Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy

Prospective observational study

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR M.S. GENERAL SURGERY BRANCH I EXAMINATION OF THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI, TO BE HELD IN MAY 2020

REGISTRATION NO. 221711458

DECLARATION

I hereby declare that this dissertation titled **"Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy"** is my original work done under the guidance and supervision of Dr. Inian Samarasam, Professor, General Surgery Unit-III, Christian Medical College, Vellore. This dissertation is submitted in partial fulfillment of the rules and regulations for the degree of MS in General Surgery examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held on May 2020.

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CERTIFICATE

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ABBREVIATIONS:

PCT	Procalcitonin
CRP	C-reactive protein
PD	Pancreaticoduodenectomy
SSI	Surgical site infection
DGE	Delayed gastric emptying
NO	Nitric oxide
SIRS	Systemic inflammatory response syndrome
IL	Interleukin
ESR	Erythrocyte sedimentation rate
SOFA	Sequential organ failure assessment
MAP	Mean arterial pressure
ERCP	Endoscopic retrograde cholangiopancreaticogram
PTBD	Percutaneous trans-hepatic biliary drainage
CDC	Centers for Disease Control and Prevention
SSISS	Surgical Site Infection Surveillance Service
NHSN	National Healthcare Safety Network
UTI	Urinary tract infection
POD	Post-operative day
BUN	Blood urea nitrogen
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
PSC	Pancreas specific complications

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ABSTRACT

TITLE OF THE ABSTRACT: Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy.

DEPARTMENT: General Surgery, Hepatopancreaticobiliary Surgery

NAME OF CANDIDATE: Dr. Nitin Paul Ambrose

DEGREE AND SUBJECT: M.S. General Surgery

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INTRODUCTION:

Pancreaticoduodenectomy is a major abdominal operation associated with high morbidity. Infective complications are a common cause of the morbidity associated with this operation. Early prediction of the infectious complication could help in taking preventive measures for the same, especially in the preoperative setting. Procalcitonin and C-reactive protein have been widely considered as biomarkers of sepsis and infections. Finding an association between preoperative values of Procalcitonin, C-reactive protein, and the postoperative complications, may help reduce the morbidity associated with the infectious complications following pancreaticoduodenectomy. Currently, there are no preoperative markers to identify

the likelihood of developing postoperative infective complications. Hence, this study was undertaken to assess the use of preoperative Procalcitonin and C-reactive protein measurements as a biomarker of postoperative infective complications of Pancreaticoduodenectomy.

METHODS:

A prospective observational study was conducted on 50 patients who underwent Pancreaticoduodenectomy for various indications, the majority of which was for pancreatic and periampullary malignancy between December 2017 and February 2019. These patients planned for Pancreaticoduodenectomy were tested for serum Procalcitonin and C-reactive protein one day prior to the date of surgery and were postoperatively monitored for sepsis, surgical site infections, pneumonia and urinary tract infection on postoperative days 3, 7, 10 and at discharge. Data collected were entered using software Epidata version 3.1. Analysis was done using software SPSS version 23. Univariate analysis was done using measures of central dispersion for continuous variables and proportions for categorical variables. Bivariate analysis was done using chi-square and Fisher's Exact Test.

RESULTS:

Postoperative sepsis was seen among 22 (44%) patients, no specific time point like post-operative day 3, 7, 10 or the time at discharge had increased risk of sepsis. Surgical site infection was seen among 32 (62%) patients of which superficial surgical site infection was more common. Features of sepsis and surgical site

infections were found to be more among patients with elevated preoperative C-reactive protein measurements, however, there was no statistically significant association. No statistical significance was established for associations between preoperative measurements of Procalcitonin, C-reactive protein and postoperative infectious complications of Pancreaticoduodenectomy.

CONCLUSIONS:

The role of preoperative measurements of Procalcitonin and C-reactive protein as a biomarker of postoperative infective complications of Pancreaticoduodenectomy could not be established from this study. The power of the study to have any statistically significant association was limited by a small sample size. Hence, we would recommend this study to be conducted in a larger number of patients over a longer duration and observe the significance if any to reach a statistically significant conclusion.

KEYWORDS:

Pancreaticoduodenectomy, Procalcitonin, C-reactive protein, preoperative measurements, biomarker, post-operative infective complications.

INTRODUCTION:

Pancreaticoduodenectomy is a major operation in which the head of the pancreas, duodenum & proximal jejunum, gall bladder, common bile duct and a portion of the stomach are removed as a part of the procedure. It is considered an operation with high morbidity. Infective complications are a common cause of morbidity.

The other causes of morbidity following pancreaticoduodenectomy are delayed gastric emptying, characterized by the need for prolonged nasogastric decompression and/or inability to tolerate oral intake. The frequency of delayed gastric emptying following pancreaticoduodenectomy is 18% followed by pancreatic fistulas with 17%. Anastomotic leaks from the hepaticojejunostomy and gastrojejunostomy are rare and occur in less than 5% of these procedures. Infectious complications (e.g., intra-abdominal abscess, wound infection) are slightly more common in this procedure and may often require intervention with percutaneous drainage or open wound dressing changes(1).

Early prediction of the infectious complications could help in taking preventive measures for the same, especially in the pre-operative setting. Procalcitonin and C-reactive protein have been widely considered as biomarkers of sepsis and infections. Finding an association, between pre-operative values of Procalcitonin, C-reactive protein, and post-operative infectious complications, may help reduce the morbidity associated with the infectious complications.

Procalcitonin and C-reactive protein are commonly used laboratory markers in the clinical setting for the evaluation of systemic inflammatory response to an infectious agent. It can be used as a diagnostic, predictor, and monitoring tool in patients with acute sepsis.

Various studies done in the past comparing Procalcitonin and C-reactive protein as markers for bacterial infections, have shown that Procalcitonin was more sensitive and specific than C-reactive protein level for differentiation of bacterial (infective) from non-infective causes of inflammation(2).

With the background knowledge of infectious complications as one of the leading causes of increased morbidity in pancreaticoduodenectomy, this study aims to look at the usefulness of pre-operative Procalcitonin and C-reactive protein as a marker for postoperative sepsis and infections. The standardized practice in Christian Medical College and Hospital, Vellore involves administration of Intravenous antibiotics to patients undergoing pancreaticoduodenectomy only prior to skin incision at the time of induction of anaesthesia and there is no role for routine administration of antibiotics in the pre-operative or post-operative period. From this study, we hope to find if pre-operative Procalcitonin and C-reactive protein measurements are useful biomarkers of post-operative infective complications In the event of a significant association, there might be a role for prolonged administration of antibiotics in the post-operative period in patients with elevated measurements of pre-operative Procalcitonin and C-reactive protein.

AIM:

To assess the diagnostic value of elevated pre-op Procalcitonin, C-reactive protein in post-pancreaticoduodenectomy infective complications.

OBJECTIVES:

1. To assess the role of pre-operative Procalcitonin and C-reactive protein as predictors of postoperative infective complications in patients undergoing pancreaticoduodenectomy

2. To compare the efficacy of each as a better predictor among the two.

LITERATURE REVIEW

Pancreaticoduodenectomy:

Pancreaticoduodenectomy is a complex surgical procedure with significant morbidity. Pancreaticoduodenectomy is the preferred resection of choice for malignant disorders of the pancreatic head and periampullary region and occasionally for benign disorders. The lowest operative mortality rates and best long-term cancer outcomes following surgery have been seen at high-volume centers(3)(4). Although previously associated with high mortality rates in the postoperative period, advances in surgical technique and perioperative management have reduced mortality rates to 5 percent or less in high-volume centers(5). One of the main factors for this achievement was the concept of centralization(6).

Resection of the head of the pancreas is indicated primarily for neoplasms and required associated duodenal resection(1). The standard operation for pancreatic cancer within the head or uncinate process of the pancreas is pancreaticoduodenectomy(7). Pancreaticoduodenectomy may also be useful in the management of duodenal or pancreatic trauma, and chronic pancreatitis(1).

. Modifications of conventional pancreaticoduodenectomy (Whipple procedure) have been developed in an attempt to improve outcomes or minimize the morbidity associated with the operation(7). Some of the modifications are pylorus-preserving pancreaticoduodenectomy, duodenum preserving pancreatic head resection and subtotal stomach preserving pancreaticoduodenectomy(1). Pylorus-preserving pancreaticoduodenectomy is less aggressive and the procedure preserves the gastric

antrum, pylorus, and the proximal 3 to 4 cm of the duodenum(7). Subtotal stomach-preserving pancreaticoduodenectomy is a modification that is less frequently performed(7).

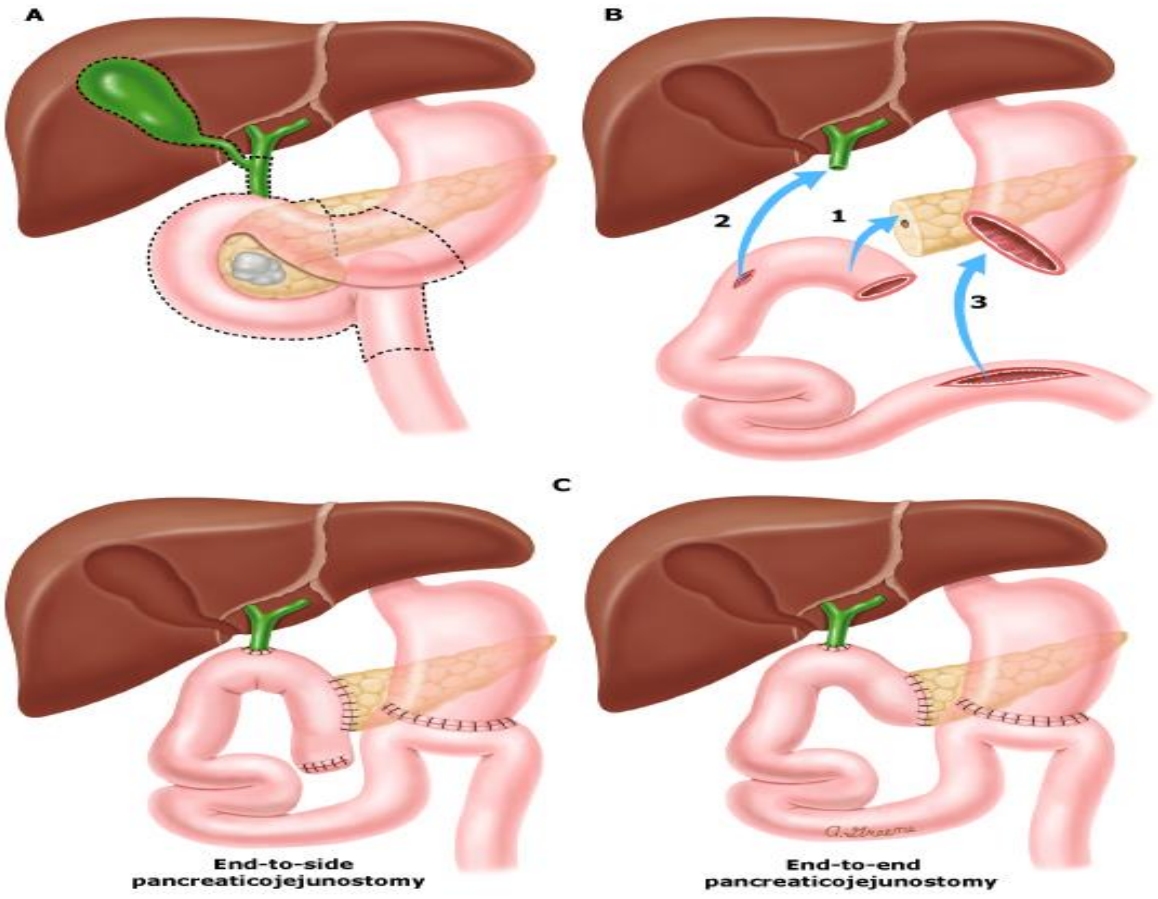

Figure 1: Conventional Pancreaticoduodenectomy (Whipple Procedure). (8)

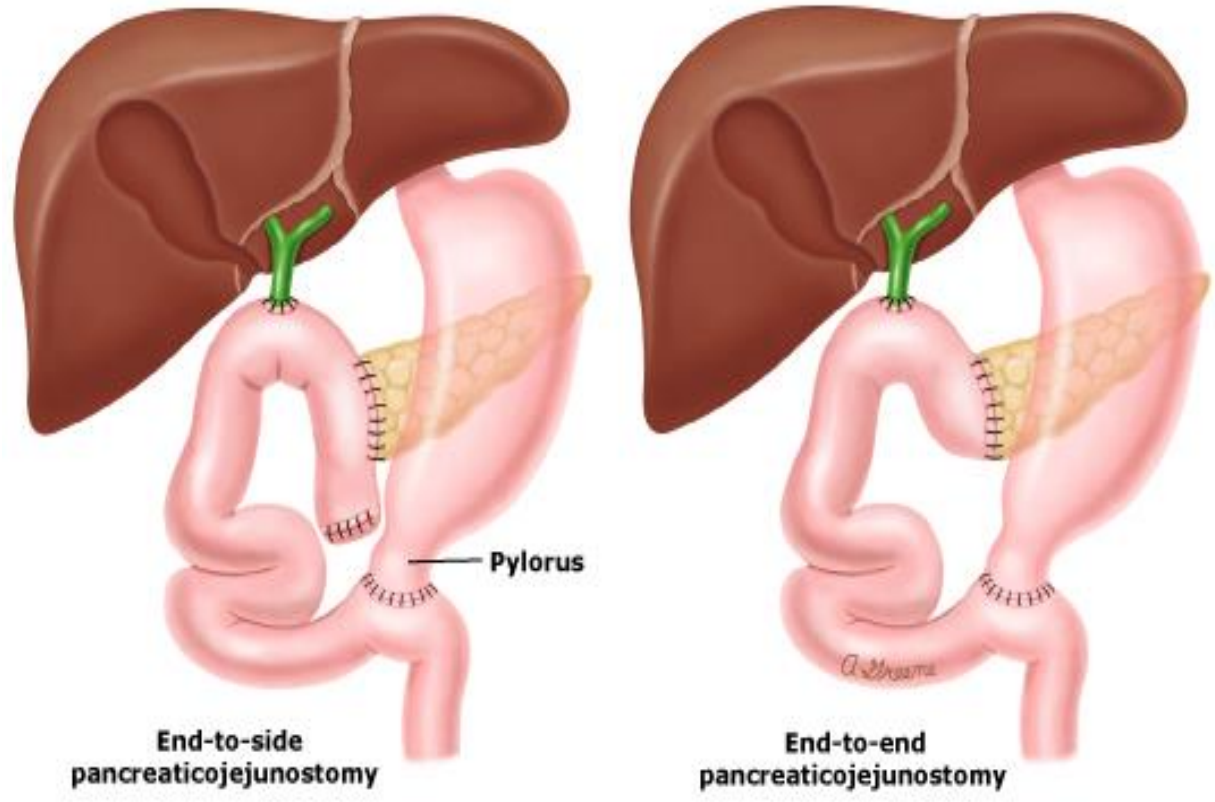

Figure 2: Pylorus preserving Pancreaticoduodenectomy(7)

The common morbidity following pancreaticoduodenectomy is delayed gastric emptying, characterized by the need for prolonged nasogastric decompression and/or inability to tolerate oral intake(1). The frequency of delayed gastric emptying following pancreaticoduodenectomy is 18% followed by pancreatic fistulas with 17%. Anastomotic leaks from the hepaticojejunostomy and duodenojejunostomy/gastrojejunostomy are rare and occur in less than 5% of these procedures(1). Infectious complications (e.g., intra-abdominal abscess, wound infection) are slightly more common in this procedure and may often require intervention with percutaneous drainage or open wound dressing(1).

Table 1: Morbidity following Pancreaticoduodenectomy (Sabiston textbook of surgery: the biological basis of modern surgical practice. 19th ed)

MORBIDITY	**FREQUENCY (%)**
Delayed gastric emptying	18
Pancreas fistula	12
Wound infection	7
Intra-abdominal abscess	6
Cardiac events	3
Bile leak	2
Overall reoperation	3

Despite being a complex surgical technique, the advances in surgical techniques have reduced the overall 30-day mortality rates to as low as 5%, or even less(6), thereby shifting the focus towards the other post-operative complications which contribute to the morbidity of the procedure and subsequently to the overall mortality(6). The four frequent complications following pancreatic resection that contributed to post-procedure morbidity included pancreatic fistula, delayed gastric emptying (DGE), septic complications(intra-abdominal abscess), and abdominal hemorrhage(6).

A study done by House et al showed that 38% of the patients who underwent pancreaticoduodenectomy had postoperative complications, most common of which were pancreatic fistula and abscess among 15%, wound infection among 14%, and delayed gastric emptying among 4% of the patients who had postoperative

complications(9). Another study done by Fathy et al showed that among 216 patients with periampullary tumors treated by pancreaticoduodenectomy, operative mortality occurred in 7(3.2%), 77(33%) patients developed 1 or more complications, pancreatic leak occurred in 23 (10.6%) patients, abdominal collection in 23 patients (10.6%) and delayed gastric emptying in 19 (8.8%) patients(10)

With the background knowledge of infectious complications as one of the leading causes of increased morbidity in pancreaticoduodenectomy, this study aims to look at the usefulness of pre-operative Procalcitonin and C-reactive protein as a marker for postoperative sepsis and infections

Procalcitonin:

Procalcitonin was described as a sepsis marker in 1993(11). Procalcitonin (PCT), is a protein that consists of 116 amino acids with a molecular weight of 13kDa, and the peptide precursor of calcitonin. This is synthesized by the parafollicular C cells of the thyroid and also produced by the neuroendocrine cells of the lung and intestine(12). It is also released as an acute-phase reactant in response to inflammatory stimuli, especially those of bacterial origin. This elevated level of Procalcitonin during inflammation is associated with bacterial endotoxin and inflammatory cytokines(13). PCT detected in plasma during inflammation is not produced in C-cells of the thyroid and the probable site of its production during inflammation are the neuroendocrine cells in the lungs or intestine(12). Thus, when standard assays are used, serum Procalcitonin is not detectable in healthy persons(12).

The physiology and regulation of Procalcitonin production is not well understood. Various hypotheses suggest that procalcitonin may be involved in the metabolism of calcium, cytokine network, nitric oxide (NO) synthesis, and its modulation, as well as pain-relieving effects(12). There are no plasma enzymes that break down Procalcitonin. Therefore, once Procalcitonin enters the circulation, it remains unchanged, with a half-life of around 30 hours, with no evidence that serum Procalcitonin binds to cellular receptors of calcitonin or any other specific Procalcitonin receptors(12). Serum levels of Procalcitonin rise within two to four hours and peak within 24 to 48 hours of an inflammatory stimulus(14). After reaching the peak levels, with resolution of inflammation, there is a decline in serum Procalcitonin levels by about 50% every 1 to 1.5 days(14).

Other non-infectious causes of systemic inflammation that can induce Procalcitonin production include trauma, shock, surgery, burn injury, chronic kidney disease, however, their correlation with Procalcitonin induction is less when compared to bacterial infection(15). Procalcitonin is said to have the highest accuracy for diagnosing sepsis in various settings(16). Hence procalcitonin measurement helps in early confirmation of systemic inflammation and sepsis(16). Also for patient in sepsis, several studies have shown that immediate initiation of right antibiotics have helped improve the overall survival rates(17). Hence PCT has also proved to be useful in guiding antibiotic therapy(16).

The other markers of sepsis used currently like C-reactive protein, lactate or other pro-inflammatory cytokines (Interleukin 6,8) are different in comparison to Procalcitonin in that, it belongs to a class of molecules which may be called 'hormokines' (16,18). During systemic inflammation and infection, this explains the cytokine-like behavior of PCT(16). The specificity of other marker s like C-reactive protein is considered to be low when it comes to diagnosing sepsis and its peak levels do not indicate the severity of the inflammation(16). Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, published in 2012, indicate that PCT can be used for the diagnosis of sepsis and to terminate antibiotic therapy in patients who initially appeared septic, but have no subsequent evidence of infection(19). Also in patients with local infection or bacterial colonization is present, PCT can be used as a tool to exclude severe systemic inflammation(16).

Levels of >0.5 to >2.0 ng/mL (high PCT levels) have a high positive predictive value to rule in diagnosis of sepsis, severe sepsis, or septic shock and similarly levels of<0.25 to <0.5 ng/mL (normal or very low PCT levels) have a high negative predictive value to rule out severe systemic inflammation or sepsis(16). Elevation of serum PCT levels correlate with the severity of the systemic inflammatory response. Bacterial infection appears to be a strong stimulus for PCT induction when compared to non-bacterial causes of PCT induction(16). Also, Procalcitonin induction that occurs in patients with systemic inflammatory response syndrome (SIRS) is not as high as it would be in patients with severe sepsis(16). Also, in patients with bacteremia, if there is no systemic inflammatory response,

PCT levels may be low(16). But, significantly high PCT levels are usually noted in patients with bacteremia and, hence, if PCT levels are found to be normal, bacteremia is unlikely(16).

Assicot et al mentioned that among the 79 children with suspected infection who were investigated thoroughly for the same, 19 with severe bacterial infection had serum procalcitonin levels in the range of 6-53ng/mL while 21 children with no signs of infection had procalcitonin baseline levels <0.1 ng/mL(11)

Procalcitonin is a good biological marker for the diagnosis of sepsis in critically ill patients and after surgery or trauma(20). PCT is superior to C-reactive protein and should be used as in the diagnostic guideline for sepsis(20).

C-reactive protein (CRP):

At the Rockefeller University in 1930, Tillet and Francis discovered C reactive protein(21,22). CRP, an acute-phase serum protein, is a surrogate for the pro-inflammatory interleukin IL-6(23,24). It is a member of the pentraxin family of proteins and is synthesized by the liver(23–25). Primarily synthesized in the liver, C-reactive protein is a part of the acute phase response(22).

CRP is also produced by cells in the vascular wall such as endothelial cells, smooth muscle cells, and also by adipose tissue(23,24). Interleukin (IL)- 6 and IL-1 are major stimuli for the synthesis of CRP(22). Being primarily synthesized in the liver, patients with severe hepatocellular impairment may have a decreased CRP response while renal impairment can elevate CRP concentrations(26).

Du Clos et al mentioned that CRP is a classical acute phase reactant primarily because its serum levels rapidly rise from <1 ug/mL to 600-1000ug/mL at the peak of an acute phase response(22). Like the other acute phase reactants such as ESR (Erythrocyte sedimentation rate), CRP levels correlate with inflammation. However, CRP is considered more useful to follow clinical course and response to treatment when compared with the other acute phase reactants because the rise and fall of the serum levels of CRP in correlation with underlying inflammation are very dramatic(22). Similarly, significant elevation of serum CRP levels indicate clinically relevant inflammation and also infection/inflammation can be excluded in the absence of high CRP levels(27).

C-reactive protein also plays an important role in the host's defense mechanism against infection(26,28). It derives its name as it reacts with the C-polysaccharide of Streptococcus pneumoniae(26) and is not related to protein C or C-peptide(27). Since interleukin (IL)-6, an inflammatory cytokine is a major stimulus for the production of CRP, it is commonly used as a screening tool for inflammation or infection(29). According to Prasad et al, sequential measurement of CRP levels may provide a more accurate assessment in response to treatment(27). Also in patients with isolated elevation of ESR (Erythrocyte sedimentation rate), CRP helps in determining the non-inflammatory cause for the elevation of ESR values(27).

The median normal CRP levels are 0.8mg/L, while among the apparently healthy people 90% have CRP levels less than 3 mg/L and 99% less than 12mg/L according to Reeves et al(26). It is also recommended to perform serial monitoring of CRP when necessary through a single laboratory to minimize error, as test results can vary between laboratories(26). According to Pepys et al, the median CRP concentration is 0.8mg/L, with 99th centile being 12mg/L and 90th centile 3mg/L(30). However, following an acute phase stimulus, CRP levels may rise 10,000-fold where values may increase from less than 50 ug/L to more than 500mg/L(30). With a plasma half-life of about 19 hours, the sole determinant of CPR levels being the synthesis rate, the levels of CRP reflect the intensity of the pathological process stimulating synthesis (30). Similarly, CRP levels rapidly fall as the stimulus for synthesis of CRP ceases completely(30). Hence, Pepys et al mentioned that CRP is a nonspecific marker of inflammation which helps in screening for disease pathology, monitoring response to treatment and detection of intercurrent infection among immunocompromised individuals(30).

Though CRP is widely used as a screening tool for infection/inflammation, it does not have diagnostic specificity as a wide range of clinical conditions can cause elevation of CRP levels(27). While the specificity of elevated CRP levels are low, it has a sensitivity of > 90% for inflammation(26). CRP can also be used as an adjunct to clinical assessment in differentiating bacterial and viral infections(26). A very high value (>100 mg/L) is likely to be due to bacterial rather than viral infection and also in the presence of a significant bacterial infection, a normal CRP value is unlikely(26).

Hence measurement other acute phase reactants like ESR, Procalcitonin may be advocated as alternative markers as mentioned by Reeves et al(26) and they concluded that when used as an adjunct to clinical assessment, CRP can be a useful tool for the evaluation of infective/inflammatory diseases(26).

Various studies done in the past comparing Procalcitonin and C-reactive protein as markers for bacterial infections, have shown that Procalcitonin was more sensitive and specific than C-reactive protein level for differentiation of bacterial (infective) from non-infective causes of inflammation(2).

Identifying Sepsis:

Sepsis, a syndrome of physiologic, pathologic and biochemical abnormalities induced by infection is a major health concern. Sepsis is a systemic host response to underlying infection that induces a series of physiologic, pathologic and biochemical abnormalities (31). In 1991, a consensus conference developed initial definitions. These definitions focused on the then-prevailing view that sepsis resulted from a host's systemic inflammatory response syndrome (SIRS) to infection (31,32).

SIRS criteria(31,32) : 2 or more of

Temperature >38 or <36 C

Heart rate > 90/min

Respiratory rate > 20/min or Paco2 < 32 mm Hg (4.3kPa)

White blood cell count > 12,000/cu mm or <4000/cu mm or > 10% immature bands.

Any patient who satisfies SIRS criteria only indicates an ongoing infection and a probable underlying suspicion of sepsis.

Due to the need for re-examining these definitions, the European Society of Intensive Care Medicine and the Society of Critical Care Medicine convened a task force in 2014 and forged agreement on updated definitions and the potential clinical criteria (33). This helped in improved understanding of sepsis pathobiology.

The Third International Consensus definitions for sepsis and septic shock (sepsis-3) (31) elicited the key concepts of sepsis which included the following:

1. The primary cause of death from infection, if not recognized and treated was sepsis and, hence, its recognition mandates urgent attention.

2. An aberrant or dysregulated host response and presence of organ dysfunction is what differentiates sepsis from infection. It is a syndrome of pathogen factors and host factors with features that evolve over time.

