidity in emergency general surgery. *Am J Surg* 2011; 201: 456-62.
- [14] Kwan TL, Lai F, Lam CM, Yuen WC, Wai A, Siu YC, Shung E and Law WL. Population-based information on emergency colorectal surgery and evaluation on effect of operative volume on mortality. *World J Surg* 2008; 32: 2077-82.
- [15] Ohene-Yeboah M. Acute surgical admissions for abdominal pain in adults in Kumasi, Ghana. *ANZ J Surg* 2006; 76: 898-903.
- [16] Iversen LH, Bülow S, Christensen IJ, Laurberg S and Harling H; Danish Colorectal Cancer Group. Postoperative medical complications are the main cause of early death after emergency surgery for colonic cancer. *Br J Surg* 2008; 95: 1012-19.

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- [17] Sørensen LT, Malaki A, Wille-Jørgensen P, Kallehave F, Kjaergaard J, Hemmingsen U, Møller LN and Jørgensen T. Risk factors for mortality and postoperative complications after gastrointestinal surgery. *J Gastrointest Surg Off J Soc Surg Aliment Tract* 2007; 11: 903-10.
- [18] Patel SS, Patel MS, Goldfarb M, Ortega A, Ault GT, Kaiser AM and Senagore AJ. Elective versus emergency surgery for ulcerative colitis: a national surgical quality improvement program analysis. *Am J Surg* 2013; 205: 333-8.
- [19] Silber JH, Williams SV, Krakauer H and Schwartz JS. Hospital and patient characteristics associated with death after surgery. A study of adverse occurrence and failure to rescue. *Med Care* 1992; 30: 615-29.
- [20] Wu SJ, Lin YX, Ye H, Xiong XZ, Li FY and Cheng NS. Prognostic value of alkaline phosphatase, gamma-glutamyl transpeptidase and lactate dehydrogenase in hepatocellular carcinoma patients treated with liver resection. *Int J Surg* 2016; 36: 143-151.
- [21] Chen Q, Zhao H, Wu J, Cai J, Li C, Zhao J, Bi X, Li Z, Huang Z, Zhang Y, Cui W and Zhou J. Preoperative D-dimer and gamma-glutamyltranspeptidase predict major complications and survival in colorectal liver metastases patients after resection. *Transl Oncol* 2019; 12: 996-1004.
- [22] Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC and De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? *BMC Res Notes* 2017; 10: 12.
- [23] Wannamethee G, Ebrahim S and Shaper AG. Gamma-glutamyltransferase: determinants and association with mortality from ischemic heart disease and all causes. *Am J Epidemiol* 1995; 142: 699-708.
- [24] Malik HZ, Prasad KR, Halazun KJ, Aldoori A, Al-Mukhtar A, Gomez D, Lodge JP and Toogood GJ. Preoperative prognostic score for predicting survival after hepatic resection for colorectal liver metastases. *Ann Surg* 2007; 246: 806-14.
- [25] Walsh SR, Cook EJ, Goulder F, Justin TA and Keeling NJ. Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. *J Surg Oncol* 2005; 91: 181-4.
- [26] Ishizuka M, Shimizu T and Kubota K. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. *Int Surg* 2012; 97: 299-304.
- [27] Simpson G, Saunders R, Wilson J and Magee C. The role of the neutrophil: lymphocyte ratio (NLR) and the CRP: albumin ratio (CAR) in predicting mortality following emergency laparotomy in the over 80 age group. *Eur J Trauma Emerg Surg* 2018; 44: 877-82.
- [28] Kulkarni SV, Naik AS and Subramanian N Jr. APACHE-II scoring system in perforative peritonitis. *Am J Surg* 2007; 194: 549-52.
- [29] Ragg JL, Watters DA and Guest GD. Preoperative risk stratification for mortality and major morbidity in major colorectal surgery. *Dis Colon Rectum* 2009; 52: 1296-303.
- [30] Oliver CM, Walker E, Giannaris S, Grocott MP and Moonesinghe SR. Risk assessment tools validated for patients undergoing emergency laparotomy: a systematic review. *Br J Anaesth* 2015; 115: 849-60.
- [31] Stewart B, Khanduri P, McCord C, Ohene-Yeboah M, Uranues S, Vega Rivera F and Mock C. Global disease burden of conditions requiring emergency surgery. *Br J Surg* 2014; 101: e9-22.