

Evaluation of Procalcitonin (PCT) As a Marker of Infection in Early Post Living Donated Liver Transplant Period.

Eman Ibrahim El-Desoki Mahmoud (✉ eman18350@gmail.com)

National Hepatology and tropical Medicine Research Institute (NHTNMRI) <https://orcid.org/0000-0002-0882-7016>

Mohammad A. Algendy

Ain Shams University

Adel M. Al-Ansary

Ain Shams University

Maissa K. Noaman

National cancer institute, Cairo university

Research

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Abstract

Background: Procalcitonin (PCT) has been increasingly used as a biomarker of bacterial infection and as a tool to guide antimicrobial therapy. Despite its increased use, data in patients with solid organ transplants are limited.

The study aim is to assess the frequency of rising procalcitonin associated with infectious complications in immunosuppressed living donated liver transplantation.

Methods: A single center, retrospective observational study. Preoperative patients' demographic data, operative, anesthetic data and postoperative clinical course are analyzed till discharge from intensive care unit.

Results: Sixty patients were classified according to the culture results' into a positive culture group & a negative one, then following up sepsis variables in each group. Total leukocyte count (TLC) and procalcitonin (PCT) were high in the positive culture group in the first 4 and 5 days respectively and was statistically significant (P -value < 0.05).

PCT at a cutoff value ≥ 9 ng/ml had higher specificity, especially on day three postoperative (90.7%). The TLC cutoff value of $\geq 17.3/\text{mm}^3$ on day one; had the specificity of > 90%.

Conclusions: following up PCT level on day one with TLC is essential and will help to detect sepsis and guide early antimicrobial initiation post liver transplantation.

Trial registration: NHTMRI, NCT03389360. Registered 7 February, 2018,

<https://register.clinicaltrials.gov/prs/app/action/SelectProtocol?sid=S000706F&selectaction=Edit&uid=U0003W0U&ts=2&cx=fwyacz>

Introduction:

Clinical signs of infection in immunosuppressed LDLTR are difficult to be determined.¹ Microbiological cultures, identifying pathogenic agents are the gold standard for the diagnosis of infection, but require time, which leads to a substantial diagnostic and therapeutic delay.²

Moreover, microbiological evidence of infection might not develop simultaneously with signs of clinically significant infections (CSIs). In addition, serum levels of common biochemical markers such as C-reactive protein (CRP) or the total leukocyte count (TLC) are frequently inaccurate; their increase might reflect graft rejection rather than infection. Thus, there is an obvious need for an accurate marker that can differentiate the infectious from noninfectious complications in LTx recipients.³

Procalcitonin (PCT) has been increasingly used as a biomarker of bacterial infection and as a tool to guide antimicrobial therapy. Despite its increased use, data in patients with solid organ transplants are

limited. Even without the presence of infection, PCT increases as a result of surgical procedures during transplantation, implantation of devices, and use of induction immunosuppressive therapy.⁴

Aim Of The Work:

The study aim is to determine the association between rising serum procalcitonin and the occurrence of infectious complications in immunosuppressed LDLTRx.

Patients & Methods:

Study type:

This is a single center, retrospective study in ICU-NHTMRI (Clinicaltrials.gov registration number: NCT03389360).

Inclusion criteria:

All patients that were included were adults aged between 18 to 65 years old who are recipients of living donated liver transplantation at the Department of Liver Transplant, between January 2015 and January 2018 and with no contraindications for early (immediately postoperative) immunosuppression.

Exclusion criteria:

Patients were excluded from the study if they were repeatedly admitted to ICU after first admission.

***Early post-transplant infections:**

Early infections will be defined from 0–30 days after transplant. Bacteria and yeast are the most frequent pathogens in the first 30 days after transplant. While post-transplant period will be defined as the period since transplant till less than 4 weeks.⁴

Symptoms & signs of infection post liver transplant may include generally; malaise, chills, low grade fever, and rigor. However because of their immunosuppressed state, transplant recipients may not manifest fever as readily as the general population. Specific signs according to the site of infection include e.g. pulmonary infections; cough, dyspnea, and chest pain. Urinary tract infections; dysuria, pyuria, and hematuria, while intra-abdominal & surgical site infections; abdominal pain, erythema at incision site, and/or elevated liver enzymes.⁵

Study Design:

The data in this study was collected from the medical records; showing that all patients transferred from operative theatre to the ICU were sedated, intubated, and ventilated. They received empiric antimicrobial prophylaxis (piperacillin-tazobactam; ICU\ICU Protocol\Liver transplant protocol\Adult LT\Protocol for ICU

management of.docx) upon admission and early immunosuppression (from day zero) according to the clinical practice guidelines in our center; they received Tacrolimus with Methyl Prednisolone with/without Mycophenolate Mofetil. Preoperative patients' demographic data were obtained. Also, Child-Pugh score prior transplant, and the primary cause of liver transplant.

Operative and anesthetic details as; operation time, units of blood, blood products transfusion, ischemic time, type of preservatives used, back table procedures, extra-hepatic procedure, and graft to recipient weight ratio (GRWR) were recorded.