3. Organ dysfunction secondary to sepsis may be occult – hence it should be considered in any patient presenting with infection. On the contrary, an unrecognized infection may cause new-onset organ dysfunction- hence, any unexplained organ dysfunction should raise suspicion of underlying infection.

4. Pre-existing acute illness, long-standing comorbidities, medication, and intervention can modify the clinical and biochemical phenotype of sepsis.

5. Specific infection may result in local organ dysfunction without generating any dysregulation in systemic host response.

A better understanding of sepsis pathobiology helped in arriving at discrete definitions and removal of terms that were used interchangeably. (31) The task force considered the current use of 2 or more SIRS criteria to identify sepsis as unhelpful and deemed that SIRS criteria do not necessarily indicate a dysregulated, life-threatening response.

Similarly, for the severity of organ dysfunction, the predominantly used score is the SOFA (Sequential Organ Failure Assessment). A higher SOFA score is associated with a higher probability of mortality and the score grades abnormality by organ system accounts for clinical interventions. However, several variables are required for the full computation of the SOFA score (APPENDIX III) and it is not well known outside the critical care community (34).

After arriving at a consensus, The Third International Consensus definitions for sepsis and septic shock (sepsis-3) described the various definitions as follows. (31)

Sepsis:

It is defined as life-threatening organ dysfunction caused by dysregulated host response to infection.

Organ dysfunction:

Acute change in total SOFA score ≥ 2 points consequent to the infection.

The baseline SOFA score can be assumed to be zero in patients not known to have pre-existing organ dysfunction.

SOFA score ≥ 2 reflects an overall mortality risk of 10% in patients with suspected infection. Even patients presenting with modest dysfunction can deteriorate

further, thereby emphasizing the seriousness of this condition and the need for appropriate intervention.

Septic Shock:

It is a subset of sepsis in which the underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality (31,35). Septic shock can also be defined as severe Sepsis plus hypotension not reversed with fluid resuscitation (19).

Such patient is identified by those with sepsis with persisting hypotension requiring vasopressors to maintain MAP (Mean arterial pressure) ≥ 65mmHg and a serum lactate level ≥ 2 mmol/L (18 mg/dL) despite adequate volume resuscitation. In this setting, the hospital mortality is >40%.

Diagnostic criteria for Sepsis and Severe Sepsis as described by Surviving Sepsis Campaign 2012 (19) (APPENDIX IIA).

In other simple terms, a patient in Sepsis would have features that satisfy SIRS with a documented source of the underlying infection i.e.,

Sepsis = SIRS + documented source of infection and

Severe Sepsis = Sepsis + Organ dysfunction/tissue hypoperfusion

MATERIALS AND METHODOLOGY:

With a background knowledge based on literature review that serum Procalcitonin and C-reactive protein levels checked in the preoperative setting could be useful to predict the infectious complications in patients undergoing pancreaticoduodenectomy, this study was conducted in Christian Medical College and Hospital, Vellore.

This prospective observational study included 50 patients who underwent Pancreaticoduodenectomy for various indications, the majority of which was for pancreatic and periampullary malignancy between December 2017 and January 2019. The total number of patients who were planned for Whipple pancreaticoduodenectomy during this period was 61. Among these, 50 patients were enrolled for this study, while the others were not enrolled either due to unwillingness to be a part of this study or because pancreaticoduodenectomy was not the procedure they underwent. Data of these patients undergoing Pancreaticoduodenectomy under our specialized Hepato-pancreaticobiliary surgical department were entered in a prospective database (Epidata) and data analysis was done using SPSS.

Patients planned for Pancreaticoduodenectomy were tested for serum Procalcitonin and C-reactive protein (CRP) one day prior to the date of operation and were postoperatively monitored for sepsis, surgical site infections, pneumonia and urinary tract infection on postoperative days 3, 7, 10 and at discharge.

CRP was measured by the nephelometry method at the serology lab of our institution and an elevated value as per the assay kit was taken as >6 g/L

Procalcitonin was measured by the immunochromatographic technique using the trace technology method at the biochemistry lab of our institution and a lab value >0.5 ng/mL was taken as an elevated value.

Other factors taken into consideration included patients' comorbid conditions, preoperative serum Bilirubin levels and Intervention on the biliary tract in the form of ERCP (Endoscopic retrograde cholangiopancreaticogram) and stenting/ PTBD (Percutaneous trans-hepatic biliary drainage)/ previous surgery on the biliary tract. Also, on a routine basis, bile was aspirated prior to transection of the bile duct and was cultured.

In Christian Medical College and Hospital, Vellore, the standardized practice involves the administration of intravenous antibiotics to patients undergoing Pancreaticoduodenectomy only prior to skin incision at the time of induction of Anaesthesia and there is no role for routine antibiotic administration of antibiotics in the preoperative or postoperative period. Hence, patients who received an antibiotic in the pre or postoperative setting for any indication were also studied to assess the correlation between administration of antibiotics, preoperative elevation of Procalcitonin, CRP and postoperative infectious complications.

Postoperative parameters assessed were:

1. Sepsis, surgical site infections, pneumonia, urinary tract infections.
2. Bile culture
3. Antibiotic use
4. Duration of hospital stay

Postoperatively all patients were examined for infective complications on postoperative days 1, 3, 7 and at discharge. Postoperative day 1 was taken as the day following the date on which the surgery was performed. This calculation of postoperative day was standard under our specialized Hepato-pancreaticobiliary surgery department. All parameters were assessed on all these postoperative days and were also assessed prior to discharge as the mean duration of stay of a patient undergoing pancreaticoduodenectomy in our institution was 14-21 days.

Postoperative sepsis, surgical site infections, pneumonia, and urinary tract were assessed based on standard definitions.

Definitions:

Sepsis was defined by Surviving Sepsis campaign/Sepsis-3 guidelines(31,35). **The sepsis screening tool** described by CDC/NHSN (36) was adapted and used for this study which is as shown below.

Surgical site infection (SSI):

Defining an SSI requires evidence of clinical signs and symptoms of infection. Pure microbiological evidence isn't sufficient to define an SSI since skin is normally colonized by a range of microorganisms that could cause infection(37). The majority of the SSIs become apparent within 30 days following an operative procedure and most often occur between the 5^{th} and 10^{th} postoperative period. Also SSIs frequently only affect superficial tissues and occasionally affect the deeper tissue indicate more serious infections (37).

The standard definition described by the Centers for Disease Control and Prevention (CDC) is most commonly used to measure the outcome for SSI. Surgical Site Infection Surveillance Service (SSISS) (38), Southampton wound grading system in SSI and ASEPSIS scoring system systems are a few other methods that are used to define SSIs.

Southampton wound grading system in SSI is used to grade the severity of postoperative wound infection (39,40).

ASEPSIS scoring method is another methodology used for assessing wound healing as it defines the characteristics to be considered and how they are to be awarded points. Objective criteria are also included in the assessment and points are given (41).

Points are given for:

Additional treatment required –

Antibiotics/Incision and drainage/Debridement

Presence of **S**erous discharge

Erythema

Purulent exudate

Separation of deep tissues

Isolation of bacteria

Duration of in-patient **S**tay

A score is given for each only on 3 of the first 7 postoperative days.

These point total represents a category of infection:

0-10: Satisfactory healing

11-20: Disturbance of healing

21-30: Minor wound infection

31-40: Moderate infection

>40: Severe wound infection

Despite few other well-accepted standardized definition/scoring systems for SSIs, CDC definitions are widely used and SSIs in this study were identified using CDC/NHSN Surveillance Definitions for Specific Types of Infections(42).

Wound classification as described by CDC/NHSN (National Healthcare Safety Network) is adapted from the American College of Surgeons wound classification schema (42).

Wounds are classified into four classes: (42)

1. Clean:
    a. An uninfected operative wound in which no inflammation is encountered.
    b. Alimentary, genital, respiratory or uninfected urinary tracts are not entered.
    c. Primary closed and, if necessary, drained with closed drainage.
    d. Operative incisional wounds following blunt (nonpenetrating) trauma should be included in this category.

2. Clean-contaminated:
    a. Wounds in which respiratory, alimentary, genital or urinary tracts are entered under controlled conditions and without unusual contamination.
    b. Operations involving the biliary tract, vagina, appendix, oropharynx should be included in this category if there is no evidence of infection or there is a major break in technique.
3. Contaminated:
    a. Open, fresh, accidental wounds.
    b. Operations with major break in sterile technique (open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, non-purulent inflammation is encountered (e.g., dry gangrene) are included in this category.
4. Dirty or infected:
    a. Old traumatic wounds with retained devitalized tissue and those involving perforated viscera or existing clinical infection.
    b. This definition suggests that the operative field was already contaminated by the organisms that cause postoperative infection.

Surgical site infection (SSI) criteria described by CDC (APPENDIX-IIC) was adapted and used for this study(42)**.** As defined by CDC, surgical site infections were classified as

1. Superficial SSI
2. Deep incisional SSI and
3. Organ/space SSI

Pneumonia defined by CDC, Centers for Disease Control and Prevention criteria for nosocomial pneumonia is as shown in figure 3.

Centers for Disease Control and Prevention criteria for nosocomial pneumonia

Pneumonia must meet one of the criteria (only in patients >12 months of age)

1. **Rales or dullness to percussion on physical examination of chest and *any* of the following:**
   - new onset of purulent sputum or change in character of sputum;
   - organism isolated from blood culture;
   - isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing or biopsy.
2. **Chest radiographic examination shows new or progressive infiltrate, consolidation, cavitation or pleural effusion and *any* of the following:**
   - new onset of purulent sputum or change in character of sputum;
   - organism isolated from blood culture;
   - isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing or biopsy;
   - isolation of virus or detection of viral antigen in respiratory secretions;
   - diagnostic single antibody titre (IgM) or four-fold increase in paired serum samples (IgG) for pathogen.

Figure 3: CDC criteria for nosocomial pneumonia

Urinary tract infection as defined by CDC is the presence of clinical evidence with a documented positive urine culture. Sepsis screening tool was adapted and used on postoperative days 3, 7, 10 and at discharge to identify postoperative sepsis. CDC definitions for Pneumonia, SSI, and Urinary tract infection were adapted for this study (Definitions in Appendix-II).

Sample size calculation:

The sample size for the study was calculated based on Two proportion hypothesis testing that was done using software – nMaster 2.0 version.

Reference study: The role of preoperative C-reactive protein and procalcitonin as predictors of post-pancreaticoduodenectomy infective complications: A prospective observational studyVerushka Mansukhani, Gunjan Desai, Rajiv Shah, Palepu Jagannath July 2017(43).

Two Proportion - Hypothesis Testing - Large Proportion - Equal Allocation		
Expected Proportion of subjects with complications in elevated CRP group	0.56	0.56
Expected Proportion of subjects complications in not elevated CRP group	0.07	0.07
Estimated risk difference	0.49	0.49
Power (1- beta) %	80	90
Alpha error (%)	5	5
1 or 2 sided	2	2
Required sample size in elevated group	13	17
Required sample size in not elevated group	13	17

Table 2: Two proportion-hypothesis testing for C-reactive protein

Based on Mansukhani et al (43), 30% of the samples had elevated CRP values, hence the approximate number of subjects to be collected to sample 13 elevated values are 43 subjects.

Table 3: Two Proportion - Hypothesis Testing - Procalcitonin

Two Proportion - Hypothesis Testing - Large Proportion - Equal Allocation		
Expected Proportion of subjects complications in elevated PCT group	0.4	.4
Expected Proportion of subjects complications in not elevated PCT group	0.05	.05
Estimated risk difference	0.35	.35
Power (1- beta) %	80	90
Alpha error (%)	5	5
1 or 2 sided	2	2
Required sample size in elevated group	21	28
Required sample size in not elevated group	21	28

Based on Mansukhani et al (43), 50% of the samples had elevated PCT values, hence the approximate number of subjects to be collected to sample 21 elevated values were 42 subjects.

Forty-three being the higher value among the two groups, the minimum sample size required for the study was 43 and the sample size was taken as 50 for the purpose of convenience.

Data collected were entered using software Epidata version 3.1. Analysis was done using software SPSS version23.

Univariate analysis was done using measures of central dispersion for continuous variables and proportions for categorical variables. Bivariate analysis was done using chi-square and Fisher's Exact Test.

RESULTS:

A total number of 50 patients were enrolled for the study. The median age of the patients in the study was found to be 55.6 [9.7] with a mean age of 54.06. The oldest patient was 72 years and the youngest was 32 years of age.

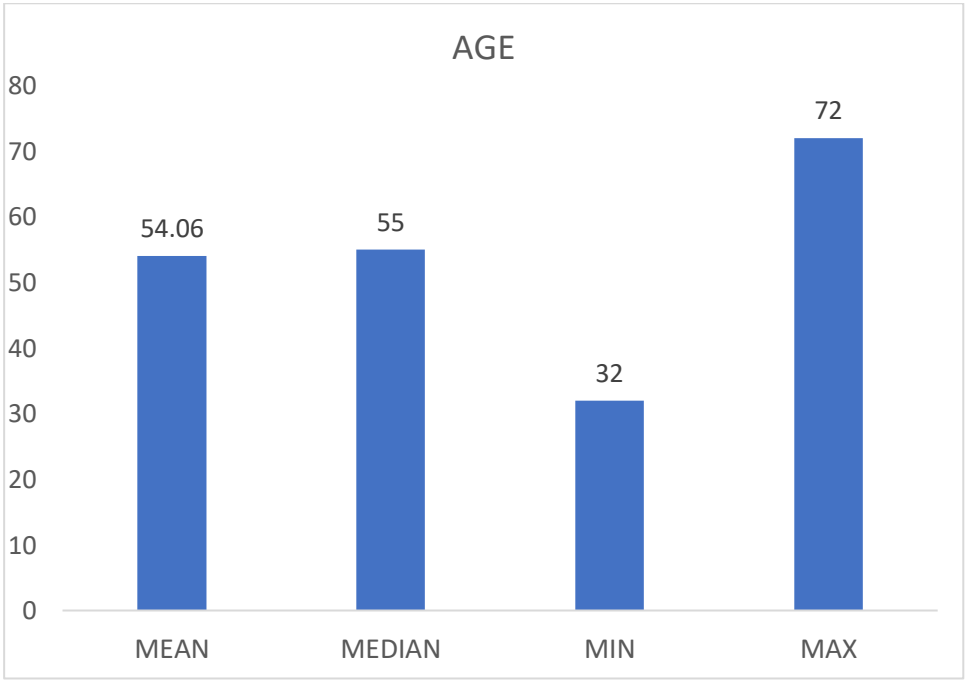

Figure 4: Age distribution

Male patients constituted 70% of the study population.

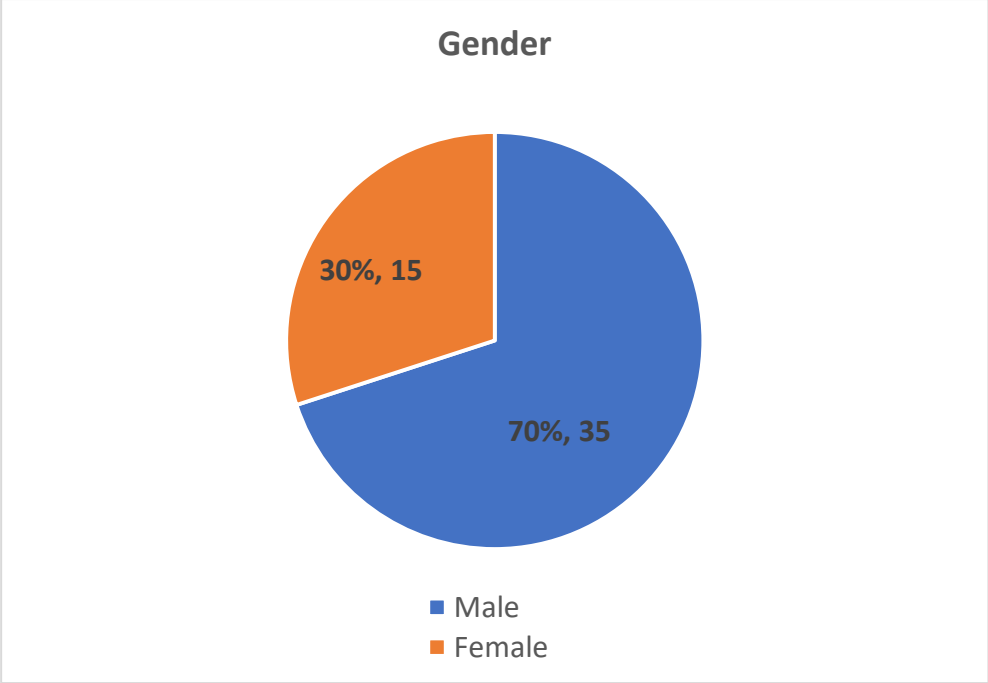

Figure 5: Gender distribution

Of the 50 patients, 25 of them had no known medical comorbidities while Bronchial asthma among 26 patients was the most common comorbidity. Diabetes and Hypertension were present among 16 and 15 patients respectively, 3 patients had Ischemic heart disease and 10 patients had other comorbidities such as tuberculosis, dyslipidemia, chronic kidney disease.

The preoperative parameters looked at were elevated Procalcitonin, C-reactive protein, serum bilirubin levels, and preoperative biliary interventions.

About 96% of the patients did not have elevated preoperative Procalcitonin levels while only 4% had elevated preoperative Procalcitonin levels.

Preoperative C-reactive protein (CRP) levels were found to be elevated among 40% (20) of the patients and significantly elevated preoperative Procalcitonin levels was observed in only 4 %.

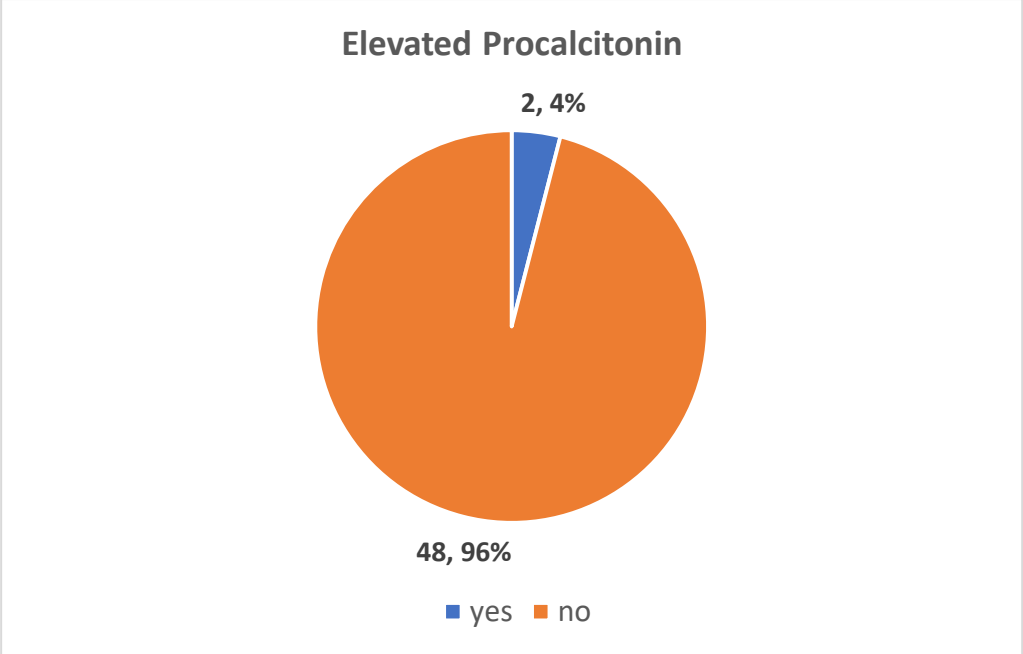

Figure 6: Preoperative elevated Procalcitonin distribution

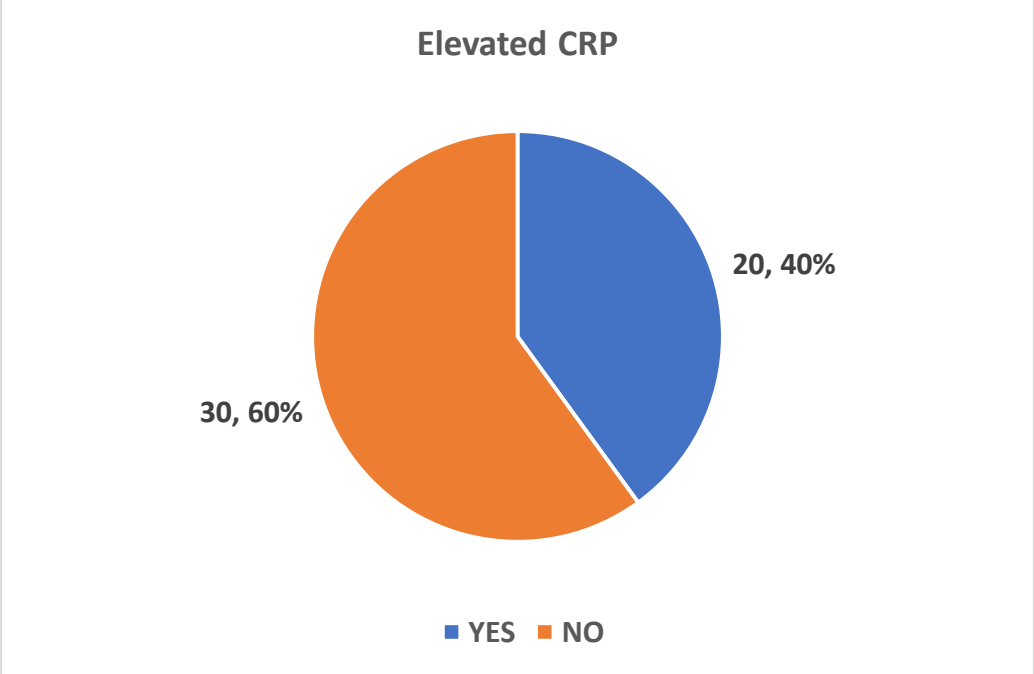

Figure 7: Preoperative elevated CRP distribution

Forty-six percent (23) of the patients had elevated preoperative serum bilirubin levels while 54% (27) of them did had normal preoperative serum bilirubin levels.

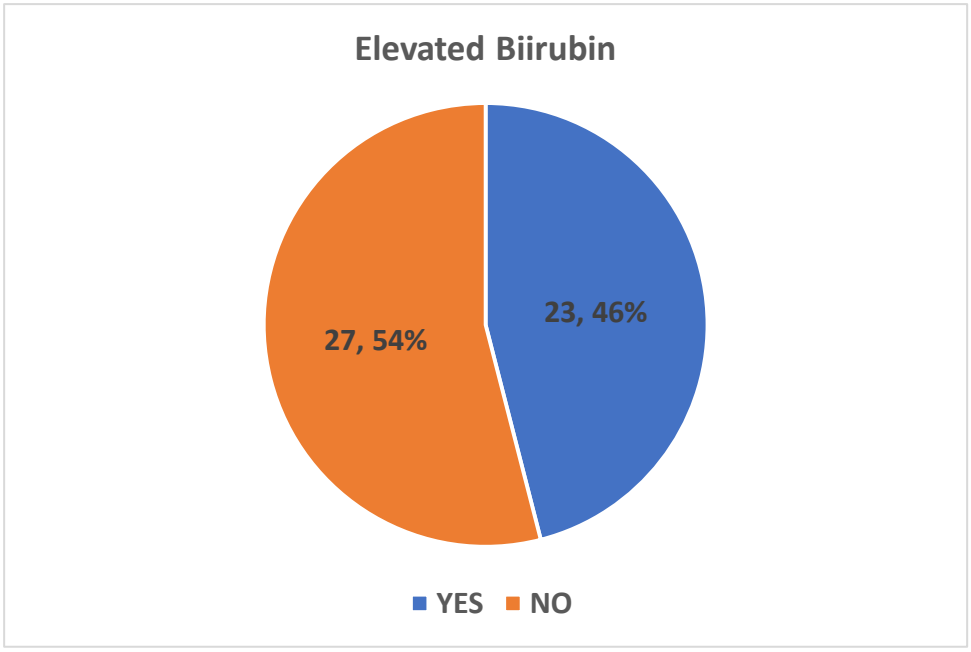

Figure 8: Distribution of serum Bilirubin levels

Of the total 50 patients, 52% (26) had preoperative biliary intervention in the form of ERCP (Endoscopic retrograde cholangiopancreaticogram), PTBD (Percutaneous transhepatic biliary drainage) or previous surgery on the biliary tract. Twenty-four patients making up for 48% of the total had no previous biliary intervention.

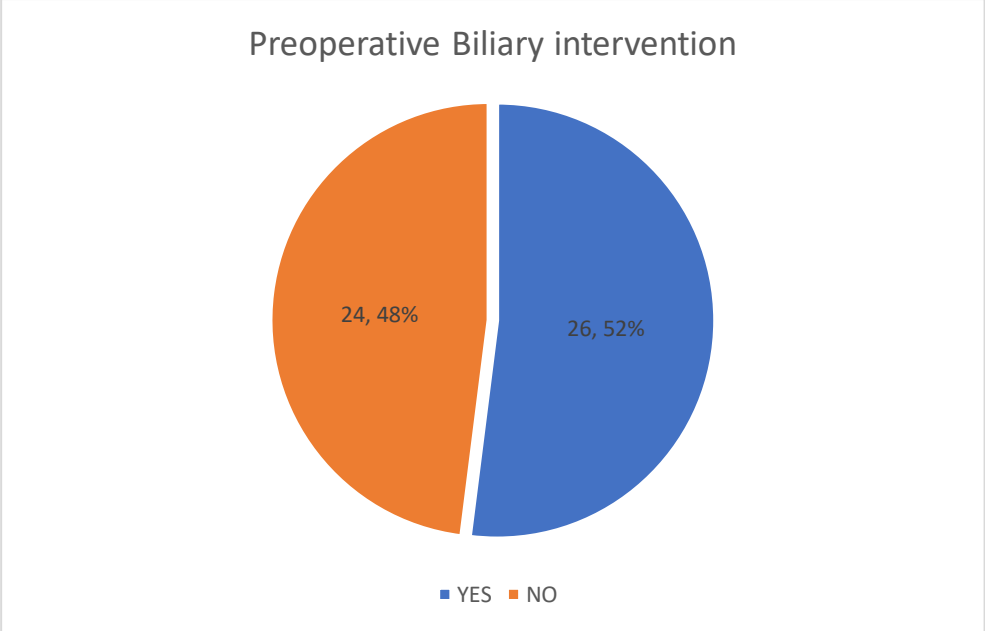

Figure 9: Preoperative biliary intervention

Among the 52% (26) who had previous biliary intervention, 23 patients had undergone ERCP, two of them - PTBD and eight of them had previous surgery in the biliary tract. Some of these 26 patients had more than one intervention on the biliary tract.

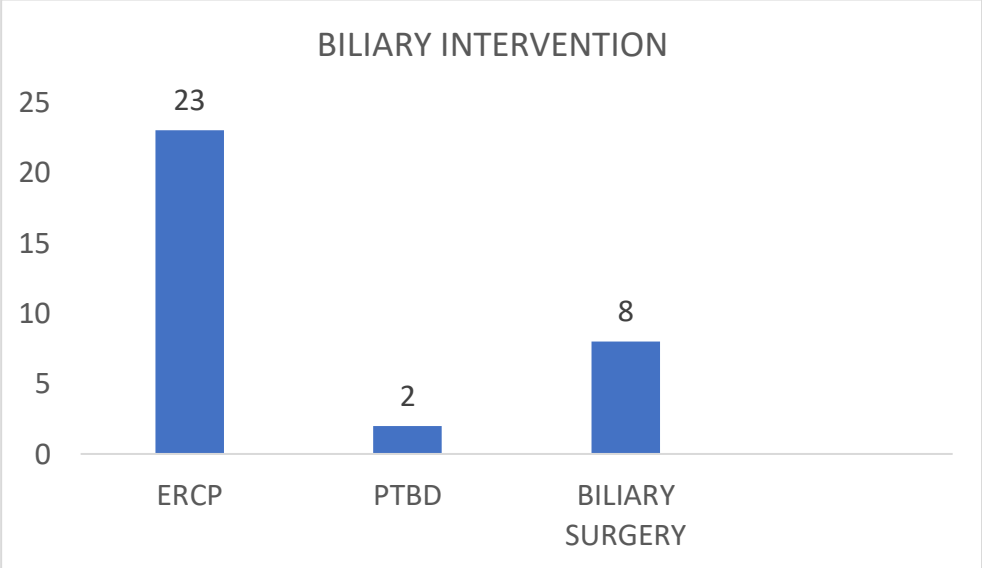

Figure 10: Distribution of type of biliary intervention

The following table summarizes the demographic details and preoperative parameters.

Table 4: Demographic details and preoperative parameters

Patient characteristics	**Total 50**
Median age in years	55
Sex (male/female)	35/15
Comorbid illness	
Diabetes mellitus	16
Hypertension	15
Bronchial asthma	26
No comorbidities	25
Preoperative parameters	
Elevated procalcitonin	2
Elevated C-reactive protein	20
Elevated serum bilirubin	23
Preoperative ERCP	23
Preoperative PTBD	2
Previous biliary surgery	8

The postoperative parameters assessed were sepsis, surgical site infection (SSI), urinary tract infection and pneumonia. Each of these parameters was assessed separately on postoperative days 3, 7, 10 and at discharge. Any of these being present may not indicate the presence of sepsis, SSI, urinary tract infection or pneumonia on

those specific days the patients were assessed. Infective parameters being present at discharge and not on day 10 would simply mean they occurred in the time frame between post-op day 10 and discharge.

Postoperative day 3:

Looking at the infective parameters on post-operative day 3, sepsis was present among 14% (7) of the patients and were absent among 86% (43). Surgical site infection was present among 7(14%) patients, of which superficial surgical site infection was present in 7 patients, deep incisional SSI and organ/space SSI was present in 1 patient each. Urinary tract infection and pneumonia on postoperative day-3 were not seen among any of the study patients. Also, none of the patients had undergone re-surgery on or before the third postoperative day.

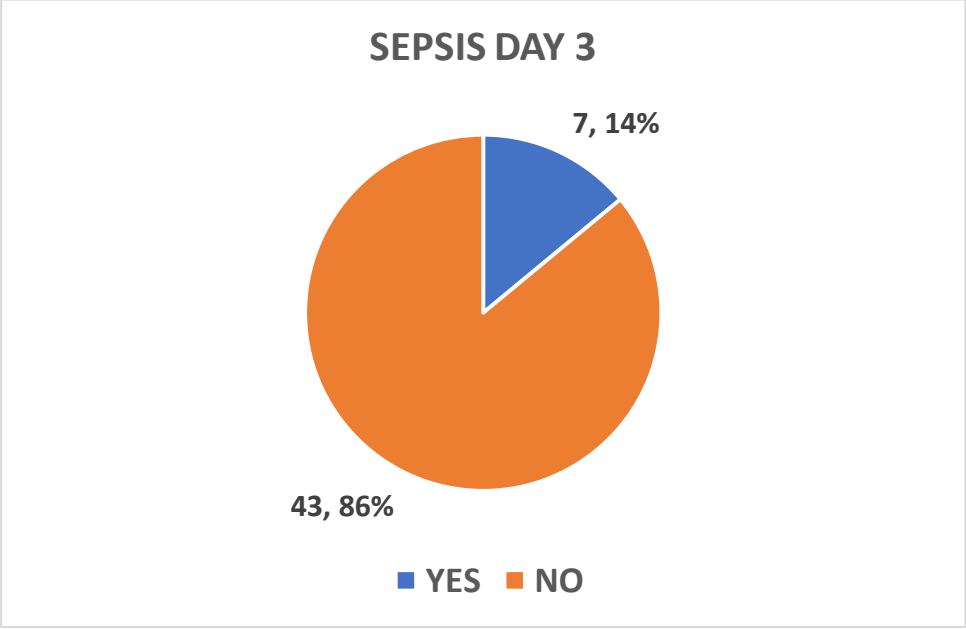

Figure 11: Sepsis assessment on POD3

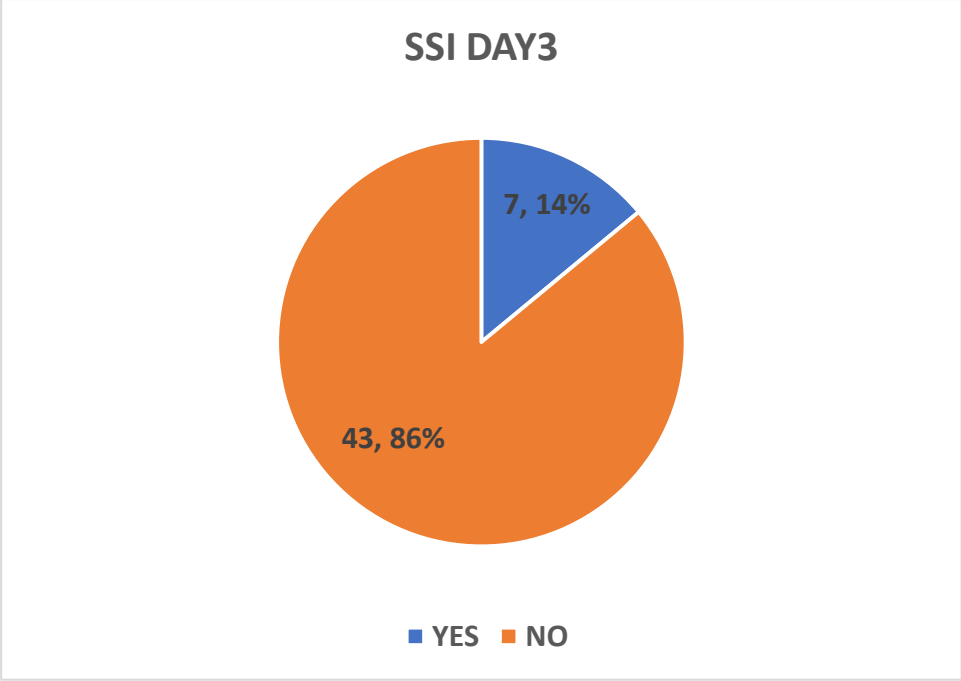

Figure 12: SSI assessment on POD3

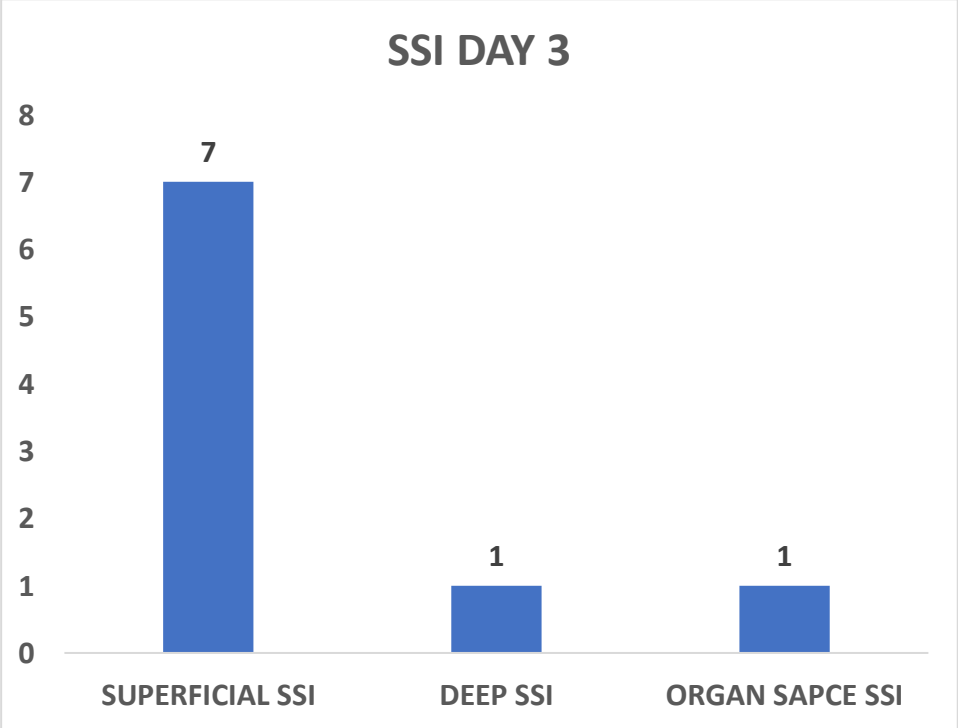

Figure 13: SSI distribution on POD3

Postoperative day 7:

On the 7th postoperative day, sepsis was present among 16% (8) of the patients and were absent among 84% (42). Surgical site infection was present among 15(30%) patients, of which all of them had only superficial surgical site infection. No patients assessed on the 7th postoperative day had deep incisional SSI or organ/space SSI. Urinary tract infection on postoperative day 7 was not seen among any of the study patients. Three (6%) patients had pneumonia as assessed on the 7th post-operative day which tells us that these 3 patients developed pneumonia after the 3rd postoperative day. Also, none of the patients had undergone re-surgery on or before the seventh postoperative day.

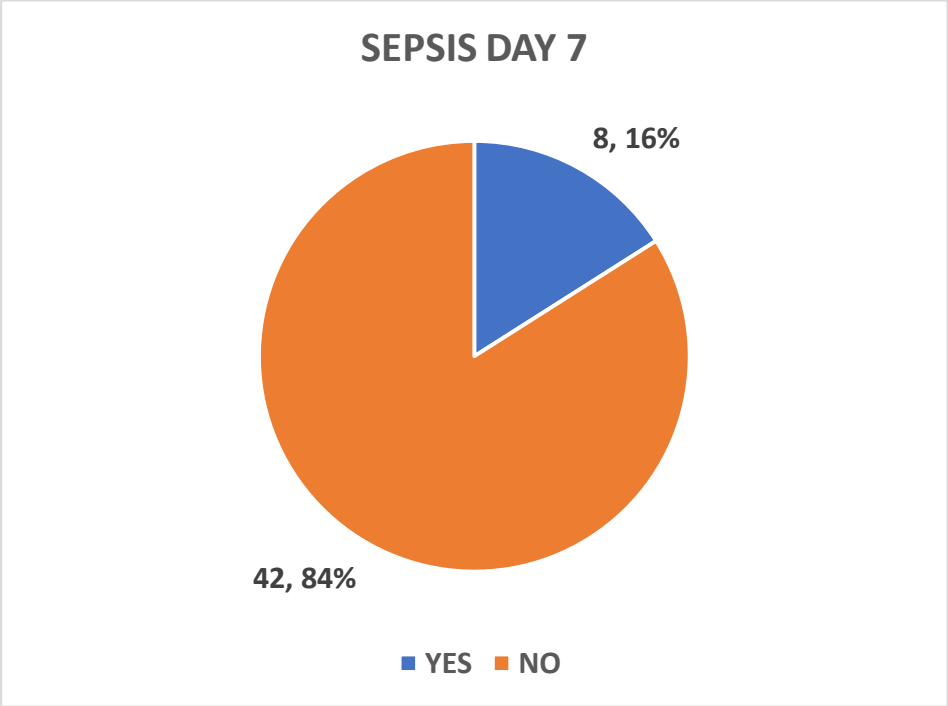

Figure 14: Sepsis assessment on POD7

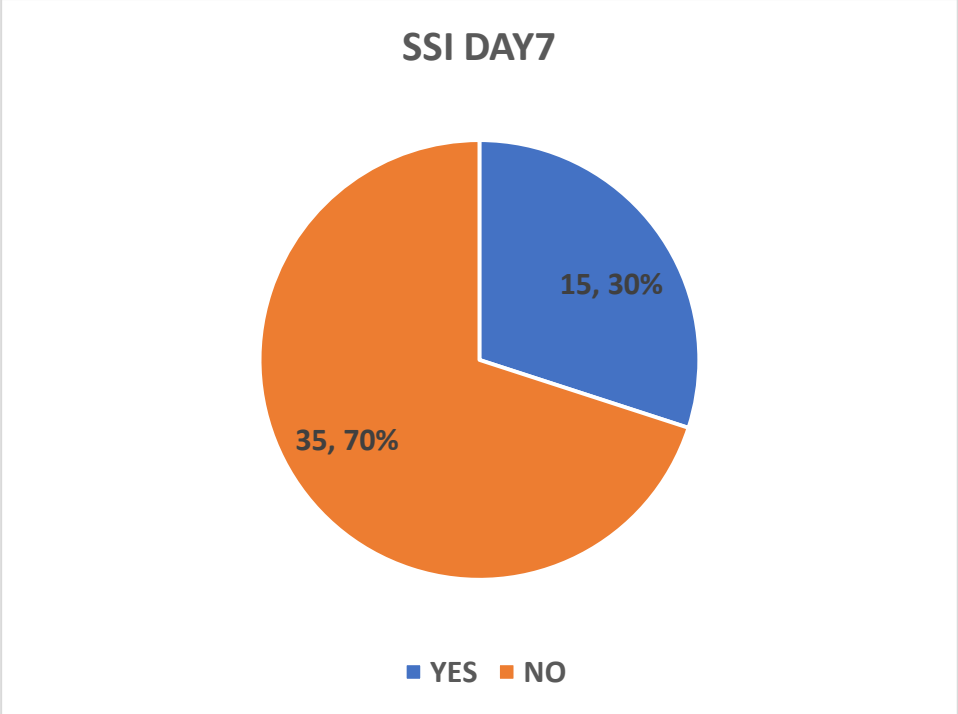

Figure 15: SSI assessment on POD7

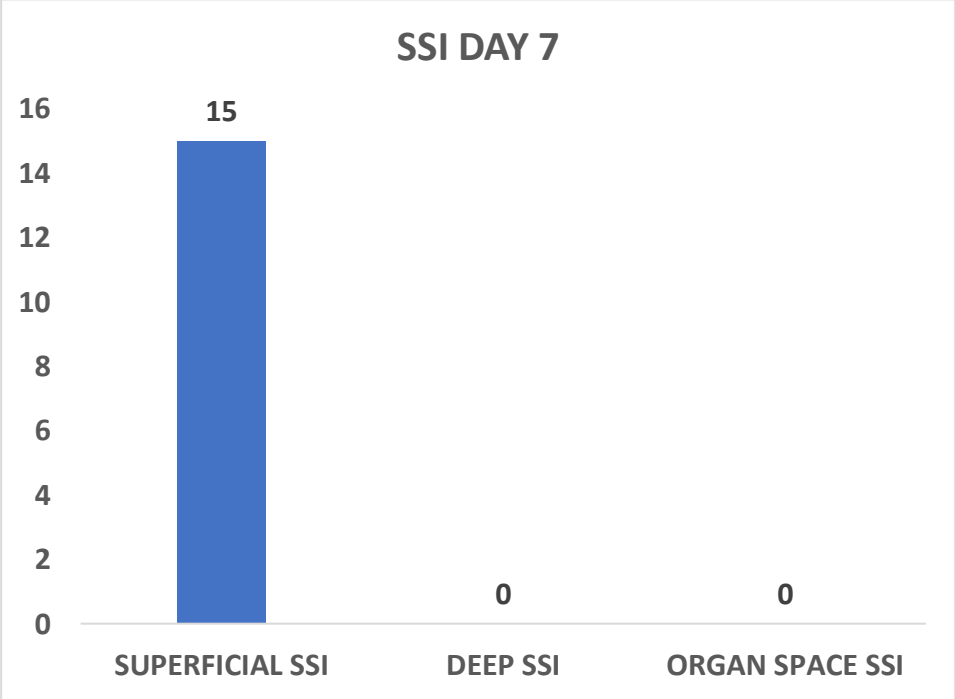

Figure 16: SSI distribution on POD7

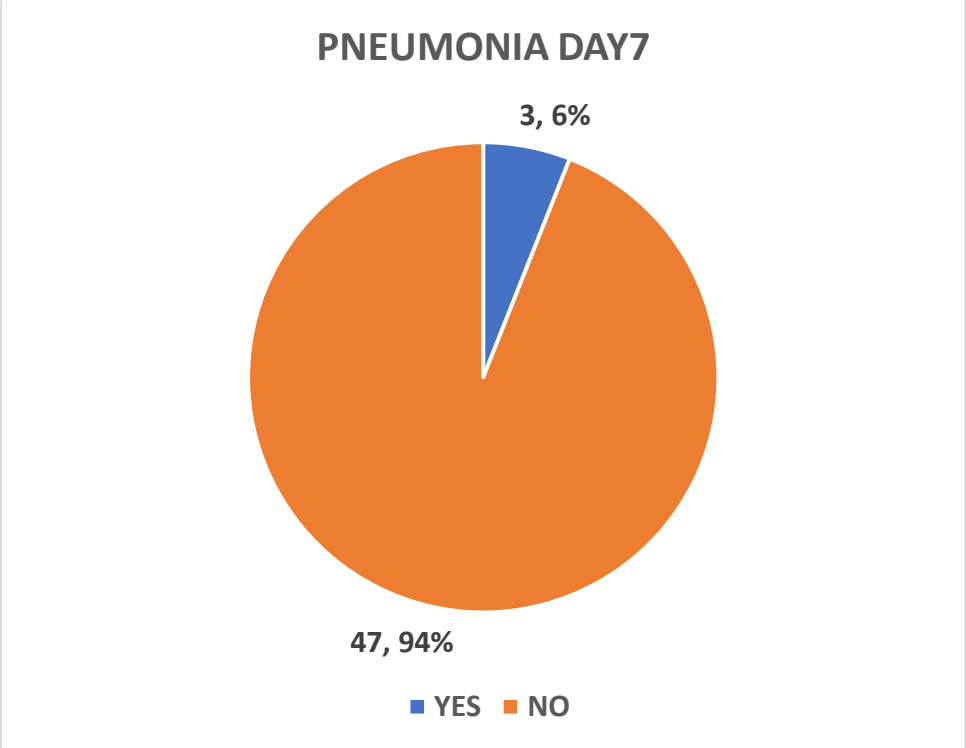

Figure 17: Pneumonia assessment on POD7

Postoperative day 10:

On the 10th postoperative day, sepsis was present among 12% (6) of the patients and were absent among 88% (44). Surgical site infection was present among 18(36%) patients and was absent among 32(64%) patients. The number of patients who had superficial surgical site infection was 14, 6 patients had organ/space SSI, none of them had deep incisional SSI. Urinary tract infection on postoperative day 10 was not seen among any of the study patients. Two (4%) patients had pneumonia as assessed on the 10th post-operative day.

On the 10th postoperative day, 2(4%) patients had undergone re-surgery for organ/space SSI with hemodynamic instability secondary to an anastomotic dehiscence.