Postoperative patient evaluation that included; Sequential Organ Failure Assessment (SOFA) on admission and /48h, hemodynamic monitoring, including hourly measurement of heart rate, mean arterial pressure (MAP), temperature, central venous pressure (CVP), arterial oxygen saturation (SaO₂), daily total volume of fluid infused, daily urine output, fluid balance daily, blood gas analysis / 6h, and daily mean values were recorded till hospital discharge.

Routine laboratory work-up included biochemical markers of liver, kidney function and hematological parameters (complete blood count and coagulation profile) were obtained.

Also routine patient evaluation for infection was obtained from the medical records through scheduled measurements of PCT every other day during ICU stay and upon needed during hospital stay. Other markers of infections were recorded till hospital discharge as C-reactive protein (CRP) every other day, daily total leukocyte count (TLC) and band cells %.

Microbiological evidence of infection was confirmed by cultures that were followed from the medical records as they were regularly sampled every 48-72 hours during ICU stay and upon any clinical, laboratory biomarker (TLC, band cells, CRP, and PCT), and/or radiological findings (e.g. pulmonary infiltrates in chest X-ray, cholangitis or hepatic abscess by CT abdomen) suggestive of infection.

Management of suspected infection as shown by the medical records; when PCT value was elevated with clinical, radiological and/or laboratory evidence of infection (TLC, CRP, band %), culture from the suspected site of infection was withdrawn. If the source of infection was not evident, cultures from blood, urine, sputum, surgical wound, drains and nasal swab were obtained and empiric antimicrobial against gram positive bacteria was added (as indicated by the local antibiogram). While the management of proven infection will be a culture based antimicrobial initiation.

Primary outcome measures:

The primary outcome of the study is to determine the association between rising procalcitonin and the occurrence of infectious complications in immunosuppressed LDLTR.

Secondary outcome measures:

To detect the non-infectious causes of rising procalcitonin post living donated liver transplant, its relation to the length of ICU and hospital stay.

Statistical Analysis:

Data were analyzed using SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL, USA) version 21 for Microsoft Windows. Numerical data were presented as mean \pm SD, median and range as appropriate. Categorical data were presented as frequency and percentage. Numerical data were explored for normality using Kolmogorov-Smirnov test and Shapiro-Wilk test. Comparisons between the two groups for normally distributed numerical variables were done using the Student's t-test while for non-parametric numeric variables Mann-Whitney test was used. Associations between qualitative data were done using Chi-square test or Fisher's exact test as appropriate. The receiver operating characteristic (ROC) curve was conducted for PCT to calculate sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Probability (p-value) equal or less than 0.05 is considered significant.

Results:

Patients' demographic variables:

Sixty patients enrolled in the study underwent liver transplantation. They were categorized mainly according to the culture results withdrawn in the early postoperative care (in the first ICU admission) into; the positive culture group and negative culture group. Seventeen patients had positive culture results and the remainder had negative results.

The same patient may have more than one positive culture specimen. Positive culture results were mainly withdrawn from sputum (N=10/17), nasal swabs (N= 6/17), Drain (N= 2/17), and urine (N= 1/17). The microorganisms isolated from cultures was; gram positive (N=8/17, 47%), gram negative organism (N= 6/17, 35%), and multi-drug resistant organism (N=3/17, 17.65%).

The age of positive culture group range (mean \pm SD), (49.3 \pm 9.2) years old and in the negative culture group was (45.9 \pm 10.6) years old and it was statistically not significant (*P*-value= 0.285). The body mass index (BMI) in the positive and negative culture groups, consequently was (mean \pm SD); (35.9 \pm 43.1), (26.6 \pm 2.6), and (*P*-value= 0.163).

Comparison of the remaining demographic data (Table 1) could not be performed due to either large number of groups or small number of patients per group.

Anesthetic & operative variables:

Regarding to the type of graft, it was mainly right lobe graft (N= 40/43, 93%), and left lobe graft was (N= 3/43, 7%) in the negative culture group. While in the positive culture group, right lobe graft was (N=13/17, 76.5%), and left lobe graft was (N= 4/17, 23.5%). Patients need extrahepatic procedures as splenectomy, splenic artery ligation, and left inguinal hernia repair were (N= 8/43, 18.6%) in the negative culture group

and were (N= 7/17, 41.2%) in the positive culture group. Porto-caval shunt was done in the negative culture (N= 11/43, 25.6%) & (N= 9/17, 52.9%) in the positive culture group.

In table 2 (anesthetic and operative variables), only the amount of blood loss and blood transfused intraoperatively had the association with positive culture results and they were statistically significant (*P-value* <0.05).

Laboratory variables:

Regarding the laboratory variables (shown in table 3) used to help diagnose infection; only total leukocyte count (TLC) was elevated in the positive culture group in comparison to the negative culture one and was statistically significant (*P-value* <0.05) till the fourth day postoperative. While band cells% & CRP was not statistically significant in both groups.

Procalcitonin assessed in both groups (Table 4); it was higher in the positive culture group than in the negative one on days 1, 3, and 5 postoperative and was statistically significant (*P-value* <0.05).