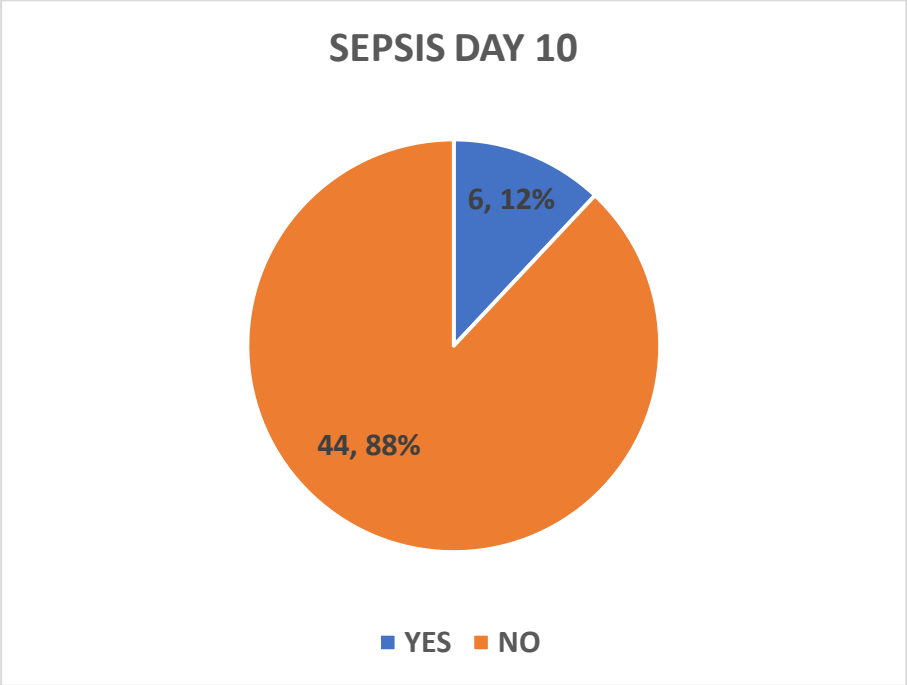

Figure 18: Sepsis assessment on POD10

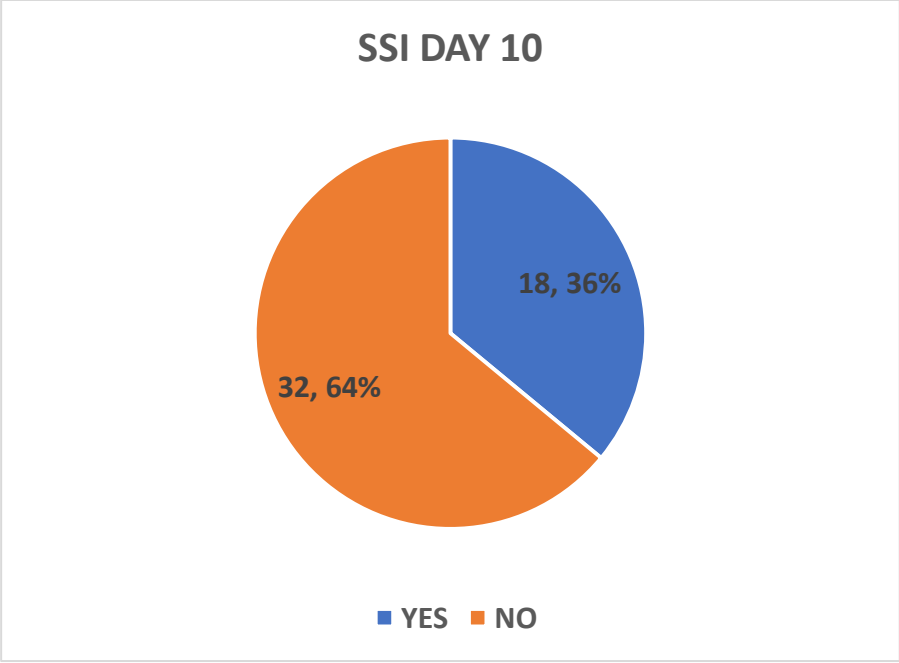

Figure 19: SSI assessment on POD10

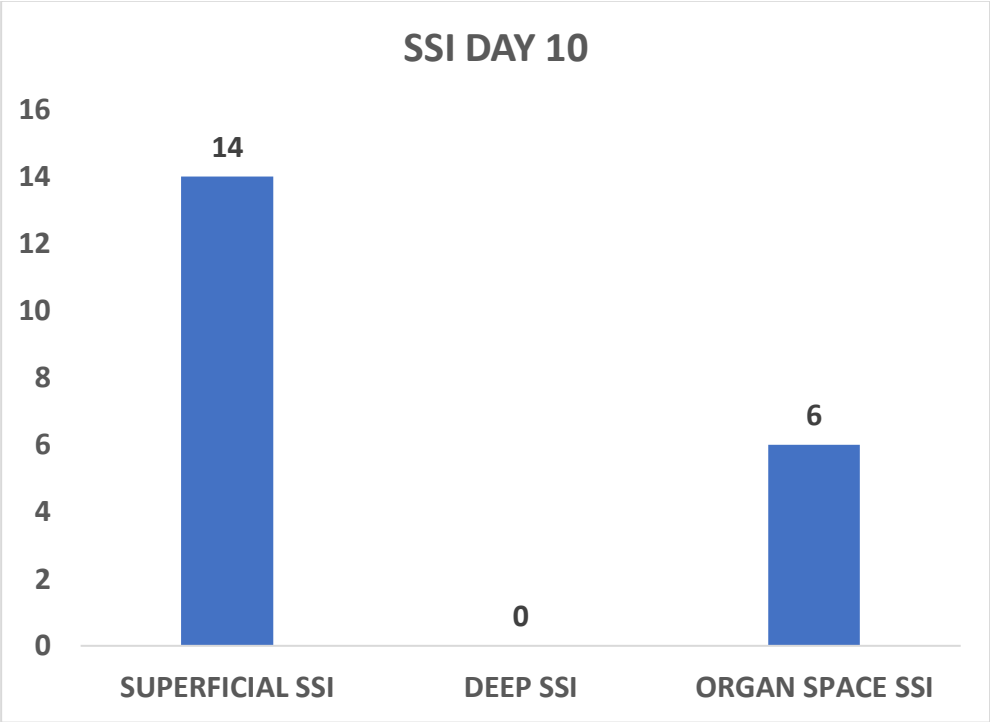

Figure 20: SSI distribution on POD10

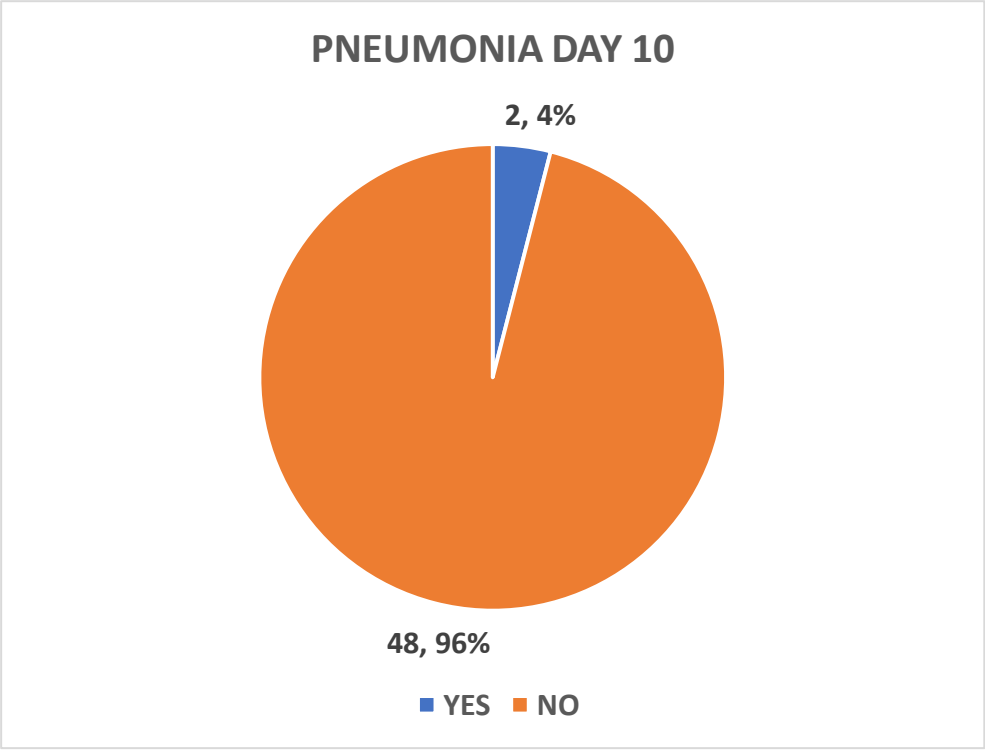

Figure 21: Pneumonia assessment on POD10

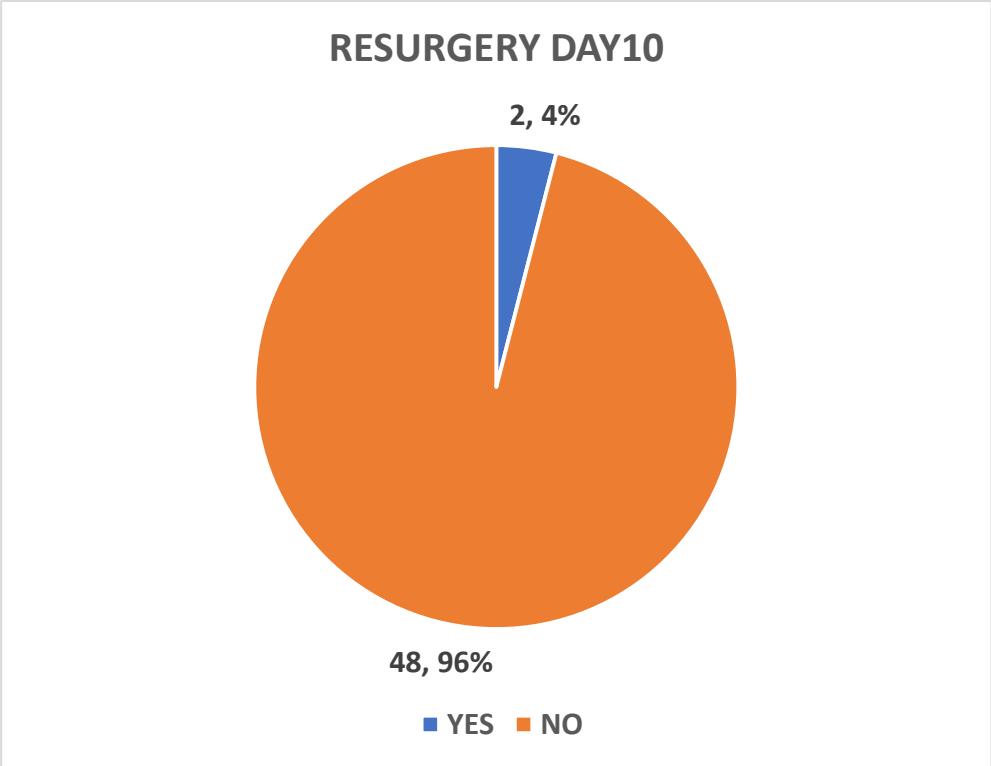

Figure 22: Resurgery on POD10

At discharge:

Surgical site infection was present among 13(26%) patients and was absent among 37(74%) patients. The number of patients who had superficial surgical site infection was 9, 7 patients had organ/space SSI and none of them had deep incisional SSI. Urinary tract infection at discharge was seen in 1(2%) patient. Two (4%) patients had pneumonia as assessed at discharge.

At discharge, 1(2%) patient had undergone re-surgery for organ/space SSI with hemodynamic instability secondary to an anastomotic dehiscence.

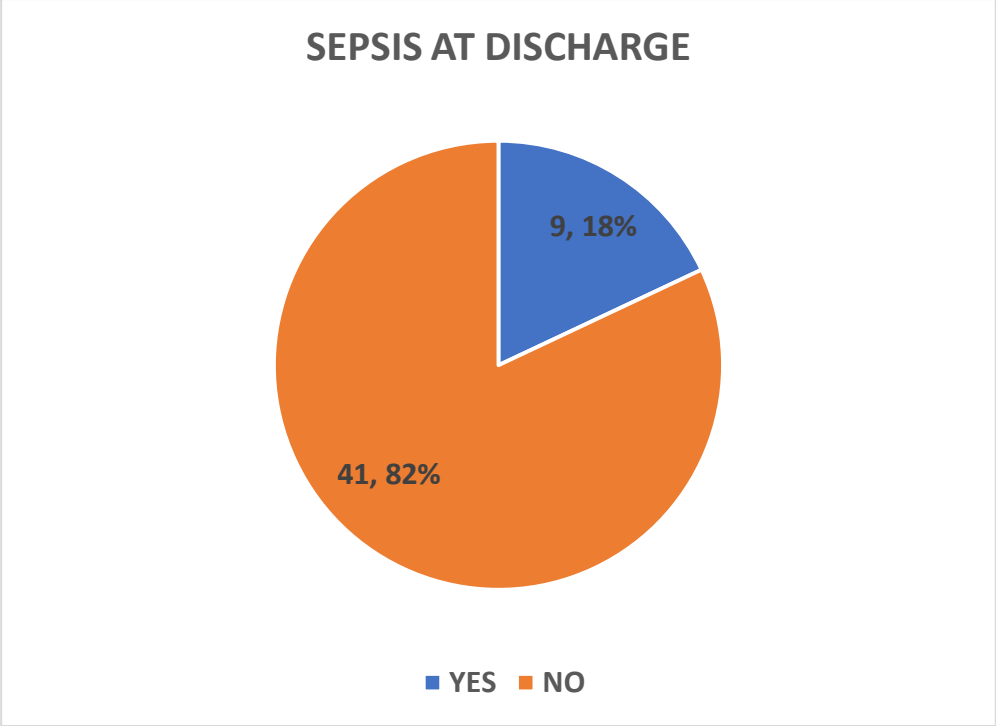

Figure 23: Sepsis assessment at discharge

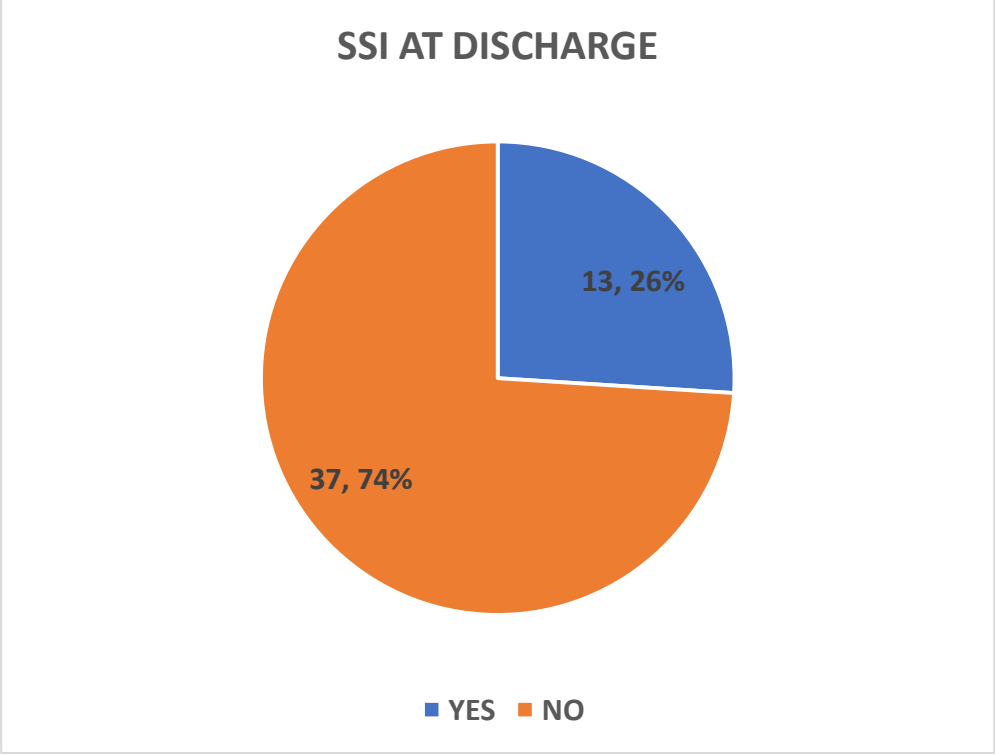

Figure 24: SSI assessment at discharge

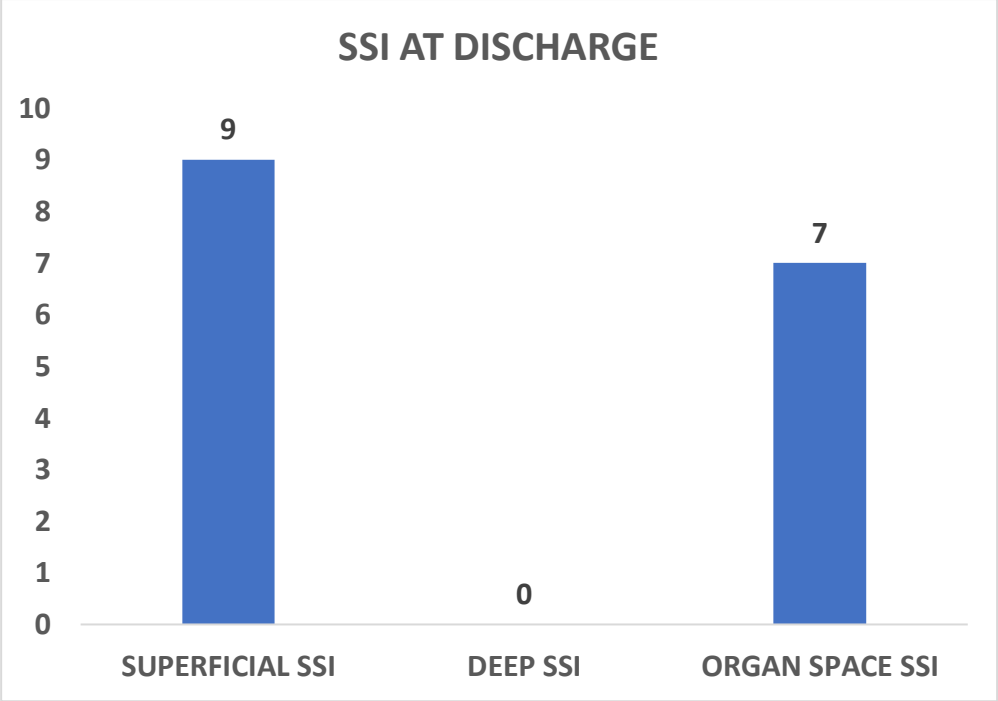

Figure 25: SSI distribution at discharge

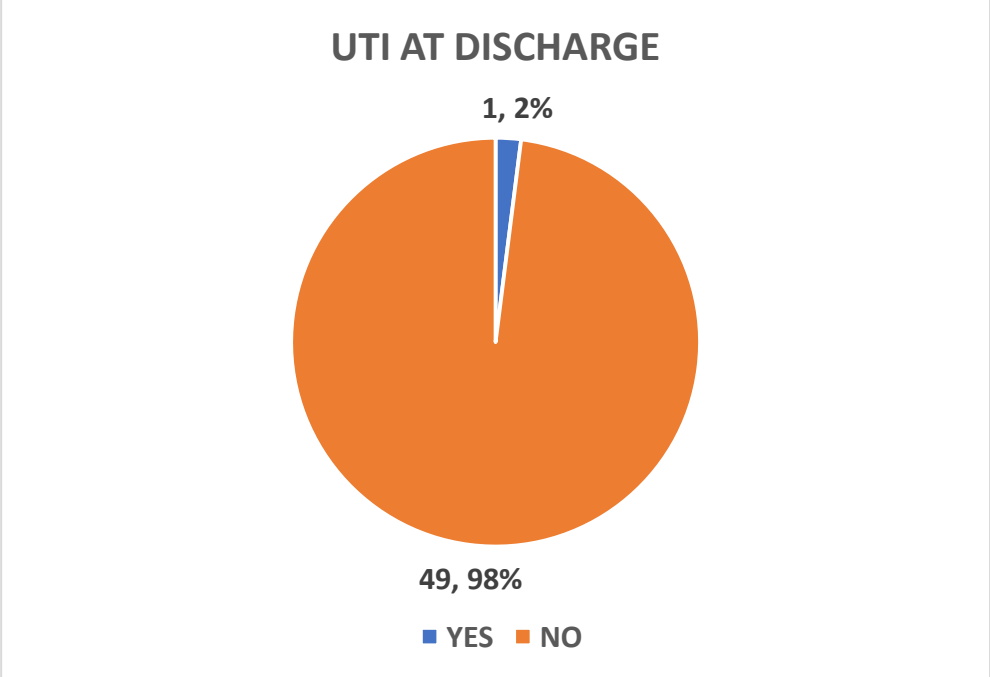

Figure 26: UTI at discharge

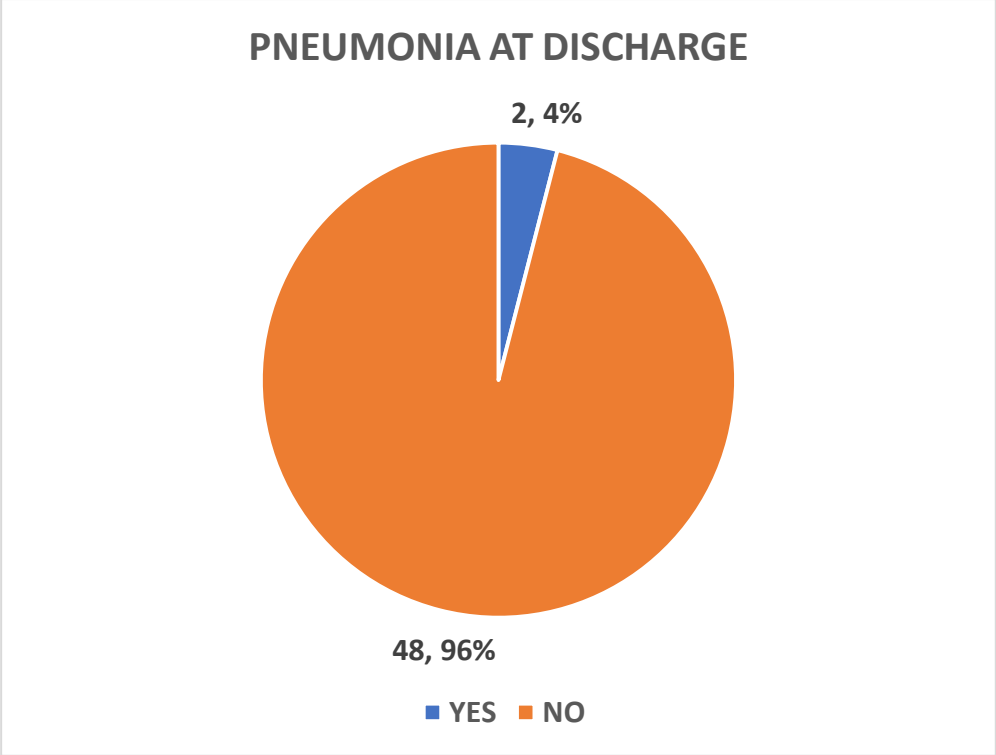

Figure 27: Pneumonia at discharge

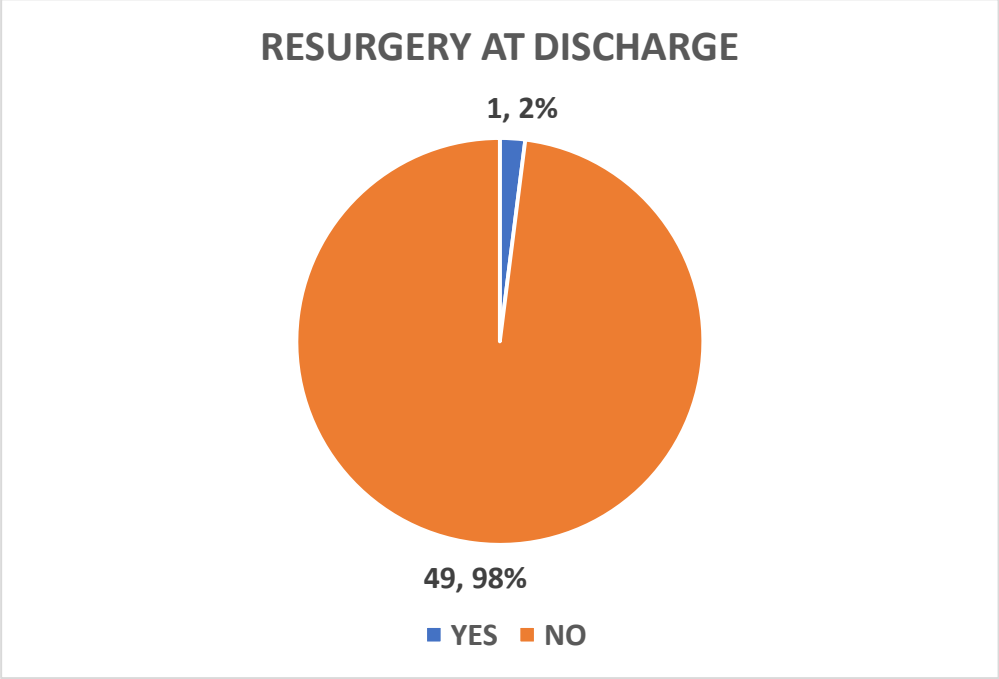

Figure 28: Resurgery at discharge

The standardized practice in Christian Medical College and Hospital, Vellore involves the administration of intravenous antibiotics to patients undergoing pancreaticoduodenectomy only prior to skin incision at the time of induction of Anaesthesia and there is no role for routine administration of antibiotics in the pre-operative or post-operative period.

Hence the patients who received intravenous antibiotics in the postoperative period for various indications were assessed. Among the 50 study patients, 33 (66%) patients had received postoperative antibiotics while only 17 (34%) did not receive post-op intravenous antibiotics.

Indications for administering antibiotics and the statistics are as described in the table below.

Table 5: Indication for postoperative antibiotic administration

Indication for antibiotic	**Total n=33(%)**
High-grade fever with features of sepsis	12 (36.36)
High grade fever with SSI	2 (6.06)
High-grade fever with features of sepsis/pneumonia	2 (6.06)
Intraoperative hypotension	7 (21.21)
Intraoperative fever	1 (3.03)
Recent cholangitis	5 (15.15)
Persistent low grade fever	1 (3.03)
Sepsis with SSI	3 (9.09)

The most common indication for administration of postoperative intravenous antibiotic was high-grade fever with features of sepsis.

Mortality rate was 4% (2).

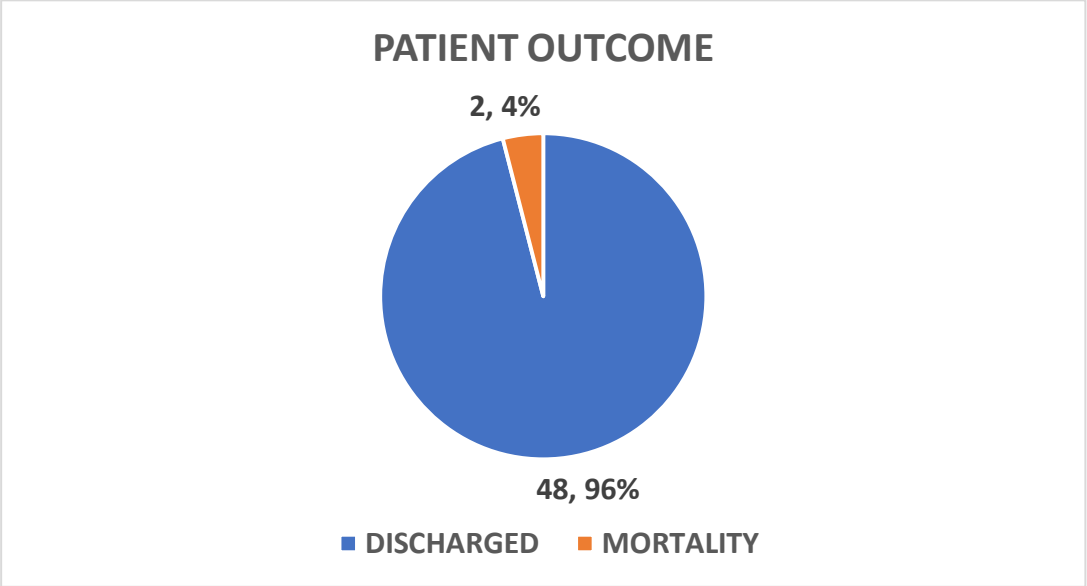

Figure 29: Patient outcome

Looking into the duration of hospital stay, the maximum duration was 67 days while the minimum duration was 11 days. The mean duration of hospital stay was 22.8 while the median for the same was 20.

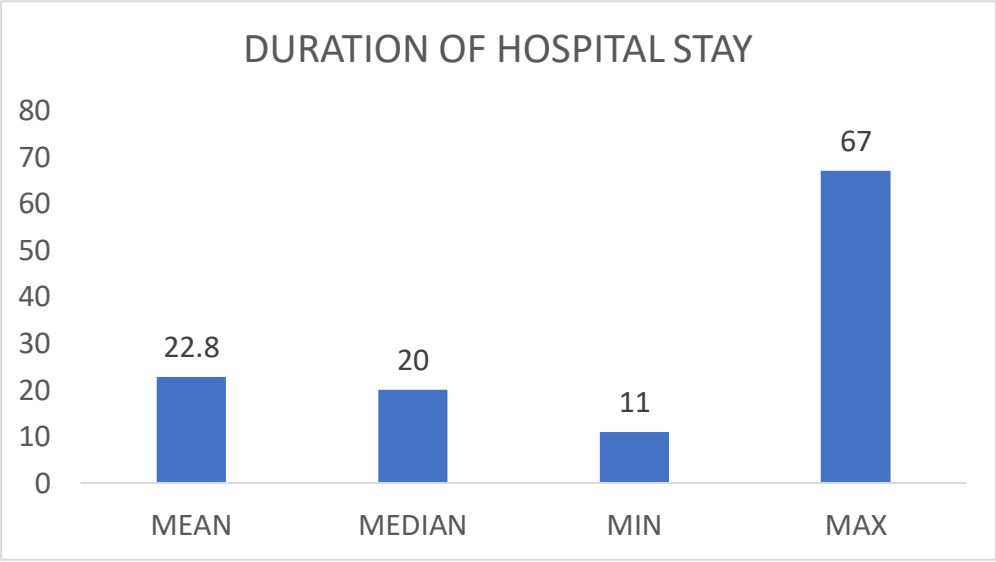

Figure 30: Duration of hospital stay

Table 6: summary of postoperative parameters

Postoperative patient characteristics	**Total: 50**
Sepsis	22 (44%)
Postoperative day 3	7
Postoperative day 7	8
Postoperative day 10	6
At discharge	9
SSI	31 (62%)
Postoperative day 3	7
Superficial/deep/organ space SSI	7, 1, 1
Postoperative day 7	15
Superficial/deep/organ space SSI	15, 0, 0
Postoperative day 10	18
Superficial/deep/organ space SSI	14, 0, 6
At discharge	13
Superficial/deep/organ space SSI	9, 0, 7
Pneumonia	3 (6%)
Postoperative day 3	0
Postoperative day 7	3
Postoperative day 10	2
At discharge	2
UTI	1
Re-surgery	3
Mortality	2
Median duration of hospital stay	20 days

Comparison of preoperative parameters with postoperative infectious complications:

1. **Sepsis on post-op day 3:**

Table 7: Comparison between preoperative parameters and sepsis on POD3

Variables		Sepsis day3		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	7(8.97)	41(85.4)		
Elevated CRP	Yes	5(25)	15(75)	0.100	4.667 (0.80-27.0)
	No	2(6.66)	28(93.33)		
Elevated bilirubin	Yes	4(17.39)	19(82.60)	0.689	1.6842 (0.33-8.45)
	No	3(11.11%)	24(88.88)		
Biliary intervention	Yes	1(3.84)	25(96.15)	0.045	0.12 (0.01-1.08)
	No	6(25)	18(75)		

On the third postoperative day, it was found that only 2(4%) patients had elevated serum Procalcitonin levels, however none of them with elevated levels had sepsis. On the contrary, 7(8.97%) of those who did not have elevated Procalcitonin levels had sepsis on post-op day 3. But since the P-value for the tests of significance was 1, the correlation between elevated Procalcitonin and sepsis on post-op day 3 was considered insignificant.

Twenty (40%) patients had elevated serum CRP levels, but only 5(25%) of those with an elevated CRP level had features with sepsis on post-op day 3. Among patients with normal CRP levels, 2(6.66%) patients had features of sepsis. However, with a P-value of 0.100, this association was statistically insignificant.

Among the 23(46%) patients who had elevated preoperative serum bilirubin levels, 4(17.39%) of them had features with features of sepsis and among the 27(54%) patients who had normal bilirubin levels, 3(11.11%) had features of sepsis.

Twenty-six (52%) of the patients had biliary intervention in the form of ERCP, PTBD or previous biliary intervention. Among those who had previous biliary intervention, 25 (96.15%) of the patients did not have any features of sepsis on post-op day 3. Among the patients who did not have any previous biliary intervention 18(36%), 6(25%) of them had features of sepsis. P-value calculated using Fisher's exact test was 0.045 and hence this correlation was considered to be significant. Hence it can be said that patients who had biliary intervention prior to the pancreaticoduodenectomy are at a lesser risk of developing Sepsis in the immediate postoperative setting within the first 3 days.

2. **Sepsis on post-op day 7:**

Table 8: Comparison between preoperative parameters and sepsis on POD7

Variables		Suspected sepsis day 7		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	8(16.66)	40(83.33)		
Elevated CRP	Yes	1(5)	19(95)	0.123	0.1729 (0.0195-1.5323)
	No	7(23.33)	23(76.66)		
Elevated bilirubin	Yes	4(17.39)	19(82.6)	1.00	1.2105 (0.2665-5.4977)
	No	4(14.82)	23(85.18)		
Biliary intervention	Yes	6(23.07)	20(76.91)	0.250	3.3 (0.5962-18.2651)
	No	2(8.33)	22(91.66)		

Among the patients who had elevated serum Procalcitonin on day7, none of them had features of sepsis.

Twenty patients (40%) had elevated serum CRP levels among which only 1(5%) had features of sepsis while 19(95%) did not have any features of sepsis. Among those who had normal serum Procalcitonin levels, 7(23.33%) had features of sepsis. The P-value for this comparison being 0.123, the association was statistically insignificant.

Among the 23(46%) patients who had preoperative elevated serum bilirubin levels, 4(17.39) had features of sepsis, while among those who had normal bilirubin levels 4(17.39%) had features of sepsis. Sepsis among the group with elevated serum bilirubin levels was higher but the P-value based on Fisher's exact test being 1.000 was considered statistically insignificant.

Twenty-six (52%) of the patients had undergone previous biliary intervention, among whom 6(23.07%) had features of sepsis on post-op day 7 while among those who had no previous biliary intervention 2 (8.33%) patients had features of sepsis. The P-value for this comparison was 0.250 and hence there was no statistical significance.

3. Sepsis on post-op day 10:

Table 9: Comparison between preoperative parameters and sepsis on POD10

Variables		**Suspected sepsis day 10**		**P-value**	**Odds ratio 95%(CI)**
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	6(12.5)	42(87.5)		
Elevated CRP	Yes	1(5)	19(95)	0.381	0.2632 (0.0283-2.4434)
	No	5(16.66)	25(83.33)		
Elevated bilirubin	Yes	3(13.04)	20(86.95)	1.00	1.2 (0.2177-6.6136)
	No	3(11.11)	24(88.88)		
Biliary intervention	Yes	3(11.53)	23(88.46)	1.000	0.913 (0.1658-5.0289)
	No	3(12.5)	21(87.5)		

On postoperative day 10, among the patients who had preoperative elevated serum Procalcitonin levels, none of them had features of sepsis while among those who had normal Procalcitonin levels, 6(12.5) patients had features of sepsis. Since the P-value was 1.000, there was no statistically significant association between preoperative elevated procalcitonin levels and post-op sepsis on post-op day 10.

Among the patients with preoperative elevated CRP levels, 1(5%) had features of sepsis and among those with normal CRP levels, 5(16.66%) had features of sepsis. P-value being 0.381, there was no statistically significant association.

Features of sepsis among patients with preoperative elevated serum bilirubin levels were present in 3(13.04%) patients and among those who had normal preoperative bilirubin levels, suspicion for sepsis was found among 3(11.11%). The percentage of sepsis among those with elevated bilirubin levels was found to be high, however since the P-value was 1.000, there is no statistically significant association.

11.53% (3) of the patients who had previous biliary intervention had features of sepsis on post-operative day 10, while 12,5% (3) of the patients who had no biliary intervention had features of sepsis. The percentage of sepsis among patients who had previous biliary intervention was found to be lower than patients who did not undergo any biliary intervention. However, since the P-value was 1.000, this association was considered statistically insignificant.

4. Sepsis at discharge:

Table 10: Comparison between preoperative parameters and sepsis at discharge

Variables		Suspected sepsis at discharge		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	9(18.75)	39(81.25)		
Elevated CRP	Yes	1(5)	19(95)	0.067	0.1447 (0,0166-1.2646)
	No	8(26.66)	2273.33()		
Elevated bilirubin	Yes	4(17.39)	19(82.6)	1.00	0.9263 (0.2171-3.9531)
	No	5(18.51)	22(81.48)		
Biliary intervention	Yes	6(23.07)	20(76.91)	0.467	2.1 (0.4615-9.5556)
	No	3(12.5)	21(87.5)		

None of the patients who had elevated preoperative serum Procalcitonin levels had features of sepsis. 9(18.75%) of the patients who had normal serum Procalcitonin levels had features of sepsis after post-op day ten and prior to discharge. P-value was 1.000 and there was no statistically significant association.

Among the 20 patients who had elevated preoperative serum CRP levels, only 1 (5%) had features of sepsis, while among those with normal serum CRP levels, 8 (26.66%) had features of sepsis. P-value calculated by Fisher's exact test was 0.067 and hence the association was considered statistically insignificant.

Among the 23 patients who had elevated serum bilirubin levels, 4(17.39%) had features of sepsis and among those with normal serum bilirubin levels, 5(18.51%) had features of sepsis. Since the P-value was 1.000, there was no statistically significant association between elevated bilirubin levels and sepsis at discharge.

23.07%(6) patients among those who had previous biliary intervention had features of sepsis after day 10 and prior to discharge while among those who had no previous biliary intervention, only 3(12.5) patients had features of sepsis. P-value of this comparison being 0.467, this association is considered statistically insignificant.

5. **SSI on post-op day 3:**

Table 11: Comparison between preoperative parameters and SSI on POD3

Variables		**SSI day 3**		**P-value**	**Odds ratio 95%(CI)**
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	1(50)	1(50)	0.263	7 (0.3848-127.3273)
	No	6(12.5)	42(87.5)		
Elevated CRP	Yes	6(30)	14(70)	0.12	12.4286 (1.362-113.4142)
	No	1(3.33)	29(96.66)		
Elevated bilirubin	Yes	3(13.04)	20(86.95)	1.00	0.8625 (0.172-4.3256)
	No	4(14.81)	23(85.18)		
Biliary intervention	Yes	3(11.53)	23(88.46)	0.697	0.6522 (0.13-3.2708)
	No	4(16.66)	20(83.33)		

One (50%) patient among the 2 who had elevated preoperative Procalcitonin level had SSI on the third post-op day, while among those who had normal serum Procalcitonin levels preoperatively, only 12.5% (6) of patients had SSI. A higher percentage of SSI was found to be present on post-op day 3 among those with preoperative elevated serum Procalcitonin levels. Since the P-value calculated by Fisher's exact test was 0.263, there was no statistically significant association between preoperative elevated levels of serum Procalcitonin and SSI on post-op day 3.

Among the patients who had elevated serum CRP levels preoperatively, 6(30%) of them had SSI while among the 30 patients with normal CRP levels, only 1(3.33%) patient had SSI and 29(96.66%) did not have SSI on post-op day 3. The percentage of SSI in patients with preoperative elevated serum CRP levels was found to be higher than those with normal CRP levels. However, since the P-value was 0.12, there was no statistically significant association between SSI and preoperative levels of C-reactive protein.

Among the patients with preoperative elevated serum bilirubin levels, 3(13.04%) had features of SSI while among the patients with normal bilirubin levels, 4(14.81%) patients had features of SSI. Since the P-value was1.000, there was no statistically significant association.

Among the 26 patients who had previous biliary intervention, 3 (11.53%) patients had features of SSI while among the 24 patients who did not have previous biliary intervention, 4(16.6%) patients had features of SSI on the third postoperative day. The percentage of SSI among patients who had previous biliary intervention is

higher than among those who did not have any biliary intervention. However, since the P-value was 0.697, there was no statistically significant association between preoperative biliary intervention and SSI on the third following the surgery.

6. SSI on post-op day 7:

Table 12: Comparison between preoperative parameters and SSI on POD7

Variables		SSI day 7		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	1(50)	1(50)	0.514	2.4286 (0.1414-41.6034)
	No	14(29.16)	34(70.83)		
Elevated CRP	Yes	6(30)	14(70)	1.000	1 (0.2909-3.4373)
	No	9(30)	21(70)		
Elevated bilirubin	Yes	5(21.79)	18(78.26)	0,239	0.4722 (0.1337-1.6676)
	No	10(37.03)	17(62.96)		
Biliary intervention	Yes	9(34.61)	17(65.38)	0.459	1.5882 (0.4654-5.4196)
	No	6(25)	18(75)		

One (50%) patient among the 2 who had elevated preoperative Procalcitonin level had SSI on the seventh post-op day, while among those who had normal serum Procalcitonin levels preoperatively, only 29.16% (14) of patients had SSI. A higher percentage of SSI was found to be present on post-op day 3 among those with preoperative elevated serum Procalcitonin levels. Since the P-value calculated by

Fisher's exact test was 0.514, there is no statistically significant association between preoperative elevated levels of serum Procalcitonin and SSI on post-op day 7.

Among the patients who had elevated serum CRP levels preoperatively, 6(30%) of them had SSI while among the 30 patients with normal CRP levels, 9 (30%) patients had SSI and 21(70%) did not have SSI on post-op day 3. The percentage of SSI in patients with preoperative elevated serum CRP levels was the same as those with normal CRP levels. However, since the P-value was 1.000, there is no statistically significant association between SSI and preoperative levels of C-reactive protein.

Among the patients with preoperative elevated serum bilirubin levels, 5(21.79%) had features of SSI while among the patients with normal bilirubin levels, 10(37.03%) patients had features of SSI. Since the P-value was 0.239, there was no statistically significant association.

Among the 26 patients who had previous biliary intervention, 9 (34.61%) patients had features of SSI while among the 24 patients who did not have previous biliary intervention, 6(25%) patients had features of SSI on the seventh postoperative day. However, since the P-value was 0.459, there was no statistically significant association between preoperative biliary intervention and SSI on the third following the surgery.

7. SSI on post-op day 10:

Table 13: Comparison between preoperative parameters and SSI on POD10

Variables		SSI day 10		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	2(100)	0	0.241	NA
	No	16(33.33)	32(66.66)		
Elevated CRP	Yes	8(40)	12(60)	0.630	1.333 (0,4125-4.3101)
	No	10(33.33)	20(66.66)		
Elevated bilirubin	Yes	9(39.13)	14(60.86)	0.670	1.2857 (0.4038-4.0941)
	No	9(33.33)	18(66.66)		
Biliary intervention	Yes	11(42.30)	15(57.69)	0.333	1.781 (0.5501-5.7657)
	No	7(29.16)	17(70.83)		

Both the patients who had elevated preoperative serum Procalcitonin levels had SSI on the 10th post-op day while among the 48 patients who did not have elevated Procalcitonin levels, 16(32.66%) patients had SSI. Since the P-value calculated was 0.241, there was no statistically significant association between preoperative elevated levels of serum Procalcitonin and SSI on post-op day 10.

Among the patients who had elevated serum CRP levels preoperatively, 8(40%) of them had SSI while among the 30 patients with normal CRP levels, 10 (33.33%) patients had SSI and 21(66.66%) did not have SSI on post-op day 3. The percentage of SSI in patients with preoperative elevated serum CRP levels was

higher than those with normal CRP levels. However, since the P-value was 0.630, there was no statistically significant association between SSI and preoperative levels of C-reactive protein.

Among the patients with preoperative elevated serum bilirubin levels, 9(39.13%) had features of SSI while among the patients with normal bilirubin levels, 9(33.33%) patients had features of SSI. Since the P-value was 0.670, there was no statistically significant association.

Among the 26 patients who had previous biliary intervention, 11 (42.30%) patients had features of SSI while among the 24 patients who did not have previous biliary intervention, 7(29.16%) patients had features of SSI on the tenth postoperative day. However, since the P-value was 0.333, there was no statistically significant association between preoperative biliary intervention and SSI on the third following the surgery.

8. SSI at discharge:

Table 14: Comparison between preoperative parameters and SSI at discharge

Variables		SSI at discharge		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	2(100)	0	0.107	NA
	No	11(22.91)	37(77.08)		
Elevated CRP	Yes	5(25)	15(75)	0.895	0.9167 (0.2509-3.3496)
	No	8(26.66)	22(73.33)		
Elevated bilirubin	Yes	6(26.08)	17(73.91)	0.990	1.0084 (0.2838-3.5826)
	No	7(25.92)	20(74.07)		
Biliary intervention	Yes	7(26.92)	19(73.07)	0.877	1.1053 (0.3114-3.9229)
	No	6(25)	18(75)		

Both the patients who had elevated preoperative serum Procalcitonin levels had SSI while among the 48 patients who did not have elevated Procalcitonin levels, 11(22.91%) patients had SSI. The percentage of patients with elevated Procalcitonin levels having SSI was more than those with normal Procalcitonin levels. Since the P-value calculated was 0.107, there was no statistically significant association between preoperative elevated levels of serum Procalcitonin and SSI at discharge.

Among the patients who had elevated serum CRP levels preoperatively, 5(25%) of them had SSI while among the 30 patients with normal CRP levels, 8 (26.66%) patients had SSI and 22(73.33%) did not have SSI at discharge. However,

since the P-value was 0.895, there was no statistically significant association between SSI and preoperative levels of C-reactive protein.

Among the patients with preoperative elevated serum bilirubin levels, 6(26.08%) had features of SSI while among the patients with normal bilirubin levels, 7(25.92%) patients had features of SSI. Since the P-value was 0.990, there was no statistically significant association.

Among the 26 patients who had previous biliary intervention, 7 (26.92%) patients had features of SSI while among the 24 patients who did not have previous biliary intervention, 6(25%) patients had features of SSI. However, since the P-value was 0.877, there was no statistically significant association between preoperative biliary intervention and SSI at the time of discharge.

9. Pneumonia at post-op day 3:

Table 15: Comparison between preoperative parameters and pneumonia on POD3

Variables		Pneumonia day 3		P-value
		Yes (n)	No (n)	
Elevated Procalcitonin	Yes	0	2	NA
	No	0	48	
Elevated CRP	Yes	0	20	NA
	No	0	30	
Elevated bilirubin	Yes	0	23	NA
	No	0	27	
Biliary intervention	Yes	0	26	NA
	No	0	24	

On the third post-op day, none of the patients had Pneumonia. Hence no association could be calculated based on the preoperative values of serum Procalcitonin, CRP, serum bilirubin or previous biliary intervention.

10. Pneumonia at post-op day 7:

Table 16: Comparison between preoperative parameters and pneumonia on POD7

Variables		Pneumonia day 7		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	3(6.25)	45(93.75)		
Elevated CRP	Yes	0	20(100)	0.395	NA
	No	3(10)	27(90)		
Elevated bilirubin	Yes	0	23(100)	0.293	NA
	No	3(11.11)	24(88.88)		
Biliary intervention	Yes	3(11.58)	23(88.46)	0.263	NA
	No	0	24(100)		

On the 7th postoperative day, none of the patients with preoperative elevated serum Procalcitonin levels developed Pneumonia. Three (6.25%) of the patients with normal Procalcitonin levels developed pneumonia. Since the P-value was not significant, there was no statistically significant association between Procalcitonin and post-op pneumonia.

None of the patients with elevated preoperative CRP levels had pneumonia. Three (10%) of those with normal preoperative levels developed pneumonia on the 7th post-op day. However, since the P-value was not significant, there was no statistically significant association between CRP and post-op pneumonia.

None of the patients with preoperative elevated bilirubin levels developed pneumonia. Three (11.11%) of those with normal bilirubin levels developed pneumonia on the 7th post-op day. Since the P-value was not significant, there was no statistically significant association between bilirubin levels and post-op pneumonia.

Among the 26 patients who had previous biliary intervention, 3 (11.58%) had developed pneumonia. And none of the patients who had no previous biliary intervention developed pneumonia. However, since the P-value was not significant, there was no statistically significant association between previous biliary intervention and post-op pneumonia.

11. Pneumonia at post-op day 10:

Table 17: Comparison between preoperative parameters and pneumonia on POD10

Variables		Pneumonia day 10		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	2(4.16)	46(95.83)		
Elevated CRP	Yes	0	20(100)	0.659	NA
	No	2(6.66)	28(93.33)		
Elevated bilirubin	Yes	0	23(100)	0.543	NA
	No	2(7.40)	25(92.59)		
Biliary intervention	Yes	2(7.69)	24(92.30)	0.506	NA
	No	0	24(100)		

On the 10th postoperative day, none of the patients with preoperative elevated serum Procalcitonin levels developed Pneumonia. Two (4.16%) of the patients with normal Procalcitonin levels developed pneumonia. Since the P-value was not significant, there was no statistically significant association between Procalcitonin and post-op pneumonia.

None of the patients with elevated preoperative CRP levels had pneumonia. Two (6.66%) of those with normal preoperative levels developed pneumonia on the 10th post-op day. However, since the P-value was not significant, there was no statistically significant association between CRP and post-op pneumonia.

None of the patients with preoperative elevated bilirubin levels developed pneumonia. Two (7.40%) of those with normal bilirubin levels developed pneumonia on the 10th post-op day. Since the P-value was not significant, there was no statistically significant association between bilirubin levels and post-op pneumonia.

Among the 26 patients who had previous biliary intervention, 2 (7.69%) had developed pneumonia. And none of the patients who had no previous biliary intervention developed pneumonia. However, since the P-value was not significant, there was no statistically significant association between previous biliary intervention and post-op pneumonia.

12. Pneumonia at discharge:

Table 18: Comparison between preoperative parameters and pneumonia at discharge

Variables		Pneumonia-discharge		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	2(4.16)	46(95.83)		
Elevated CRP	Yes	0	20(100)	0.659	NA
	No	2(6.66)	28(93.33)		
Elevated bilirubin	Yes	0	23(100)	0.543	NA
	No	2(7.40)	25(92.59)		
Biliary intervention	Yes	2(7.69)	24(92.30)	0.506	NA
	No	0	24(100)		

At discharge, none of the patients with preoperative elevated serum Procalcitonin levels developed Pneumonia. Two (4.16%) of the patients with normal Procalcitonin levels developed pneumonia. Since the P-value was not significant, there was no statistically significant association between Procalcitonin and post-op pneumonia.

None of the patients with elevated preoperative CRP levels had pneumonia. Two (6.66%) of those with normal preoperative levels developed pneumonia at

discharge. However, since the P-value was not significant, there was no statistically significant association between CRP and post-op pneumonia.

None of the patients with preoperative elevated bilirubin levels developed pneumonia. Two (7.40%) of those with normal bilirubin levels developed pneumonia at discharge. Since the P-value was not significant, there was no statistically significant association between bilirubin levels and post-op pneumonia.

Among the 26 patients who had previous biliary intervention, 2 (7.69%) had developed pneumonia. And none of the patients who had no previous biliary intervention developed pneumonia. However, since the P-value was not significant, there was no statistically significant association between previous biliary intervention and post-op pneumonia.

13. Urinary tract infection:

a) On the third postoperative day, among the patients who had preoperative elevated levels of Procalcitonin, CRP, serum bilirubin or previous biliary intervention, none of them developed UTI.

b) On post-op day 7, among the patients who had preoperative elevated levels of Procalcitonin, CRP, serum bilirubin or previous biliary intervention, none of them developed UTI.

c) On post-op day 10, among the patients who had preoperative elevated levels of Procalcitonin, CRP, serum bilirubin or previous biliary intervention, none of them developed UTI.

d) At discharge:

Table 19: Comparison between preoperative parameters and UTI at discharge

Variables		UTI at discharge		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	1(2.08)	97.91()		
Elevated CRP	Yes	1(5)	19(95)	0.837	NA
	No	0	30(100)		
Elevated bilirubin	Yes	0	23(100)	1.000	NA
	No	1(3.70)	26(96.29)		
Biliary intervention	Yes	1(3.84)	25(96.15)	1.000	NA
	No	0	24(100)		

At discharge, none of the patients who had preoperative elevated serum Procalcitonin levels had developed UTI. One (2.08%) patient among those with normal preoperative Procalcitonin level developed UTI. Since the P-value was not significant, no statistically significant association was found between Procalcitonin levels and UTI.

Among the 20 patients who had preoperative elevated serum CRP levels, 1 (5%) patient had developed UTI at discharge. None of the patients with a normal preoperative serum CRP level developed UTI. However, since the P-value was not

significant, there was no statistically significant association between CRP levels and UTI levels.

None of the patients who had elevated preoperative serum bilirubin levels developed UTI while among those who had normal serum bilirubin, 1 (3.70%) patient developed UTI. P-value calculated was not significant and hence there was no statistically significant association between preoperative bilirubin levels and post-op UTI.

Among the 26 patients who had previous biliary intervention, only 1 (3.84%) developed UTI at discharge. Among those who did not have any previous biliary intervention, none of them developed UTI. Since the P-value was not significant, there was no statistically significant association between biliary intervention and UTI.

14. Comparison of Bactibilia with preoperative parameters:

Table 20: Comparison between preoperative parameters and bactibilia

Variables		Bactibilia		P-value	Odds ratio
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	2(100)	0	0.875	NA
	No	33(68.75)	15(31.25)		
Elevated CRP	Yes	13(65)	7(35)	0.529	0.6753 (0.1985-2.2975)
	No	22(73.33)	8(26.66)		
Elevated bilirubin	Yes	17(73.91)	6(26.98)	0.577	1.4167 (0.4152-4.8342)
	No	18(66.66)	9(33.33)		
Biliary intervention	Yes	21(80.76)	5(19.23)	0.084	3 (0.8435-10.6696)
	No	14(58.33)	10(41.66)		

Intraoperative bile culture was sent for 46 of the 50 patients enrolled in the study. Among the 46 patients, 35 &76.98%) of them had bactibilia.

Among the two patients who had preoperative elevated serum Procalcitonin levels, both of them (100%) had bactibilia. Among the 48 who had normal serum Procalcitonin levels, 33 (68.75%) patients had bactibilia. The percentage of patients having bactibila was higher among the group of patients with preoperative elevated serum Procalcitonin levels. However, since the P-value was not significant, there was no statistically significant association between Procalcitonin levels and bactibilia.

Among the 20 patients who had preoperative elevated serum CRP levels, 13 (65%) had bactibilia. Among the 30 who had normal serum Procalcitonin levels, 22 (73.33%) patients had bactibilia. However, since the P-value was not significant, there was no statistically significant association between CRP levels and bactibilia.

Among the 23 patients who had preoperative elevated serum bilirubin levels, 17 (73.91%) had bactibilia. Among the 27 who had normal serum Procalcitonin levels, 18 (66.66%) patients had bactibilia. The percentage of patients having bactibila was higher among the group of patients with preoperative elevated serum bilirubin levels. However, since the P-value was not significant, there was no statistically significant association between bilirubin levels and bactibilia.

Among the 26 patients who had previous biliary intervention, 21 (80.76%) had bactibilia. Among the 24 who had no biliary intervention, 14 (58.33%) patients had bactibilia. The percentage of patients having bactibila was higher among the group of patients with preoperative elevated serum Procalcitonin levels. However, since the P-value was not significant, there was no statistically significant association between previous biliary intervention and bactibilia.

15. Re-surgery/re-operation:

a) On the third post-op day, among the patients who had elevated serum Procalcitonin, bilirubin, CRP, previous biliary intervention, none of them underwent re-operation.

b) On post-op day 7, among the patients who had elevated serum Procalcitonin, bilirubin, CRP, previous biliary intervention, none of them underwent re-operation.

c) On post-op day 10:

Table 21: Comparison between preoperative parameters and re-operation on POD10

Variables		**Re-operation day 10**		**P-value**	**Odds ratio 95%(CI)**
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	2(4.16)	46(95.83)		
Elevated CRP	Yes	0	20(100)	0.659	NA
	No	2(6.66)	28(93.33)		
Elevated bilirubin	Yes	1(4.37)	22(95.65)	1.000	1.1818 (0.0698-20.0147)
	No	1(3.70)	26(96.29)		
Biliary intervention	Yes	0	26(100)	0.435	NA
	No	2(8.33)	22(91.66)		

Among those with elevated preoperative serum Procalcitonin levels, none of them underwent re-operation on post-op day 10. Two (4.16%) patients among those with normal serum Procalcitonin levels underwent re-operation. Since the P-value was insignificant, there was no statistically significant association between Procalcitonin levels and re-operation.

None of the patients with elevated preoperative CRP levels underwent re-operation on post-op day 10. Two (6.66%) of the patient who had normal CRP levels underwent re-operation. There was no statistically significant association between elevated CRP levels and re-operation on post-op day 10 since the P-value was insignificant.

Among the 23 patients who had elevated preoperative serum bilirubin levels, one (4.37%) patient underwent re-operation and one (3.70%) patient among those with normal preoperative serum bilirubin level underwent reoperation on post-op day 10. Since the P-value was insignificant, there was no statistically significant association between bilirubin levels and re-operation on post-op day 10.

None of the patients who had previous biliary intervention underwent re-operation on post-op day 10. Since P-value was insignificant, there was no statistically significant association between previous biliary intervention and re-operation on post-op day 10.

d) At discharge:

Table 22: Comparison between preoperative parameters and re-operation at discharge

Variables		Re-operation at discharge		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	0	2(100)	1.000	NA
	No	1(2.08)	47(97.91)		
Elevated CRP	Yes	0	20(100)	1.000	NA
	No	1(3.33)	29(96.66)		
Elevated bilirubin	Yes	1(4.34)	22(95.65)	0.460	NA
	No	0	27(100)		
Biliary intervention	Yes	1(3.84)	25(96.15)	1.000	NA
	No	0	24(100)		

At discharge, none of the patients with preoperative elevated serum Procalcitonin levels underwent re-operation while 1(2.08%) patient among those with normal Procalcitonin level underwent reoperation. P-value being 1.000 was considered insignificant and hence there was no statistically significant association between Procalcitonin levels and reoperation.

Among the 20 patients with preoperative elevated serum CRP levels, none of them underwent reoperation while 1(3.33%) patient among those with normal CRP levels underwent reoperation. P-value being 1.000 was considered

insignificant and hence there was no statistically significant association between CRP levels and reoperation.

Among the 23 patients with preoperative elevated serum bilirubin levels, one (4.34%) patient underwent reoperation while none of those with normal bilirubin levels underwent reoperation. P-value being 0.460, there was no statistically significant association between bilirubin levels and reoperation.

Among the 26 patients who had previous biliary intervention, one (3.84%) patient underwent reoperation while none among the 24 patients who had no previous biliary intervention underwent reoperation. P-value being 1.000 there was no statistically significant association between previous biliary intervention and reoperation.

Comparison of post-op antibiotics with preoperative parameters and postoperative infective complications:

1. Preoperative serum Procalcitonin, CRP, bilirubin levels, previous biliary intervention, and post-op antibiotics:

Table 23: Comparison between preoperative parameters and the use of postoperative antibiotics

Variables		Post-op antibiotics		P-value	Odds ratio 95%(CI)
		Yes n (%)	No n (%)		
Elevated Procalcitonin	Yes	1(50)	1(50)	1.000	0.5 (0.0293-8.5244)
	No	32(66.66)	16(33.33)		
Elevated CRP	Yes	13(65)	7(35)	0.623	0.9286 (0.282-3.058)
	No	20(66.66)	10(33.33)		
Elevated bilirubin	Yes	16(69.56)	7(30.43)	0.623	1.3345 (0.412-4.3879)
	No	17(62.96)	10(37.03)		
Biliary intervention	Yes	19(73.07)	7(26.92)	0.272	1.9388 (0,5914-6.3554)
	No	14(58.33)	10(41.66)		

Among the 2 patients who had preoperative elevated serum Procalcitonin levels, one patient received post-op antibiotics while among the 48 patients who had normal Procalcitonin levels, 32 (66.66%) patients received post-op antibiotics. The P-value for this comparison was insignificant and hence there was no statistically

significant association between the need for post-op antibiotic and preoperative elevated serum Procalcitonin levels.

Among the 20 patients who had preoperative elevated serum CRP levels, 13(65%) patients were administered post-op antibiotics while among those with normal CRP levels, 20(66.66%) patients were also administered antibiotics in the post-operative period. The percentage of patients who were administered post-op antibiotics were similar in the groups with normal as well as elevated CRP levels. Since the P-value was insignificant, there was no statistically significant association between the need for post-op antibiotic and preoperative elevated serum CRP levels.

2. Post-op antibiotics and post-op sepsis:

Table 24: Comparison between postoperative sepsis and postoperative use of antibiotics

Variables		**Post-op antibiotics**		**P-value**
		Yes n (%)	No n (%)	
Sepsis day 3	Yes	7(100)	0	0.106
	No	26(60.46)	17(39.53)	
Sepsis day 7	Yes	8(100)	0	0.071
	No	25(59.52)	17(40.47)	
Sepsis day 10	Yes	6(100)	0	0.157
	No	27(61.36)	17(38.63)	
Sepsis at discharge	Yes	9(100)	0	0.047
	No	24(58.53)	17(34.69)	

Among the 7 patients who had features suspicious for sepsis on the third post-op day, all of them required antibiotics postoperatively. Also, 26(60.46%) patients among those who had no features of sepsis received antibiotics in the postoperative period. P-value being insignificant, there was no statistically significant association between the need for antibiotics and features with suspicion for sepsis.

On the 7th post-op day, all 8 patients who had features of sepsis continued to require post-op antibiotics. Similarly, 25(59.52%) patients who did not have features of sepsis received antibiotics. P-value being insignificant, there was no statistically significant association between the need for antibiotics and features with suspicion for sepsis.

On the 10th post-op day, all 6 patients who had features of sepsis required post-op antibiotics. Similarly, 27(61.63%) patients who did not have features of sepsis required antibiotics. P-value being insignificant, there was no statistically significant association between the need for antibiotics and features with suspicion for sepsis.

At discharge, 9 patients who had sepsis required antibiotics and the others who did not have features of sepsis did not require any antibiotics. The P-value for this association was 0.047. However, no association can be derived from this statistical significance.

3. Post-op antibiotics and SSI:

Table 25: Comparison between postoperative SSI and the use of postoperative antibiotics

Variables		Post-op antibiotics		P-value
		Yes n (%)	No n (%)	
SSI day 3	Yes	4(57.14)	3(42.85)	0.677
	No	29(67.44)	14(32.55)	
SSI day 7	Yes	11(73.33)	4(26.66)	0.474
	No	22(62.85)	13(37.14)	
SSI day 10	Yes	14(77.77)	4(22.22)	0.187
	No	19(59.37)	13(40.62)	
SSI at discharge	Yes	9(69.23)	4(30.76)	1.000
	No	24(64.86)	13(35.13)	

Among the seven patients who had features of SSI on post-op day 3, 4(57.14%) patients required antibiotics. Also, among the 43 patients who had no features of SSI, antibiotics were required and administered in 29(62.85%) patients. P-value calculated was insignificant and hence there was no statistically significant association between the need for antibiotics and features of SSI.

Among the 15 patients who had SSI on post-op day 7, 11(73.33%) patients required antibiotics. Among the 35 patients who had no SSI, 22(62.85%) required antibiotics. P-value calculated was insignificant and hence there was no statistically significant association between the need for antibiotics and features of SSI.

On the 10th post-op day, 18 patients had SSI, among them 14(77.77%) patients required antibiotics and among the 32 patients who had no SSI, 19(59.37%) patients were administered antibiotics. P-value calculated was insignificant and hence there was no statistically significant association between the need for antibiotics and features of SSI.

Among the 13 patients who had SSI at discharge, 9(69.23%) patients required antibiotics and among the 37 patients who had no SSI, 24(64.86%) patients were administered antibiotics. P-value calculated was insignificant and hence there was no statistically significant association between the need for antibiotics and features of SSI.

4. Post-op antibiotics and pneumonia:

Table 26: Comparison between postoperative pneumonia and the use of postoperative antibiotics

Variables		**Post-op antibiotics**		**P-value**
		Yes n (%)	No n (%)	
Pneumonia day 3	Yes	0	0	NA
	No	33(66)	17(34)	
Pneumonia day 7	Yes	3(100)	0	0.513
	No	30(63.82)	17(36.17)	
Pneumonia day 10	Yes	2(100)	0	0.784
	No	31(64.58)	17(35.41)	
Pneumonia at discharge	Yes	2(100)	0	0.784
	No	31(64.58)	17(35.41)	

On the third post-op day, none of the patients had features of pneumonia and on the 7th post-op day, all the 3 patients who had features of pneumonia had received antibiotics.

On the 10th post-op day, 2 patients had features of pneumonia with both of them having received antibiotics and at discharge, 2 patients who had features of pneumonia received antibiotics.

P-value calculated for all the above association are insignificant and hence there is no association between post-op pneumonia and the need for antibiotics.

5. Post-op antibiotics and UTI:

Table 27: Comparison between postoperative UTI and the use of postoperative antibiotics

Variables		**Post-op antibiotics**		**P-value**
		Yes n (%)	No n (%)	
UTI day 3	Yes	0	0	NA
	No	33(66)	17(34)	
UTI day 7	Yes	0	0	NA
	No	33(66)	17(34)	
UTI day 10	Yes	0	0	NA
	No	33(66)	17(34)	
UTI at discharge	Yes	1(100)	0	1.000
	No	32(65.30)	17(34.69)	

On post-op days 3, 7 and 10, none of the patients had UTI. At discharge, 1 patient had UTI who also received an antibiotic. There was no significant P-value calculated.

Combined comparison between CRP and Procalcitonin:

In order to assess the combined efficacy of preoperatively elevated procalcitonin and C-reactive protein levels as a biomarker for postoperative infectious complications, the following analysis was done.

1. Association between Sepsis and Preoperative elevated levels of CRP and PCT

Table 28: Comparison between patients with elevated levels of both CRP, PCT and post-op Sepsis

Variables		**Elevated CRP and PCT**	
		Yes	No
Sepsis POD3	Yes	0	7(14.58%)
	No	2(100%)	41(85.41%)
Sepsis POD7	Yes	0	8(16.66%)
	No	2(100%)	40(83.33%)
Sepsis POD10	Yes	0	6(12.5%)
	No	2(100%)	42(87.5%)
Sepsis at discharge	Yes	0	9(18.75%)
	No	2(100%)	39(81.25%)

Among the 50 patients who were a part of this study, only 2 (4%) patients had preoperatively elevated C-reactive protein and procalcitonin. Also, neither of these two patients had any features of sepsis on postoperative days 3, 7, 10 or at the time of their discharge.

2. Association between SSI and Elevated CRP and Procalcitonin

Table 29: Comparison between patients with elevated levels of both CRP, PCT and post-op SSI

Variables		**Elevated CRP and PCT**	
		Yes n(%)	No n(%)
SSI POD3	Yes	1(50)	6(12.5)
	No	1(50)	42(87.5)
SSI POD7	Yes	1(50)	14(29.16)
	No	1(50)	34(70.83)
SSI POD10	Yes	2(100)	6(12.5)
	No	0	42(87.5)
SSI at discharge	Yes	2(100)	9(18.75)
	No	0	39(81.25)

Among the two patients who had elevated levels of both C-reactive protein and procalcitonin, only one patient developed SSI on or before the 3rd post-op day while the other patient developed SSI on or before the 7th postoperative day. However, from the table above, SSI being present on the 10th post-op day and at discharge only means that both these patients went on to

have prolonged superficial surgical site infection lasting till their discharge from the hospital. Also, the sample is only two, the 'p' value could not be calculated for this comparison and hence there was no statistical significance.

3. Association between Pneumonia and elevated levels of CRP and PCT

Table 30: Comparison between patients with elevated levels of both CRP, PCT and post-op Pneumonia

Variables		**Elevated CRP and PCT**	
		Yes n(%)	No n(%)
Pneumonia POD3	Yes	0	0
	No	2(100)	48(100)
Pneumonia POD7	Yes	0	3(6.25)
	No	2(100)	45(93.75)
Pneumonia POD10	Yes	0	2(4.16)
	No	2(100)	46(95.83)
Pneumonia at discharge	Yes	0	2(4.16)
	No	2(100)	46(95.83)

4. Association between UTI and preoperative elevated CRP and PCT:

Table 31: Comparison between patients with elevated levels of both CRP, PCT and post-op UTI

Variables		Elevated CRP and PCT	
		Yes n(%)	No n(%)
Pneumonia POD3	Yes	0	0
	No	2(100)	48(100)
Pneumonia POD7	Yes	0	0
	No	2(100)	48(100)
Pneumonia POD10	Yes	0	0
	No	2(100)	48(100)
Pneumonia at discharge	Yes	0	1(2.08)
	No	2(100)	47(97.91)

Neither of the two patients with elevated levels of both CRP and PCT developed pneumonia or urinary tract infection during their hospital stay.

5. Association between postoperative use of antibiotics and preoperative elevated CRP and PCT:

Table 32: Comparison between patients with elevated levels of both CRP, PCT and post-op use of antibiotics

Variables		Elevated CRP and PCT	
		Yes n(%)	No n(%)
Post-op antibiotic	Yes	1 (50)	32 (66.66)
	No	1 (50)	16(33.33)

One patient with elevated levels of both CRP and PCT required antibiotic administration during the hospital stay for SSI.

DISCUSSION

Advances in surgical technique and perioperative management have reduced mortality rates for Whipple procedure to 5 percent or less in high-volume centers(5). Similar studies have shown that the lowest operative mortality rates and best long-term cancer outcomes following surgery have been seen in high-volume centers(3,4). House et al in 2008 showed that infective complications following pancreaticoduodenectomy were 14% for wound infection and 15% for pancreatic fistula(9). Fathy et al published that among 216 patients with periampullary tumors treated by pancreaticoduodenectomy, operative mortality occurred in 7(3.2%), 77(33%) patients developed 1 or more complications, pancreatic leak occurred in 23 (10.6%) patients, abdominal collection in 23 patients (10.6%) and delayed gastric emptying in 19 (8.8%) patients(10).

With this background knowledge that infectious complications as one of the leading causes of increased morbidity in pancreaticoduodenectomy, preoperative parameters that can possibly help as predictors for postoperative infective complications were looked into. Thereby an attempt at prevention of these infective complications can be made with the help of accurate preoperative prediction.

Several biochemical markers have been used in the past to predict morbidity and mortality after pancreaticoduodenectomy. Winter et al in 2007 analyzed preoperative levels of serum amylase, glucose, creatinine, blood urea nitrogen (BUN), hematocrit, alkaline phosphatase, liver enzymes - alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, serum bilirubin within two weeks from surgery as predictive markers of postoperative morbidity and mortality after

pancreaticoduodenectomy(44). High peak postoperative amylase (>292 μL) and preoperative BUN levels >20 mg/dL along with preoperative albumin level <2.5 g/dL and/or peak postoperative ALT/AST >200 U/L were associated with an increased morbidity(44). Also, patients with preoperative albumin level <3.5 g/dL had a relatively higher incidence of infective complications.

Procalcitonin was described as a sepsis marker in 1993(11). Synthesized by the parafollicular C cells of the thyroid gland, it is also released as an acute-phase reactant in response to inflammatory stimuli, especially those of bacterial origin(12,13). An update on procalcitonin measurements in 2014 showed that PCT is said to have the highest accuracy for diagnosing sepsis in various settings(16). Hence procalcitonin measurement helps in early confirmation of systemic inflammation and sepsis(16). Also for patient in sepsis, several studies have shown that immediate initiation of right antibiotics have helped improve the overall survival rates(17). Hence PCT has also proved to be useful in guiding antibiotic therapy(16).

Giardino et al in 2016, studied 84 patients who underwent pancreaticoduodenectomy and assessed PCT and CRP as predictive markers for postoperative inflammatory complications(45). The overall complication rates were found to be higher in patients with CRP <84 mg/dL on the first postoperative day, CRP > 127 mg/dL on the third postoperative day. The delta PCT and CRP levels that were calculated as the difference between preoperative levels and levels on 3rd postoperative day showed a positive trend toward correlation with morbidity(45). Giordino et al concluded that the use of CRP and PCT would guide better

postoperative management when complications arise, further studies to arrive at a statistically significant conclusion were advised(45).

C-reactive protein was discovered by Tillet and Francis in 1930 at the Rockefeller University(21). Du Clos et al mentioned that CRP is a classical acute phase reactant primarily because its serum levels rapidly rise from <1ug/mL to 600-1000ug/mL at the peak of an acute phase response(22). Like the other acute phase reactants such as ESR (Erythrocyte sedimentation rate), CRP levels correlate with inflammation. However, CRP is considered more useful to follow clinical course and response to treatment when compared with the other acute phase reactants because the rise and fall of the serum levels of CRP in correlation with underlying inflammation are very dramatic(22).

Several studies have shown that CRP has been used as a parameter to predict septic complications after colorectal, gastric, upper gastrointestinal surgeries, as well as to predict anastomotic leaks in gastrointestinal surgeries(46–48). Witczak et al showed that serial measurement of CRP in the first week following surgery is predictive of postoperative infective complications following abdominal surgeries(46). According to this study, the CRP levels on the 5^{th} postoperative day greater than half the maximum CRP level on the 2^{nd} postoperative day or CRP>150 mg/dL on 3^{rd} postoperative day can predict infective complications. Also, the correlation was not significant when the CRP levels were calculated before postoperative day 3.

Palanivelu et al studied the trend of CRP levels on postoperative days 1 to 4 and their postoperative morbidity in patients undergoing pancreaticoduodenectomy(49). Pancreas specific complications (PSCs) such as postoperative pancreatic fistula, hemorrhage, and intra-abdominal collections were looked. Serum CRP more than or equal to 180 mg/dL on the 2nd postoperative day was associated with PSCs, prolonged critical care stay and relaparotomy. However, in this study, the incidence of cardiopulmonary complications and surgical site infections after pancreaticoduodenectomy did not reveal any significant association(49).

Welsch et al who conducted a similar study to assess the correlation between CRP levels and inflammatory complications showed that CRP>140mg/dL on the 4th postoperative day was associated with the development of inflammatory complications and should prompt intense clinical search for any an underlying major septic process. (50).

In 2017 Mansukhani et al studied the preoperative role of PCT and CRP as a predictor of post-pancreaticoduodenectomy infective complications. This prospective observational study included 133 patients and showed that morbidity associated with infective complications was 21.8%. Also, a significant association was found between preoperative PCT and CRP with infective complications. Hence, they concluded that preoperative PCT and CRP levels done 48 hours prior to the surgery are sensitive and specific predictors of infective complications following pancreaticoduodenectomy.

In our study, we had evaluated 50 patients to assess the value of elevated preoperative procalcitonin and C-reactive protein in post-pancreaticoduodenectomy infective complications. We had also set out to assess the preoperative levels of PCT and CRP as a predictor of postoperative infective complications in patients undergoing pancreaticoduodenectomy.

Among the study population, preoperatively elevated levels of CRP and PCT were found among 20 and 2 patients respectively. Also, two patients had elevated levels of both CRP and PCT. Twenty-three patients had elevated preoperative serum bilirubin levels, 26 patients had undergone previous biliary intervention in the form of ERCP, PTBD or previous surgery on the biliary tract.

Sepsis, SSI, UTI, and pneumonia were the postoperative infective parameters assessed as a part of this study. Postoperative sepsis was present among 22 (44%) patients, the distribution of this on the postoperative-day (POD) 3, 7, 10 and at the time of discharge was even. There was no particular postoperative period that was prone to sepsis.

Surgical site infection (SSI) was present among 31 (62%) patients. Patients. Superficial SSI was more common and was seen among 7, 15, 14 and 9 patients on PODs 3, 7, 10 and at discharge respectively. Organ space infection was seen among 1, 6 and 7 patients on PODs 3, 10 and at discharge respectively. Organ space infection included postoperative anastomotic leaks as well.

Three patients had postoperative pneumonia and one patient had urinary tract infection.

When preoperative parameters were compared with the postoperative infectious complications, on POD 3, there was no statistical significance between preoperatively elevated CRP, PCT levels and postoperative sepsis. Also, preoperative high serum bilirubin levels did not have a significance with postoperative sepsis. However, 96% of the patients who had preoperative biliary intervention did not have sepsis on POD3 and this association was statistically significant.

Regarding benefits of preoperative biliary intervention and postoperative surgical outcomes, Marignoni et al in their retrospective study of 257 patients showed that preoperative biliary drainage does not affect the early or late outcomes in patients undergoing pancreaticoduodenectomy(51). Meta-analysis data from 2015 suggested that preoperative biliary drainage before pancreaticoduodenectomy increase postoperative infectious complications and hence preoperative biliary drainage should not be routinely done in patients planned for pancreaticoduodenectomy(52).

On POD 10, features of sepsis were seen among 13% of the patients who had elevated preoperative serum bilirubin levels, while only 11% of those with a normal preoperative serum bilirubin levels had features of sepsis. This association was not statistically significant. Piyush Aggarwal et al studied the effects of preoperative bilirubin levels on postoperative morbidity among 4580 patients who underwent pancreaticoduodenectomy and suggested that there was no increase in 30-day mortality. However, postoperative morbidity with high bilirubin levels was statistically significant and there was no association with surgical site infections or overall duration of hospital stay(53).

Surgical site infection (SSI) was present among both the patients who had elevated preoperative procalcitonin levels on POD 10 and at discharge. However, there was no statistical significance for SSI among patients who had elevated procalcitonin levels. The probable reason for this could be that there were only two patients with elevated values and, hence, statistical significance could not be attained. Although 50% of patients with elevated preoperative levels had SSI on POD 3 and 10, there was no statistical significance.

SSI among patients who had an elevated preoperative CRP level was similar to those with normal preoperative CRP levels. On POD 10, 40% of the patients with preoperative elevated CRP levels had SSI in comparison to 33% with SSI among those with normal CRP. However, there was no statistical significance for SSI among patient with preoperative elevated CRP levels. This could also probably be attributed to a small group of patients with elevated CRP levels. From our study, we were also not able to identify any statistical significance for preoperative biliary intervention, serum bilirubin levels, and postoperative surgical site infections.

None of the patients with preoperative elevated levels of CRP, PCT or serum bilirubin developed pneumonia during their hospital stay which was also statistically significant. Similarly, there was no statistical significance for the association between pneumonia and preoperative biliary drainage.

Subgroup analysis was done to look into any association between bactibilia and postoperative infective complications. Bactibilia was present among both patients who had elevated preoperative PCT levels, while 68.75% of patients with normal PCT levels had bactibilia and this association was not statistically significant.

Also, there was no statistically significant association between bactibilia and preoperative elevated CRP levels. However, our subgroup analysis showed that bactibilia was more prevalent among patients who had elevated serum bilirubin level (73.91%) or previous biliary intervention (80%). The P-value for this association was not significant.

Two of the 50 patients who were a part of our study with normal PCT and CRP levels underwent re-operation while none with a preoperative elevated CRP or PCT required re-operation. However, there was no statistical significance for this association. Also, from our results, there was no statistical significance for the association between patients who had preoperative elevated CRP, PCT and those who required antibiotics in the postoperative period for infective complications.

We also looked into the combined efficacy of procalcitonin and C-reactive protein as a preoperative predictor of postoperative infective complications. We had only 2 patients who had elevated values of both PCT and CRP. Neither of the two patients had features of sepsis during their postoperative period. However, both of them had SSI after POD 10 and this association was statistically insignificant. The probability of SSI occurring after POD 10 being predicted by preoperative levels of PCT and CRP would probably not be of any significance because both PCT and CRP are acute phase reactants.

CONCLUSION

1. The association between preoperative procalcitonin and C-reactive protein and postoperative sepsis had no statistical significance and hence the role of PCT and CRP as a preoperative predictor of postoperative sepsis is doubtful.
2. Surgical site infection was notably higher among patients with elevated preoperative PCT levels and also marginally higher among patients with elevated preoperative CRP levels, however this association was not of statistical significance.
3. Subgroup analysis showed that bactibilia was more commonly seen among patients with elevated serum bilirubin levels, however, this association was not statistically significant.
4. Patients undergoing preoperative biliary intervention have a statistically significant chance of not developing features of sepsis on the third postoperative day.
5. There was no significant association between preoperative PCT, CRP levels and postoperative pneumonia or urinary tract infections.
6. On comparing the efficacy of CRP and PCT as a predictor of postoperative infective complications, neither is superior to the other as a predictor and no statistically significant association could be identified.
7. Combined efficacy of both PCT and Procalcitonin did not reveal any significant association with postoperative infective complications.

LIMITATIONS

The power of the study to have any association between preoperative elevated levels of PCT, CRP and postoperative infective complications was limited by the small sample size among the group of patients who had elevated preoperative levels of CRP and PCT.

This was an observational study where the results have the potential to be confounded by the care delivered.

Although the calculated sample size was achieved, the estimated samples with an elevated PCT and CRP for the estimated sample size could not be achieved in order to draw statistically significant conclusions. Hence, we would recommend this study to be conducted on a larger scale with larger sample size to arrive at any significant conclusion.

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APPENDIX

APPENDIX I:

Evaluation for Severe Sepsis Screening Tool

Instructions: **Use this optional tool to screen patients for severe sepsis in the emergency department, on the medical/surgical floors, or in the ICU.**

1. Is the patient's history suggestive of a new infection?

- ☐ Pneumonia, empyema
- ☐ Urinary tract infection
- ☐ Acute abdominal infection
- ☐ Meningitis
- ☐ Skin/soft tissue infection
- ☐ Bone/joint infection
- ☐ Wound infection
- ☐ Blood stream catheter infection
- ☐ Endocarditis
- ☐ Implantable device infection
- ☐ Other infection _____

___ Yes ___No

2. Are any two of following signs & symptoms of infection both present and new to the patient? Note: laboratory values may have been obtained for inpatients but may not be available for outpatients.

- ☐ Hyperthermia > 38.3 °C (101.0 °F)
- ☐ Hypothermia < 36 °C (96.8°F)
- ☐ Altered mental status
- ☐ Tachycardia > 90 bpm
- ☐ Tachypnea > 20 bpm
- ☐ Leukocytosis (WBC count >12,000 µL–1)
- ☐ Leukopenia (WBC count < 4000 µL–1)
- ☐ Hyperglycemia (plasma glucose >140 mg/dL) or 7.7 mmol/L in the absence of diabetes

___ Yes ___No

If the answer is yes, to both questions 1 and 2, *suspicion of infection* is present:

- ✓ Obtain: **lactic acid, blood cultures**, CBC with differential, basic chemistry labs, bilirubin.
- ✓ At the physician's discretion obtain: UA, chest x-ray, amylase, lipase, ABG, CRP, CT scan.

3. Are any of the following organ dysfunction criteria present at a site remote from the site of the infection that are NOT considered to be chronic conditions? Note: in the case of bilateral pulmonary infiltrates the remote site stipulation is waived.

- ☐ SBP < 90 mmHg or MAP <65 mmHg
- ☐ SBP decrease > 40 mm Hg from baseline
- ☐ Creatinine > 2.0 mg/dl (176.8 mmol/L) or urine output < 0.5 ml/kg/hour for 2 hours
- ☐ Bilirubin > 2 mg/dl (34.2 mmol/L)
- ☐ Platelet count < 100,000 µL
- ☐ Lactate > 2 mmol/L (18.0 mg/dl)
- ☐ Coagulopathy (INR >1.5 or aPTT >60 secs)
- ☐ Acute lung injury with PaO2/FiO2 <250 in the absence of pneumonia as infection source
- ☐ Acute lung injury with PaO2/FiO2 <200 in the presence of pneumonia as infection source

___ Yes ___No

If *suspicion of infection* is present AND *organ dysfunction* is present, the patient meets the criteria for SEVERE SEPSIS and should be entered into the severe sepsis protocol.

Date: ____/____/____ (circle: dd/mm/yy or mm/dd/yy) Time: ____: ____ (24 hr. clock)

APPENDIX IIA: CDC definition for Urinary tract infection:

Table 1. Urinary Tract Infection Criteria

Criterion	Urinary Tract Infection (UTI)
	Symptomatic UTI (SUTI) Must meet at least ***one*** of the following criteria:
SUTI 1a **Catheter-associated Urinary Tract Infection (CAUTI) in any age patient**	Patient must meet 1, 2, and 3 below: 1. Patient had an indwelling urinary catheter that had been in place for more than 2 consecutive days in an inpatient location on the date of event AND was either: • Present for any portion of the calendar day on the date of event†, **OR** • Removed the day before the date of event‡ 2. Patient has at least ***one*** of the following signs or symptoms: • fever (>38.0°C): Reminder: To use fever in a patient > 65 years of age, the IUC needs to be in place for more than 2 consecutive days in an inpatient location on date of event and is either still in place OR was removed the day before the DOE. • suprapubic tenderness* • costovertebral angle pain or tenderness* • urinary urgency ^ • urinary frequency ^ • dysuria ^ 3. Patient has a urine culture with no more than two species of organisms identified, at least one of which is a bacterium of $\geq 10^5$ CFU/ml (See Comments). All elements of the SUTI criterion must occur during the IWP (See IWP Definition Chapter 2 Identifying HAIs in NHSN).
	† When entering event into NHSN choose "INPLACE" for Risk Factor for IUC ‡ When entering event into NHSN choose "REMOVE" for Risk Factor for IUC *With no other recognized cause (see Comments) ^ These symptoms cannot be used when catheter is in place. An IUC in place could cause patient complaints of "frequency" "urgency" or "dysuria". **Note:** • Fever is a non-specific symptom of infection and cannot be excluded from UTI determination because it is clinically deemed due to another recognized cause.

SUTI 1b **Non-Catheter-associated Urinary Tract Infection (Non-CAUTI) in any age patient**	Patient must meet 1, 2, and 3 below: 1. One of the following is true: • Patient has/had an indwelling urinary catheter but it has/had not been in place for more than 2 consecutive days in an inpatient location on the date of event† **OR** • Patient did not have an indwelling urinary catheter in place on the date of event nor the day before the date of event † 2. Patient has at least ***one*** of the following signs or symptoms: • fever (>38°C) in a patient that is ≤ 65 years of age • suprapubic tenderness* • costovertebral angle pain or tenderness* • urinary frequency ^ • urinary urgency ^ • dysuria ^ 3. Patient has a urine culture with no more than two species of organisms identified, at least one of which is a bacterium of ≥10^5 CFU/ml. (See Comments) All elements of the SUTI criterion must occur during the IWP (See IWP Definition Chapter 2 Identifying HAIs in NHSN). † When entering event into NHSN choose "NEITHER" for Risk Factor for IUC *With no other recognized cause (see Comments) ^These symptoms cannot be used when IUC is in place. An IUC in place could cause patient complaints of "frequency" "urgency" or "dysuria". **Note:** • Fever is a non-specific symptom of infection and cannot be excluded from UTI determination because it is clinically deemed due to another recognized cause.

SUTI 2 **CAUTI or Non-CAUTI in patients 1 year of age or less**	Patient must meet 1, 2, and 3 below: 1. Patient is ≤1 year of age (with‡ or without an indwelling urinary catheter) 2. Patient has at least ***one*** of the following signs or symptoms: • fever (>38.0°C) • hypothermia (<36.0°C) • apnea* • bradycardia* • lethargy* • vomiting* • suprapubic tenderness* 3. Patient has a urine culture with no more than two species of organisms identified, at least one of which is a bacterium of ≥10^5 CFU/ml. (See Comments) All elements of the SUTI criterion must occur during the IWP (See IWP Definition Chapter 2 Identifying HAIs in NHSN). ‡ If patient had an IUC in place for more than 2 consecutive days in an inpatient location and the IUC was in place on the date of event or the previous day the CAUTI criterion is met. If no such IUC was in place, UTI (non-catheter associated) criterion is met. *With no other recognized cause (See Comments) **Note:** Fever and hypothermia are non-specific symptoms of infection and cannot be excluded from UTI determination because they are clinically deemed due to another recognized cause.

APPENDIX IIB: Sepsis definition Surviving sepsis campaign.

Severe sepsis definition = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection)
Sepsis-induced hypotension
Lactate above upper limits laboratory normal
Urine output < 0.5 mL/kg/hr for more than 2 hrs despite adequate fluid resuscitation
Acute lung injury with Pao_2/Fio_2 < 250 in the absence of pneumonia as infection source
Acute lung injury with Pao_2/Fio_2 < 200 in the presence of pneumonia as infection source
Creatinine > 2.0 mg/dL (176.8 μmol/L)
Bilirubin > 2 mg/dL (34.2 μmol/L)
Platelet count < 100,000 μL
Coagulopathy (international normalized ratio > 1.5)

APPENDIX IIB: Sepsis definition

Infection, documented or suspected, and some of the following:
General variables
Fever (> 38.3°C)
Hypothermia (core temperature < 36°C)
Heart rate > 90/min^{-1} or more than two SD above the normal value for age
Tachypnea
Altered mental status
Significant edema or positive fluid balance (> 20 mL/kg over 24 hr)
Hyperglycemia (plasma glucose > 140 mg/dL or 7.7 mmol/L) in the absence of diabetes
Inflammatory variables
Leukocytosis (WBC count > 12,000 μL^{-1})
Leukopenia (WBC count < 4000 μL^{-1})
Normal WBC count with greater than 10% immature forms
Plasma C-reactive protein more than two SD above the normal value
Plasma procalcitonin more than two SD above the normal value
Hemodynamic variables
Arterial hypotension (SBP < 90 mm Hg, MAP < 70 mm Hg, or an SBP decrease > 40 mm Hg in adults or less than two SD below normal for age)
Organ dysfunction variables
Arterial hypoxemia (Pao_2/Fio_2 < 300)
Acute oliguria (urine output < 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)
Creatinine increase > 0.5 mg/dL or 44.2 μmol/L
Coagulation abnormalities (INR > 1.5 or aPTT > 60 s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count < 100,000 μL^{-1})
Hyperbilirubinemia (plasma total bilirubin > 4 mg/dL or 70 μmol/L)
Tissue perfusion variables
Hyperlactatemia (> 1 mmol/L)
Decreased capillary refill or mottling

APPENDIX-IIC

SSI criteria as described by CDC

Criterion	Surgical Site Infection (SSI)
	Superficial incisional SSI Must meet the following criteria:
	Date of event for infection occurs within 30 days after any NHSN operative procedure (where day 1 = the procedure date) **AND** involves only skin and subcutaneous tissue of the incision **AND** patient has at least ***one*** of the following: a. purulent drainage from the superficial incision. b. organisms identified from an aseptically-obtained specimen from the superficial incision or subcutaneous tissue by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST). c. superficial incision that is deliberately opened by a surgeon, attending physician** or other designee and culture or non-culture based testing is not performed. **AND** patient has at least one of the following signs or symptoms: pain or tenderness; localized swelling; erythema; or heat. d. diagnosis of a superficial incisional SSI by the surgeon or attending physician** or other designee. www.cdc.gov/nhsn/xls/icd10-pcs-pcm-nhsn-opc.xlsx www.cdc.gov/nhsn/xls/cpt-pcm-nhsn.xlsx ** The term attending physician for the purposes of application of the NHSN SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency physician or physician's designee (nurse practitioner or physician's assistant).

APPENDIX IIC

Comments	There are two specific types of superficial incisional SSIs: 1. Superficial Incisional Primary (SIP) – a superficial incisional SSI that is identified in the primary incision in a patient that has had an operation with one or more incisions (e.g., C-section incision or chest incision for CBGB) 2. Superficial Incisional Secondary (SIS) – a superficial incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (e.g., donor site incision for CBGB)
Reporting Instructions for Superficial SSI	**The following do not qualify as criteria for meeting the NHSN definition of superficial SSI:** • Diagnosis/treatment of cellulitis (redness/warmth/swelling), by itself, does not meet criterion "d" for superficial incisional SSI. Conversely, an incision that is draining or that has organisms identified by culture or non-culture based testing is not considered a cellulitis. • A stitch abscess alone (minimal inflammation and discharge confined to the points of suture penetration). • A localized stab wound or pin site infection- Such an infection might be considered either a skin (SKIN) or soft tissue (ST) infection, depending on its depth, but not an SSI **Note:** A laparoscopic trocar site for an NHSN operative procedure is not considered a stab wound. • Circumcision is not an NHSN operative procedure. An infected circumcision site in newborns is classified as CIRC and is not an SSI • An infected burn wound is classified as BURN and is not an SSI.

APPENDIX IIC

	Deep incisional SSI Must meet the following criteria: The date of event for infection occurs within 30 or 90 days after the NHSN operative procedure (where day 1 = the procedure date) according to the list in Table 2 **AND** involves deep soft tissues of the incision (e.g., fascial and muscle layers) **AND** patient has at least ***one*** of the following: a. purulent drainage from the deep incision. b. a deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon, attending physician** or other designee and organism is identified by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST) or culture or non-culture based microbiologic testing method is not performed **AND** patient has at least ***one*** of the following signs or symptoms: fever (>38°C); localized pain or tenderness. A culture or non-culture based test that has a negative finding does not meet this criterion. c. an abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test ** The term attending physician for the purposes of application of the NHSN SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency
Comments	There are two specific types of deep incisional SSIs: 1. Deep Incisional Primary (DIP) – a deep incisional SSI that is identified in a primary incision in a patient that has had an operation with one or more incisions (e.g., C-section incision or chest incision for CBGB) 2. Deep Incisional Secondary (DIS) – a deep incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (e.g., donor site incision for CBGB)

APPENDIX IIC

	Organ/Space SSI Must meet the following criteria: Date of event for infection occurs within 30 or 90 days after the NHSN operative procedure (where day 1 = the procedure date) according to the list in Table 2 **AND** infection involves any part of the body deeper than the fascial/muscle layers, that is opened or manipulated during the operative procedure **AND** patient has at least ***one*** of the following: a. purulent drainage from a drain that is placed into the organ/space (e.g., closed suction drainage system, open drain, T-tube drain, CT guided drainage) b. organisms are identified from an aseptically-obtained fluid or tissue in the organ/space by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST). c. an abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test evidence suggestive of infection. **AND** meets at least ***one*** criterion for a specific organ/space infection site listed in Table 3. These criteria are found in the Surveillance Definitions for Specific Types of Infections chapter.

APPENDIX III: SOFA score

SOFA score	1	2	3	4
Respiration PaO_2/FiO_2, mmHg	< 400	< 300	< 200	< 100 with respiratory support
Coagulation Platelets $\times 10^3/mm^3$	< 150	< 100	< 50	< 20
Liver Bilirubin, mg/dl (μmol/l)	1.2 – 1.9 (20 – 32)	2.0 – 5.9 (33 – 101)	6.0 – 11.9 (102 – 204)	> 12.0 (< 204)
Cardiovascular Hypotension	MAP < 70 mmHg	Dopamine ≤ 5 or dobutamine (any dose)[a]	Dopamine > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1
Central nervous system Glasgow Coma Score	13 – 14	10 – 12	6 – 9	< 6
Renal Creatinine, mg/dl (μmol/l) or urine output	1.2 – 1.9 (110 – 170)	2.0 – 3.4 (171 – 299)	3.5 – 4.9 (300 – 440) or < 500 ml/day	> 5.0 (> 440) or < 200 ml/day

[a] Adrenergic agents administered for at least 1 h (doses given are in μg/kg·min)

APPENDIX-IV: IRB forms, Consent forms, information sheets, data collection proforma, data sheet.

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

November 16, 2017.

Dr. Nitin Paul Ambrose,
Postgraduate Registrar,
Department of Surgery - 3,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant: New Proposal:**
Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy.
Dr. Nitin Paul Ambrose, PG Registrar, Employment Number : 29646, Surgery III, Dr. Inian Samarasam, Employment Number : 30123, Surgery III, Dr. Philip Joseph, Employment number: 14105, Dr. Manbha Rymbai, Employment Number: 51919 Department of Hepatopancreaticobiliary Surgery.

Ref: IRB Min. No. 10949 dated 07.11.2017

Dear Dr. Nitin Paul Ambrose,

The Institutional Review Board (**Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy" on November 07,2017. I am quoting below the minutes of the meeting.

The Committee raises the following queries:

1. Why are pre-op measurements of Pro-calcitonin being done.
2. Need to define what is pre-op (how many days needs to be defined)
3. Reference for sample size calculation not present on the list
4. Need to define when antibiotics will be given; is it standardized
5. Will antibiotics be stopped pre-op if already started
6. Till when will you recruit patients
7. Section II – mention in what setting consent will be obtained
8. Hindi consent form needs to be changed

1 of 2

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. R.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
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Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Drs Nitin Paul Ambrose and Inian Samarasam were present during the presentation of the proposal and satisfactorily responded to the queries raised by the Members. After discussion, it was resolved to **ACCEPT the proposal after receiving the suggested modifications and answers to the queries.**

Note: 1. Kindly HIGHLIGHT the modifications in the revised proposal.
2. Keep a covering letter and point out the answer to the queries.
3. Reply to the queries should be submitted within 3 months duration the time of the thesis/ protocol presentation, if not the thesis/protocol has to be resubmitted to the IRB.
4. The checklist has to be sent along with the answers to queries.

Email the details to research@cmcvellore.ac.in and send a hard copy through internal dispatch to Dr. Biju George, Addl. Vice-Principal (Research), Principal's Office, CMC.

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board.

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Inian Samarasam, Department of Surgery - 3, CMC, Vellore.

IRB Min. No. 10949 dated 07.11.2017

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
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April 06, 2018

Dr. Nitin Paul Ambrose,
PG Registrar,
Department of Surgery - 3,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant: New Proposal:**
Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy.
Dr. Nitin Paul Ambrose, PG Registrar, Employment Number : 29646, Surgery III, Dr. Inian Samarasam, Employment Number : 30123, Surgery III, Dr. Philip Joseph, Employment number: 14105, Dr. Manbha Rymbai, Employment Number: 51919 Department of Hepatopancreaticobiliary Surgery...

Ref: IRB Min. No. 10949 [OBSERVE] dated 07.11.2017

Dear Dr. Nitin Paul Ambrose,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

DR. BIJU GEORGE
M.B.B.S., MD., DM
SECY. (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002

Cc: Dr. Inian Samarasam, Dept. of Surgery - 3, CMC, Vellore

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April 06, 2018

Dr. Nitin Paul Ambrose,
PG Registrar,
Department of Surgery - 3,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant: New Proposal:**
Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy.
Dr. Nitin Paul Ambrose, PG Registrar, Employment Number : 29646, Surgery III, Dr. Inian Samarasam, Employment Number : 30123, Surgery III, Dr. Philip Joseph, Employment number: 14105, Dr. Manbha Rymbai, Employment Number: 51919 Department of Hepatopancreaticobiliary Surgery,..

Ref: IRB Min. No. 10949 [OBSERVE] dated 07.11.2017

Dear Dr. Nitin Paul Ambrose,

The Institutional Review Board (**Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy" on November 07th 2017.

The Committee reviewed the following documents:

1. IRB application format
2. Patient information sheet and Consent form (English,Tamil, Hindi, Bengali, Telugu)
3. Proforma for Data Collection Form
4. Cvs of Drs. Nitin Paul Ambrose Inian Samarasam , Philip Joseph, . Manbha Rymbai, Tunny Sebastia.
5. Permission Letter
6. No. of documents 1- 5

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on November 07th 2017 in the BRTC Conference Hall, Biostatistics Building, Christian Medical College, Vellore 632 004.

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Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee). IRB, CMC, Vellore	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA (Theology), Dr. Min (Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Dr. RatnaPrabha	MBBS, MD (Pharma)	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Dr. SowmyaSathyendra	MBBS, MD (Gen. Medicine)	Professor, Medicine III, CMC, Vellore	Internal, Clinician
Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Sathish Kumar	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist &Epidemiologist
Dr. Asha Solomon	MSc Nursing	Associate Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
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Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
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Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. John Antony Jude Prakash	MBBS, MD	Professor, Clinical Microbiology, CMC, Vellore.	Internal, Clinician.
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician
Dr. Mathew Joseph	MBBS, MCH	Professor, Neurosurgery, CMC, Vellore	Internal, Clinician
Dr. RekhaPai	BSc, MSc, PhD	Associate Professor, Pathology, CMC, Vellore	Internal, Basic Medical Scientist
Ms. Grace Rebekah	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of Withdrawals for the study entitled: "Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy" on a monthly basis. Please sendcopies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:
A sum of 1,00,000/- INR (Rupees One Lakh Only) will be granted for 2 years. 50,000/- INR (Rupees Fifty Thousand only) will be granted for 12 months as an Ist Installment. The rest of the 50,000/- INR (Rupees Fifty thousand only) each will be released at the end of the first year as 2 nd Installment.

Yours sincerely,

Dr. BIJU GEORGE
M.B.B.S., M.D., D.M.
SECRETARY (ETHICS COMMITTEE)
Institutional Review Board
Christian Medical College, Vellore - 632 002

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

IRB Min. No. 10949 [OBSERVE] dated 07.11.2017

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Data collection proforma:

Christian Medical College, Vellore
Department of General Surgery

Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy

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1) Serial no.

2) Name:

3) Hospital no.

4) Age:

5) Sex:

6) Post-op day:
   a) Day 3
   b) Day 7
   c) Day 10

   d) At discharge

7) Comorbidities:
   a) None
   b) Systemic hypertension
   c) Diabetes mellitus
   d) Ischaemic heart disease
   e) Bronchial asthma
   f) Others

8) Histopathological diagnosis

9) Pre-operative parameters
   a) Elevated procalcitonin
      i) Yes
      ii) No
   b) Elevated C-reactive protein
      i) Yes
      ii) No

   c) Serum bilirubin level elevated
      i) Yes
      ii) No
   d) Biliary intervention
      i) ERCP
      ii) PTBD
      iii) Previous surgery on the biliary tract

10) Post-operative parameters

a) Infectious complications
   i) Sepsis:
      (1) Yes
      (2) No
   ii) Surgical site infections:
      (1) Yes
      (2) No
   iii) Pneumonia
      (1) Yes
      (2) No
   iv) Urinary tract infection
      (1) Yes
      (2) No

b) Bile culture – bactibilia
   i) Yes
   ii) No

c) Re-surgery/ Re-intervention
   i) Yes
   ii) No

d) Duration of hospital stay in days:

e) Post-op antibiotic and indication:

Diagnostic criteria for post-op infectious complications:
(CDC criteria)

1) Sepsis:

a) Is the patient's history suggestive of a new infection? **YES / NO**
   i) Wound infection
   ii) Skin/soft tissue infection
   iii) Pneumonia/empyema
   iv) Acute abdominal collection
   v) Urinary tract infection
   vi) Blood stream catheter infection
   vii) Other infection

b) Are any of the two following signs and symptoms of infection both present and new to patient?

YES / NO

   i) Hyperthermia >38.3 °C (101.0 F)
   ii) Hypothermia < 36 ° (96.8 F)
   iii) Tachypnea > 20/min
   iv) Tachycardia > 90/min
   v) Leukocytosis (WBC count > 12,000)
   vi) Leukopenia (WBC count < 4,000)
   vii) Altered mental status

2) Pneumonia: criteria must meet one of the following

a) Rales or dullness to percussion and any of the following: **YES / NO**

i) New onset of purulent sputum or change in character of sputum
ii) Organism isolated from blood culture
iii) Isolation of pathogen obtained form sputum or bronchial secretion

b) Chest radiograph showing new or progressive infiltrate, consolidation,cavitation or pleural effusion and any of the following:

YES / NO

i) New onset of purulent sputum or change in character of sputum
ii) Organism isolated from blood culture
iii) Isolation of pathogen obtained form sputum of bronchial secretion

3) Urinary tract infection

a) clinical evidence + positive urine culture **YES / NO**

4) surgical site infection (SSI) within 30 days after the procedure

YES / NO

a) Superficial incisional SSI
b) Deep incisional SSI
c) Organ space SSI

Informed Consent form to participate in a research study

Study Title: Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy

Study Number: _____

Subject's Name: _____

Hospital Number: _____

Date of Birth / Age: _____

Address and Phone Number:
_____

Phone: _____

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness:
_____

Date: _____/_____/_____

Name & Address of the Witness:
_____

<u>सहमति पत्र</u>

अध्ययन शीर्षक: पैनक्रिएटिकोडोडायनेटोमी ऑपरेशन से पहले अधिक मात्रा में प्रोक्लसिटोनिन और सी-रिएक्टिव प्रोटीन और ऑपरेशन के बाद संक्रमक जटिलताओं के बीच में संबंध

अध्ययन क्रमांक: _____

रोगी की नाम: _____

जन्म की तिथि / आयु: _____

(विषय)

(i) मैं इस बात की पुष्टि करता हूँ की मैंने उपरोक्त अध्ययन के लिए सूचना पत्रक दिनांकित _____ पढ़ा है, समझा है और सवाल पूछने का अवसर मिला है। [ ]

(ii) मैं समझा हूं की अध्ययन मैं मेरी भागीदारी स्वाछिक है और किसी भी समय अपना नाम बिना कोई कारण बताए, बिना अपने चिकितसा देखबाल या कानूनी अधिकार प्रभवित किया वापस लेने केलिए स्वतंत्र हूँ। [ ]

(iii) अध्ययन के आचार समिति और नियमिक अधिकारियों को मेरे स्वास्थ रिकॉर्ड देने केलिए मेरी अनुमति की जरूरत नहीं होगी, हालाँकि , मैं यह समझता हूँ कि मेरी पहचान किसी भी तीसरे पक्ष को जारी या प्रकाशित नहीं की जाएगी, इसके लिए मैं सहमत हूँ। [ ]

(iv) मैं इस प्रयोग के परिणाम को किसी भी वैज्ञानिक उद्देश्य केलिए प्रदान करने में कोई रोक नहीं लगाऊंगा। [ ]

(v) मैं ऊपर लिखित अध्ययन में भाग लेने के लिए सहमत हूँ। [ ]

रोगी के हस्ताक्षर (या अंगूठे का निशान) / या क़ानूनी स्वीकृत प्रतिनिधि

दिनांक : _____/_____/_____

हस्ताक्षर करने वाले का नाम: _____
हस्ताक्षर:

या

प्रतिनिधि: _____

दिनांक : _____/_____/_____

हस्ताक्षर करने वाले का नाम: _____

अध्ययन जांचकर्ता के हस्ताक्षर: _____

दिनांक : _____/_____/_____

अध्ययन जांचकर्ता का नाम: _____

गवाह के हस्ताक्षर।: _____

दिनांक : _____/_____/_____

गवाह का नाम और पता।:

ஒப்புதல் படிவம்

ஆய்வினில் பங்கேற்க முறையான சம்மதம் வேண்டி படிவம்

ஆய்வு: தலைப்பு: பான்கிரியாடிக்கோடியோடிநெக்டமி அறுவை சிகிச்சைக்கு முன் ஏற்படும் ப்ரொகால்சிடோனின், சி-ரியாக்டிவ் ப்ரொடீனின் அதிக அளவு மற்றும் அறுவை சிகிச்சைக்கு பின் ஏற்படும் தொற்று சம்பந்த பின்விளைவுகளை கண்டறியும் ஆற்றல் பற்றி அறிய ஒரு ஆய்வு

ஆராய்ச்சி எண்: _____

பொருளின் பெயர்: _____

பிறப்பு / வயது தேதி: _____

(தலைப்பு)

1. நான் கொடுத்திருக்கும் தகவல் தாளை படித்து புரிந்துகொண்டதுடன் எனக்கு எற்பட்ட சந்தேகங்களையும் இன்று _____ கேட்டு தெரிந்துகொண்டேன்.
2. இந்த ஆய்வில் நான் பங்குகெடுக்க முழு மனதோடு சம்மதிக்கிறேன். மேலும் எனக்கு இந்த ஆய்வில் ஒருவேளை விருப்பமின்மை ஏற்பட்டால், எவ்வித காரணம் சொல்லாமல் விலக்கொள்வேன். எனது மருத்துவ பராமரிப்புக்கும், சட்ட உரிமைக்கும் எவ்வித பாதிப்பும் எற்படாது என்பதை அறிவேன்.
3. இந்த ஆய்வின் சார்பாக வேலை செய்பவர்களுக்கும், நெறிமுறை குழு மற்றும் ஒழுங்குமுறை குழுவிற்கும், நான் இந்த ஆய்விலிருந்து விலகிக்கொண்டாள் கூட எனது மருத்துவ விவரங்களை காணவும் அதனை இந்த ஆய்வினில் மட்டுமல்லாது இதனை சேர்ந்த பின்வரும் ஆய்விற்கும் பயன்படுத்த முழு உரிமை உள்ளதென அறிவேன். எனினும் என்னை பற்றிய தகவல்களை இந்த ஆய்வில் சார்ந்தோர் அல்லாது வேறு எவரிடமும் சேராது என அறிவேன்.
4. இதில் கிடைக்கும் தரவுகளையும், முடிவுகளையும் இந்த ஆய்வுக்கு மட்டுமின்றி. ஒருவேளை அறிவியல் சார்ந்து வேறு ஆய்வுக்கும் தேவைப்பட்டால் பயன்படுத்த உரிமை உள்ளது என்பதை அறிவேன்.
5. நான் மேலே குறிப்பிட்டிருக்கும் இந்த ஆய்வில் பங்குகொள்ள சம்மதிக்கிறேன்.

கையொப்பம் (அல்லது பெருவிரல் ரேகை)

தேதி: ___ / ___ / ___

கையொப்பமி டு ம் பெயர்: _____
கையொப்பம்:

அல்லது

பிரதிநிதி: _____

தேதி: ___ / ___ / ___

கையொப்பமி டு ம் பெயர்: _____

ஆராய்ச்சியாளராக கையொப்பம்: _____

தேதி: ___ / ___ / ___

ஆய்வு ஆராய்ச்சியாளராக பெயர்: _____

சாட்சி கையொப்பம் அல்லது பெருவிரல் ரேகை: _____

தேதி: ___ / ___ / ____

பெயர் & சாட்சி முகவரி:

উচ্চতর প্রাক-অপারেটর প্রসালসিটিনিন, সি-রিঅ্যাক্টিভ প্রোটিন এবং পোস্ট-অপারেটিভ pancreaticoduodenectomy – র্ ইন্ফএকটিভ কমপলিকএশণ এর সম্বন্ধ

একটি গবেষণা অধ্যয়নে অংশগ্রহণের জন্য জ্ঞাত কনসেন্ট ফর্ম

অধ্যয়ন সংখ্যা: _____

বিষয়টির প্রাথমিক: _____ বিষয় নাম: _____

হাসপাতাল নম্বর: _____

জন্ম তারিখ / বয়স: _____

ঠিকানা ও ফোন নম্বর: _____

_____

ফোন: _____

(i) আমি নিশ্চিত করছি যে উপরের অধ্যয়নের জন্য আমি _____ এর তথ্যপত্র পড়েছি এবং বুঝতে পেরেছি এবং প্রশ্নগুলি জিজ্ঞাসা করার সুযোগ পেয়েছি। []

(ii) আমি বুঝতে পারি যে আমার গবেষণায় অংশগ্রহন স্বেচ্ছাসেবী এবং যে কোনও কারণে বিনামুল্যে আমি আমার চিকিৎসার বা আইনগত অধিকার ব্যতীত অন্য কোনও কারণে প্রত্যাহার করতে পারি। []

(iii) আমি বুঝতে পারি যে, এথিকস কমিটি এবং নিয়ন্ত্রক কর্তৃপক্ষকে আমার বর্তমান স্বাস্থ্য গবেষণাপত্রের দিকে নজর রাখার জন্য আমার অনুমতির প্রয়োজন হবে না এবং বর্তমান গবেষণা এবং তার সাথে সম্পর্কযুক্ত যে কোনও গবেষণার প্রয়োজন হয়, এমনকি যদি আমি তা থেকে সরে যাই ট্রায়াল। আমি এই অ্যাক্সেসের জন্য সম্মত। যাইহোক, আমি বুঝতে পারি যে আমার পরিচয় তৃতীয় পক্ষের কাছে প্রকাশিত বা প্রকাশিত কোন তথ্য প্রকাশ করা হবে না। []

(iv) আমি এই গবেষণা থেকে উদ্ভূত কোন তথ্য বা ফলাফল ব্যবহার সীমিত করতে সম্মত হন তবে এই ধরনের ব্যবহার শুধুমাত্র বৈজ্ঞানিক উদ্দেশ্যে (গুলি) জন্য। []

(v) আমি উপরের গবেষণায় অংশ নিতে সম্মত হই। []

Fবিষয় / আইনত গ্রহণযোগ্য এর স্বাক্ষর (বা আঙুল ছাপ)

তারিখ: _____ / _____ / _____

স্বাক্ষরকারীর নাম: _____:

তদন্তকারীর স্বাক্ষর: _____

তারিখ: _____ / _____ / _____

অধ্যয়ন তদন্তকারীর নাম: _____

সাক্ষীর স্বাক্ষর বা আঙুলের ছাপ: _____

তারিখ: _____ / _____ / _____

সাক্ষীর নাম ও ঠিকানা: _____

Christian Medical College, Vellore

Department of General Surgery

Use of pre-operative Procalcitonin and C-reactive Protein measurements as biomarker of post-operative infective complications of Pancreaticoduodenectomy

Information sheet

INVITATION:

You are invited to participate in the study, because you are having a surgical procedure at Surgery Department at CMC Hospital, Vellore.

If you take part what will you have to do?

If you agree to participate in this study, your blood sample will be collected and tested for procalcitonin and C-reactive protein values prior to the surgery. All the other treatments that you are already on will be continued and your regular treatment will not be changed during this study.

After surgery in the hospital, you will be monitored for infectious complications on days 3, 7 and 10 after the surgery. No additional procedures will be conducted routinely for this study.

If at any time you experience any problems, you can report this to the doctor.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you because of taking part in this study.

Will you have to pay anything extra to take part in the study?

You will not incur any extra charges for taking part in this study.

What happens after the study is over?

You may or may not benefit from the study that you are a part of. However the conclusions drawn from this study will be useful to manage similar patients in future.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

There will be approximately 50 participants enrolled for the study. You are urged to communicate the health condition to the best of your knowledge

If you have any further questions, please ask

Dr. Nitin Paul Ambrose,
Department of General Surgery Unit III
Christian Medical College Hospital
Vellore, Tamilnadu
632004
Tel: 04162282079
Mobile No. 8825791590
Email: snitinpaul@gmail.com

क्रिस्चियन मेडिकल कॉलेज, वेल्लोर

पैनक्रिएटिकोडोडायनेटोमी ऑपरेशन से पहले अधिक मात्रा में प्रोक्लसिटोनिन और सी-रिएक्टिव प्रोटीन और ऑपरेशन के बाद संक्रमक जटिलताओ के बीच में संबंध

सुचना पत्र।

अगर आप हिस्सा लेंगे तो होन्ग?

अगर आप इस अध्ययन का हिस्सा बनते है थो आप की स्वचिक जानकारी जमा की जाएगी। आप को एक सवाल पत्रक दिया जाएगा जिसमे आप से जोखिम के कारण पूछे जाएंगे।
आप की चिकित्सा पर कोई फर्क नहीं पड़ेगा।
अस्पताल से छुट्टी के बाद आप से फ़ोन द्वारा कुछ सवाल पूछे जयींग।
इस अध्यनन में कोई अतिरक्त प्रक्रिया या ब्लड टेस्ट नहीं किया जाईगे।
अगर आप को किसी भी समय कोई समस्या होती है थो आप किसी भी डॉक्टर को सुचित कर सकते है।

क्या अध्ययन शुरू होने के बाद आप अपना नाम वापस ले सकते है ?
आप की भाग्यदारी स्वचिक है। और आप किसी भी समय अपना नाम वापस ले सकते है। ऐसा करने पर आप की चिकित्सा प्रभावित नहीं होगी।

क्या इस अध्ययन से कोई हानि हो सकती है ?
इस अध्ययन से आप को किसी तरह की हानि नहीं होगी।

क्या इस अध्ययन में भाग लेने केलिए कोई खर्च होगा?
इस अध्ययन में आप को कोई अतिरक्त खर्च नहीं होगा।

अध्ययन की समपथी पर क्या होगा ?

आप को इस अध्ययन से शायद कोई फायदा हो या नहीं हो सकता है । लेकिन इस अध्ययन के परिणाम भविष्य में इस प्रकार की बीमारियों का इलाज करने में काम आएंगे।

क्या मेरी निजी जानकारी का खुलासा किया जायेगा?
इस अध्ययन के परिणाम केवल वैज्ञानिक पत्रिका में प्रकाशित किया जाईगे। लेकिन आप की निजी जानकारी का खुलासा नहीं किया जायेगा। लेकिन आप के स्वस्थ्य रिकॉर्ड इस अध्ययन जुड़े बाकी अधिकारियों द्वारा देखे जाएंगे।
इस अध्ययन में ३०० व्यक्ति धकील किये जाएंगे। आप से विनती है की आप के स्वस्थ के बारे में सम्पूर्ण जानकारी दे।

अगर आप के कोई थो इस डॉक्टर से पूछ सकते है
डॉ. नितिन पॉल एम्ब्रोज़
क्रिस्चियन मेडिकल कॉलेज हॉस्पिटल ,
वेल्लोर , तमिल नाडु ,
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கிறிஸ்துவ மருத்துவ கல்லூரி, வேலூர்

பான்கிரியாடிக்கோடியோடிநெக்டமி அறுவை சிகிச்சைக்கு முன் ஏற்படும் ப்ரொகால்சிடோனின், சி. ரியாக்டிவ் ப்ரொடீனின் அதிக அளவு மற்றும் அறுவை சிகிச்சைக்கு பின் ஏற்படும் தொற்று சம்பந்த பின்விளைவுகளை கண்டறியும் ஆற்றல் பற்றி அறிய ஒரு ஆய்வு

தகவல் தாள்

உங்களுக்கு ஒரு அறிவிப்பு:

நீங்கள் வேலூர் கிறித்துவ மருத்துவ கல்லூரி மருத்துவமனையின் பொது அறுவை சிகிச்சை பிரிவின் கீழ் அறுவை சிகிச்சை மேற்கொள்ள இருப்பதால் உங்களை இந்த ஆய்வில் பங்கேற்க அழைக்கிறோம்.

நீங்கள் இதில் கலந்துகொள்ள என்ன செய்ய வேண்டும் ?

இந்த ஆய்வில் பங்கேற்க ஒப்பு கொண்டால் உங்கள் அடிப்படை விவரங்கள் சேகரிக்கப்படும். அறுவை சிகிச்சைக்கு முன் உங்களுக்கு ப்ரொகால்சிடோனின் மற்றும் சி. ரியாக்டிவ் ப்ரொடீனுக்கான இரத்தப் பரிசோதனை செய்யப்படும். நீங்கள் ஏற்கனவே எடுத்து கொள்ளும் சிகிச்சைகள் அனைத்தும் தொடரும். உங்களின் வழக்கமான சிகிச்சை இந்த ஆய்வின் போது மாற்றப்பட மாட்டாது.

அறுவை சிகிச்சைக்கு பின் ஏற்படும் தொற்று சம்பந்த பின்விளைவுகள், நீங்கள் மருத்துவமனையில் தங்கியிருக்கும் நேரம் அறுவை சிகிச்சைக்கு பின் வரும் 3, 7, மற்றும் 10 ஆகிய நாட்களில் கண்காணிக்கப்படும்.

கூடுதல் நடைமுறைகள் இந்த ஆய்வுக்காக நடத்தப்பட மாட்டாது. ஏதேனும் பிரச்சனை எதிர் கொண்டால் உடனடியாக மருத்துவரிடம் தெரிவியுங்கள்.

தொடங்கியதிலிருந்து இந்த ஆய்வில் இருந்து மீளப்பெற முடியுமா?

இந்த ஆய்வில் உங்கள் பங்களிப்பு முற்றிலும் தன்னார்வற்றது. இதிலிருந்து எப்போதும் விலகிக்கொள்ள முழு அனுமதி உள்ளது. அதனால் உங்கள் வழக்கமான சிகிச்சை பாதிக்காது.

இந்த ஆய்வில் பங்கேற்பதன் மூலம் ஏதேனும் பாதிப்பு ஏற்படுமா?

இந்த ஆய்வில் பங்கேற்பதனால் எந்த பாதிப்பும் எற்படாது.

நீங்கள் இந்த ஆய்வினில் பங்கேற்க ஏதேனும் கூடுதலாக செலுத்த வேண்டுமா?

நீங்கள் இந்த ஆய்வினில் பங்கேற்க கூடுதலாக எதுவும் செலுத்த வேண்டியதில்லை.

ஆய்வு முடிந்த பின்னர் என்ன நடக்கும்?

நீங்கள் ஆய்வினில் பங்கேற்பது உங்களுக்கு பயனளிக்காமல் போகலாம். எனினும் இந்த ஆய்வில் இருந்து வரையப்பட்ட முடிவுகள் எதிர்காலத்தில் இதேபோன்ற நோயாளிகளை நிர்வகிக்க பயனுள்ளதாக இருக்கும்.

உங்கள் தனிப்பட்ட விவரங்கள் இரகசியமாக வைக்கப்படுமா?

ஆய்வின் முடிவு ஒரு பத்திரிக்கையில் அல்லது ஒரு வழங்கல் மூலமாக வெளியிடப்படலாம். உங்கள் தனிப்பட்ட விவரங்கள் மற்றும் அடையாளங்கள் வெளியிடப்படாது. எனினும், உங்கள் மருத்துவ குறிப்புகளை ஆய்வு தொடர்புடைய மக்களால், உங்கள் கூடுதல் அனுமதி இல்லாமல், மதிப்பாய்வு செய்யப்படும் 50 பேர் இந்த ஆய்வில் கலந்து கொள்கின்றனர். உங்கள் முழு மற்றும் சரியான விவரங்களை தருமாறு கேட்டுக்கொள்கிறோம்

எந்த கேள்விகள் இருந்தாலும் நீங்கள் தொடர்பு கொள்ள,

டாக்டர். நிதின் பால் ஆம்பறோல்
பொது அறுவை சிகிச்சை துறை
கிறிஸ்த்துவ மருத்துவ கல்லூரி மருத்துவமனை
வேலூர்,
தமிழ்நாடு
632004
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উচ্চতর প্রাক-অপারেটর প্রসার্সসিটিনিন, সি-রিঅ্যাক্টিভ প্রোটিন এবং পোস্ট-অপারেটিভ pancreaticoduodenectomy – র্ ইন্ফএকটিভ কমপলিকএশণ এর সম্বন্ধ

আমন্ত্রণ:

আপনি অধ্যয়নে অংশগ্রহণের জন্য আমন্ত্রণ জানানো হয়, কারণ আপনি সিএমসি হাসপাতালে জেনারেল সার্জারি বিভাগে অস্ত্রোপচার করছেন.

- আপনি যদি অংশ নেন তাহলে আপনাকে কি করতে হবে?

আপনি যদি এই গবেষণায় অংশ নিতে সম্মত হচ্ছেন, তাহলে অস্ত্রোপচারের পূর্বে আপনার রক্তের নমুনা সংগ্রহ করা হবে এবং প্রক্লেসিটিনিন এবং সি-রিঅ্যাক্টিভ প্রোটিন মূল্যের জন্য পরীক্ষা করা হবে। আপনি ইতিমধ্যে যে অন্যান্য সমস্ত চিকিত্সা অব্যাহত থাকবে এবং আপনার নিয়মিত চিকিত্সা এই গবেষণায় পরিবর্তন করা হবে না।

হাসপাতালে অস্ত্রোপচারের পর অস্ত্রোপচারের পর 3, 7 এবং 10 দিনের মধ্যে আপনার সংক্রামক জটিলতার জন্য নজর রাখা হবে। এই গবেষণা জন্য নিয়মিতভাবে কোন অতিরিক্ত পদ্ধতির পরিচালিত হবে।

যেকোনো সময় যদি আপনি কোনও সমস্যায় পড়েন, তবে আপনি ডাক্তারকে এই বিষয়ে রিপোর্ট করতে পারেন

- এটি শুরু করার পরে আপনি এই গবেষণা থেকে প্রত্যাহার করতে পারেন?

এই গবেষণায় আপনার অংশগ্রহণ সম্পূর্ণরূপে স্বেচ্ছাসেবী এবং আপনি এই গবেষণায় অংশগ্রহণের অনুমতি প্রত্যাহার করার সিদ্ধান্ত নিচ্ছেন মুক্ত। আপনি যদি তা করেন তবে এটি আপনার হাসপাতালে যে কোনো উপায়ে আপনার স্বাভাবিক চিকিত্সা প্রভাবিত করবে না।

- যদি আপনি কোনো অধ্যয়ন সম্পর্কিত আঘাত বিকাশ করবেন তাহলে কি হবে?

এই গবেষণায় অংশ নেওয়ার কারণে আমরা আপনাকে ঘটতে কোন আঘাত আশা করি না।

- অধ্যয়নে অংশ নেওয়ার জন্য আপনাকে কি অতিরিক্ত কিছু দিতে হবে?

আপনি এই গবেষণায় অংশগ্রহণের জন্য কোন অতিরিক্ত চার্জ কাটা হবে না.

- অধ্যয়ন শেষ হওয়ার পরে কি হবে?

আপনি অধ্যয়ন থেকে উপকৃত হতে পারেন বা হতে পারে না যে আপনি একটি অংশ। তবে ভবিষ্যতে এই ধরণের রোগীদের পরিচালনার জন্য এই গবেষণায় উদ্ভূত উপসংহারে সহায়ক হবে।

- আপনার ব্যক্তিগত বিবরণ গোপনীয় রাখা হবে?

এই গবেষণা ফলাফল একটি মেডিকেল জার্নাল প্রকাশিত হতে পারে কিন্তু আপনি কোনো প্রকাশন বা ফলাফল উপস্থাপনা নাম দ্বারা চিহ্নিত করা হবে না। যাইহোক, আপনার মেডিকেল নোট আপনার অতিরিক্ত অনুমতি ছাড়া, অধ্যয়ন সম্পর্কিত ব্যক্তি দ্বারা পর্যালোচনা করা হতে পারে, আপনি এই গবেষণায় অংশগ্রহণ করার সিদ্ধান্ত নিতে হবে।

গবেষণার জন্য প্রায় 50 জন অংশগ্রহণকারী অংশগ্রহণ করবে। আপনি আপনার স্বাস্থ্যের সবচেয়ে ভাল জ্ঞান স্বাস্থ্য অবস্থা যোগাযোগ করার জন্য আহ্বান করা হয়

আপনার যদি আরো প্রশ্ন থাকে, তাহলে জিজ্ঞাসা করুন

ডা। নিতিন পল অ্যামব্রোস,

জেনারেল সার্জারি ইউনিট তৃতীয় বিভাগ

খৃস্টান মেডিকেল কলেজ হাসপাতাল

ভিল্লার, তামিলনাড়ু

632004

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A1 GENNO

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
1	GENNO	SERNO	AGE	GENDER	NONE	HYPERTEN	DIABETES	IHD	ASTHMA	OTHERS	OTHERSPE	HISTOPAT	ELEVPROC	ELEVCRP	ELEVBILIR	BILIARYIN	ERCP	PTBD	PREVIOUS SU
2	1	1	52	1	2	1	2	2	2	2		ADENO CA	2	1	2	2			
3	2	2	69	1	2	1	1	2	2	1	SICK SINU	DISTAL CH	2	2	2	1	1	2	1
4	3	3	38	2	2	2	1	2	2	2		ADENO CA	2	2	2	1	1	2	2
5	4	4	65	2	2	1	1	2	2	1	POLYARTH	ADENO CA	2	1	2	2			
6	5	5	49	1	1							ADENO CA	2	2	2	2			
7	6	6	45	2	2	1	1	2	2	2		ADENO CA	2	2	2	2			
8	7	7	55	1	1							ADENO CA	2	2	2	1	1	2	2
9	8	8	45	2	2	1	1	2	2	2		ADENO CA	2	1	2	2			
10	9	9	43	1	1							ADENO CA	2	2	1	2			
11	10	10	44	1	1							ADENO CA	2	1	1	2			
12	11	11	56	1	1							ADENO CA	2	2	1	2			
13	12	12	48	1	1							DISTAL CH	2	2	1	1	1	2	2
14	13	13	40	2	1							ADENO CA	2	2	1	2			
15	14	14	50	1	2	2	2	2	2	1	RENAL CEI	ADENO CA	2	1	1	1	2	1	2
16	15	15	32	1	1							ADENO CA	2	2	1	1	1	2	2
17	16	16	65	2	2	2	1	2	2	2		DISTAL CH	2	2	1	1	1	2	2
18	17	17	46	2	1							DISTAL CH	2	1	2	1	1	2	1
19	18	18	54	1	2	1	1	1	2	1	HYPOTHYI	ADENO CA	2	2	2	1	1	2	1
20	19	19	60	2	1							ADENO CA	2	1	1	1	1	2	2
21	20	20	68	1	2	2	1	2	2	2		DISTAL CH	2	1	1	1	1	2	2
22	21	21	56	2	1							ADENO CA	2	2	2	2			
23	22	22	50	1	1							ADENO CA	2	2	2	2			
24	23	23	57	1	1							ADENO CA	2	2	2	2			
25	24	24	57	1	1							ADENO CA	2	2	2	1	1	2	1

	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK
1	PREVIOUS	SUSPSEPSI	SUSPSEPSI	SUSPSEPSI	SEPSISDIS	SSITHREE	SUPERFICI	DEEPSSI	ORGANSP/	SSISEVEN	SUPERFICI	DEEPSSI1	ORGANSP/	SSITEN	SUPERFICI	DEEPSSI2	ORGANSP/	SSIDISCHA	SUPERFICI
2		2	2	2	2	2				2				2				2	
3	1	2	1	1	1	2				2				2				2	
4	2	2	1	2	2	2				1	1	2	2	2				2	
5		1	2	2	2	2				2				2				2	
6		2	2	2	2	2				1	1	2	2	2				2	
7		2	2	2	2	2				2				2				2	
8	2	2	1	2	2	2				2				2				2	
9		2	2	2	2	2				2				2				1	1
10		2	2	2	2	2				2				2				2	
11		2	2	2	2	2				2				2				2	
12		2	2	2	2	2				2				2				2	
13	2	2	1	2	2	2				1	1	2	2	1	2	2	1	2	
14		2	2	2	2	2				2				2				1	2
15	2	2	1	1	2	2				2				1	1	2	1	2	
16	2	2	2	2	2	2				2				2				2	
17	2	2	2	2	1	2				2				2				1	1
18	1	2	2	2	2	2				2				1	1	2	2	2	
19	1	2	2	1	1	2				2				1	1	2	2	2	
20	2	2	2	2	2	2				2				2				2	
21	2	2	2	2	2	2				2				2				2	
22		2	2	2	2	2				2				2				2	
23		2	2	2	1	2				2				2				1	1
24		2	2	2	1	2				2				2				2	
25	1	2	2	2	2	2				2				2				1	1

	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB	BC	BD
1	DEEPSSI3	ORGANSP/	PNEUMON	PNEUMON	PNEUMON	PNEUMON	UTITHREE	UTISEVEN	UTITEN	UTIDISCH/	BACTIBILI/	RESURGTH	RESURGSE	RESURGTE	RESURGDI	DURATION	POSTOPAE	INDICATIC	OUTCOME
2			2	2	2	2	2	2	2	2	1	2	2	2	2	22	1	INTRA-OP	DISCHARGED
3			2	1	1	1	2	2	2	2	1	2	2	2	2	28	1	INTRA-OP	MORTALITY
4			2	2	2	2	2	2	2	2	1	2	2	2	2	14	1	HIGH GRA	DISCHARGED
5			2	2	2	2	2	2	2	2	2	2	2	2	2	28	1	HIGH GRA	DISCHARGED
6			2	2	2	2	2	2	2	2	1	2	2	2	2	14	2		DISCHARGED
7			2	2	2	2	2	2	2	2	1	2	2	2	2	18	2		DISCHARGED
8			2	1	2	2	2	2	2	2	1	2	2	2	2	19	1	HIGH GRA	DISCHARGED
9	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	17	2		DISCHARGED
10			2	2	2	2	2	2	2	2	2	2	2	2	2	21	2		DISCHARGED
11			2	2	2	2	2	2	2	2	1	2	2	2	2	16	2		DISCHARGED
12			2	2	2	2	2	2	2	2	1	2	2	2	2	13	2		DISCHARGED
13			2	2	2	2	2	2	2	2	1	2	2	2	2	15	1	HIGH GRA	DISCHARGED
14	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	25	1	INTRA-OP	DISCHARGED
15			2	2	2	2	2	2	2	2	1	2	2	2	2	33	1	INTRA-OP	DISCHARGED
16			2	2	2	2	2	2	2	2	1	2	2	2	2	14	1	RECENT CI	DISCHARGED
17	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	67	1	RECENT CI	DISCHARGED
18			2	2	2	2	2	2	2	1	2	2	2	2	2	19	1	INTRA-OP	DISCHARGED
19			2	1	1	1	2	2	2	2	1	2	2	2	2	54	1	HIGH GRA	MORTALITY
20			2	2	2	2	2	2	2	2	1	2	2	2	2	18	1	RECENT CI	DISCHARGED
21			2	2	2	2	2	2	2	2	1	2	2	2	2	17	1	INTRA-OP	DISCHARGED
22			2	2	2	2	2	2	2	2	1	2	2	2	2	30	2		DISCHARGED
23	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	38	1	HIGH GRA	DISCHARGED
24			2	2	2	2	2	2	2	2	1	2	2	2	2	24	1	HIGH GRA	DISCHARGED
25	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	27	2		DISCHARGED

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
26	25	25	70	2	2	1	1	2	2	2		ADENO CA	2	1	1	1	1	2	2
27	26	26	42	1	1							ADENO CA	2	2	2	2			
28	27	27	64	1	2	1	1	1	2	1	DYSLIPIDE	INTRA-AM	2	1	1	1	1	2	2
29	28	28	48	1	2	1	2	2	2	2		ADENO CA	2	2	2	1	2	2	1
30	29	29	62	1	1							ADENO CA	2	1	2	1	1	2	2
31	30	30	50	2	1							ADENO CA	2	1	1	2			
32	31	31	55	2	2	2	2	2	2	1	HYPOTHYI	ADENO CA	2	2	1	1	1	2	2
33	32	32	56	1	2	1	2	2	2	2		ADENO CA	2	2	2	1	1	2	1
34	33	33	55	1	2	2	1	2	2	2		DISTAL CH	2	2	1	1	1	2	2
35	34	34	57	1	2	1	2	2	2	2		ADENO CA	2	2	2	1	1	2	2
36	35	35	64	1	1							INTRA-AM	1	1	2	2			1
37	36	36	64	1	1							ADENO CA	2	1	2	1	1	2	2
38	37	37	53	1	2	2	1	2	2	2		ADENO CA	2	1	1	1	2	2	1
39	38	38	45	2	2	2	1	2	2	2		ADENO CA	2	1	2	1	1	2	2
40	39	39	58	1	1							INTRA-AM	2	2	2	1	1	2	2
41	40	40	55	1	2	2	2	2	2	1	OLD PULM	SIGNET RI	2	1	1	2			
42	41	41	64	2	2	1	2	2	2	1	DYSLIPIDE	DISTAL CH	2	2	1	2			
43	42	42	55	1	1							ADENO CA	1	1	1	2			
44	43	43	43	1	1							ADENO CA	2	2	1	2			
45	44	44	67	1	2	1	1	1	2	2		INTRA-AM	2	1	2	2			
46	45	45	39	2	2	2	1	2	2	2		ADENO CA	2	1	2	2			
47	46	46	61	1	1							INTRA-AM	2	2	1	1	1	1	2
48	47	47	72	1	1							ADENO CA	2	2	1	2			
49	48	48	54	1	2	1	1	2	2	1	MULTINOI	METASTA	2	2	2	2			
50	49	49	53	1	2	1	2	2	2	1	DYSLIPIDE	INTRA-AM	2	2	1	1	1	2	2

	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL
26	1	2	2	2	2				2				2				1	1	2
27	2	2	2	2	2				2				2				2		
28	2	2	2	1	1	1	2	2	1	1	2	2	1	1	2	2	2		
29	2	1	2	2	2				1	1	2	2	2				2		
30	2	2	2	2	2				2				2				2		
31	1	2	2	2	2				2				2				2		
32	2	2	2	2	2				2				2				2		
33	2	2	2	2	2				2				2				2		
34	2	2	2	1	2				2				2				1	2	2
35	2	2	2	2	2				1	1	2	2	1	1	2	2	1	1	2
36	2	2	2	2	1	1	2	2	1	1	2	2	1	1	2	2	1	2	2
37	2	2	2	2	1	1	2	2	1	1	2	2	1	1	2	2	1	1	2
38	2	2	2	2	1	1	1	1	2				2				2		
39	2	2	2	2	2				1	1	2	2	1	1	2	2	2		
40	2	2	2	1	2				1	1	2	2	1	1	2	2	1	1	2
41	2	2	2	2	2				2				2				2		
42	1	1	1	2	2				2				1	2	2	1	2		
43	2	2	2	2	2				2				1	2	2	1	1	2	2
44	1	2	2	2	2				1	1	2	2	1	1	2	2	2		
45	1	2	2	2	1	1	2	2	1	1	2	2	1	1	2	2	2		
46	1	2	2	2	1	1	2	2	1	1	2	2	2				2		
47	2	2	2	2	2				2				1	1	2	2	2		
48	2	1	1	1	1	1	2	2	1	1	2	2	1	1	2	1	1	1	2
49	2	2	1	2	2				2				1	2	2	1	2		
50	2	2	2	2	2				1	1	2	2	1	1	2	2	2		

	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB	BC	BD
26	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	30	1	RECENT CI	DISCHARGED
27			2	2	2	2	2	2	2	2	2	2	2	2	2	17	1	PERSISTEN	DISCHARGED
28			2	2	2	2	2	2	2	2	1	2	2	2	2	22	1	HIGH GRA	DISCHARGED
29			2	2	2	2	2	2	2	2	2	2	2	2	2	11	1	HIGH GRA	DISCHARGED
30			2	2	2	2	2	2	2	2	1	2	2	2	2	14	2		DISCHARGED
31			2	2	2	2	2	2	2	2	2	2	2	2	2	23	1	HIGH GRA	DISCHARGED
32			2	2	2	2	2	2	2	2	2	2	2	2	2	28	1	INTRA-OP	DISCHARGED
33			2	2	2	2	2	2	2	2	1	2	2	2	2	16	2		DISCHARGED
34	2	1	2	2	2	2	2	2	2	2	2	2	2	2	1	21	1	RECENT CI	DISCHARGED
35	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	26	1	HIGH GRA	DISCHARGED
36	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	29	2		DISCHARGED
37	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	15	2		DISCHARGED
38			2	2	2	2	2	2	2	2	1	2	2	2	2	17	2		DISCHARGED
39			2	2	2	2	2	2	2	2	1	2	2	2	2	15	1	HIGH GRA	DISCHARGED
40	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	33	1	SEPSIS WI	DISCHARGED
41			2	2	2	2	2	2	2	2	1	2	2	2	2	13	2		DISCHARGED
42			2	2	2	2	2	2	2	2	1	2	2	1	2	26	1	SEPSIS WI	DISCHARGED
43	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	25	1	SSI	DISCHARGED
44			2	2	2	2	2	2	2	2	1	2	2	2	2	18	1	HIGH GRA	DISCHARGED
45			2	2	2	2	2	2	2	2	2	2	2	2	2	18	1	HIGH GRA	DISCHARGED
46			2	2	2	2	2	2	2	2	2	2	2	2	2	24	1	INTRA-OP	DISCHARGED
47			2	2	2	2	2	2	2	2	1	2	2	2	2	15	2		DISCHARGED
48	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	41	1	SEPSIS WI	DISCHARGED
49			2	2	2	2	2	2	2	2	2	2	2	1	2	25	1	HIGH GRA	DISCHARGED
50			2	2	2	2	2	2	2	2	1	2	2	2	2	11	2		DISCHARGED