Table 5, showed the cutoff value of PCT in (ROC) on day one postoperative was ≥ 9 ng/ml, it had the sensitivity of 52.9% while the specificity of 83.7%. The positive predictive value (PPV) was 56.3%, the negative predictive value (NPV) was 81.8%, and the overall accuracy of the test was 75%.

According to the cutoff of PCT ≥ 9 ng/ml, TLC cutoff value on day one was determined to be of $\geq 17.3/\text{mm}^3$. It had the specificity of > 90%, sensitivity of 47.1%, PPV of 66.7%, NPV of 81.3% and the overall accuracy of the test was 78.3%.

Postoperative course:

Regarding the need for blood transfusion postoperative was (N= 17/43, 39.5%) in the negative culture group while in the positive culture group was (n= 7/17, 41.2%). Only four patients received fresh frozen plasma postoperative; two patients in each group. In the positive culture group, each given 600ml and in the negative culture group, each given 300ml. While one patient need platelet transfusion (600ml) postoperative and was in the positive culture group.

The need for re-ventilation after extubation was (N= 1/43, 2.3%) in the negative culture group and was (N= 1/17, 5.9%) in the positive culture group. One patient (2.3%) developed renal impairment requiring renal replacement therapy in the negative culture group while it was (0.0%) in a positive culture group.

Therefore, the noninfectious complications developed and recorded to be studied in this research was low enough to allow the statistical analysis.

Regarding the impact of PCT at the cutoff value of ≥ 9 and < 9ng/ml on ICU stay, was significant only on day three as expressed by median (Min-Max), were 7(4-17) days and 6(2-13) days respectively and it was

statistically significant (P -value= 0.05). While the impact of PCT at the cutoff value of ≥ 9 ng/ml on hospital stay, was not statistically significant (P -value > 0.05).

Discussion:

Diagnosis of infection post solid organ transplantation should be as early as possible, as the delay of antimicrobial administration will lead to potentially long term effects on the morbidity and mortality. While initiation of antimicrobials to treat colonization will expose both patients & centers to resistance, increase cost, and drug side effects.⁴

PCT is used as a marker of early bacterial translocation in some group of patients.⁶ However, in solid organ transplantation (SOT), PCT levels may be affected by other factors e.g. the surgical procedure, underlying disease, and immunosuppression used that interfere with its interpretation & makes it more challenging in the transplant group.⁷⁻⁹

Procalcitonin is the precursor molecule of human calcitonin, its molecular weight is about 13KD & with no hormonal activity.¹⁰ In normal individuals, it is present in very low concentration about 0.5ng/ml. However, during bacterial infection & multi-organ failure, it will exceed this value to reach 100ng/ml.¹¹ Procalcitonin has half-life about 24hours while calcitonin has a shorter half-life about 10-20 minutes.¹⁰

Regarding the primary outcome of the study is to determine the association between rising serum procalcitonin and infectious complications in immunosuppressed LDLTRx.

So, the patients were classified into the positive culture group & the negative one then retrospectively following up the sepsis laboratory variables in each group (mainly TLC, Band cells%, CRP and PCT) to allow finding simple, rapid marker that would be suitable post LDLTX to diagnose clinically significant infections.

PCT levels were higher with statistically significant (P -value < 0.05) in the positive culture group from day one till day 5 postoperative. The cutoff value that was highly specific to infection, ≥ 9 ng/ml (specificity of 83.7% on day one postoperative and specificity was highest on day three 90.7%).

Early post LTx, the cutoff value of PCT that would be associated with infection has not been defined, depending on the type of allograft and the extent of the surgery, so PCT levels may increase or remain stable after transplantation.¹²

Perrakis et al. found that post LTx, PCT values > 5ng/mL increased 11.7 times the odds of developing complications e.g. infectious complications, renal failure, bleeding, and respiratory failure.¹³

As the literature in the setting of liver or kidney transplantation is not extensive, so, in heart transplant recipients, PCT with cutoff values > 0.6ng/ml was correlated with local infection while in multiple infections & sepsis PCT levels were substantially elevated to (7.3-22.4ng/ml).¹⁴

Chen et al. showed that PCT can be used to predict catheter-related bloodstream infections post liver transplantation (LTx), where the PCT values $> 3.1\text{ng/ml}$ had a sensitivity of 72% and specificity of 87% to predict the infection.¹⁵

Study of lung transplant patients, using the PCT to differentiate between colonization & infection where PCT was mildly elevated in colonization with cutoff value <2 and $>0.5\text{ng/ml}$.^{16,17}

Kunz et al. measured PCT immediately before and daily after liver transplantation in 22 patients and found that all patients had increased PCT levels without clinical signs of infection.¹⁸

Prieto et al. reported a cutoff value of 1.92ng/mL as a predictor for both infectious and non-infectious complications with a sensitivity of 95.6% and specificity of 89.5%, although those who suffered complications had worse preoperative criteria and higher Child–Pugh scores.¹⁹

Regarding to PCT dynamics, in the study of heart and lung recipients, PCT level was high in the first 24hours postoperative & it remained high in those patients who suffered infectious complications,²⁰⁻²² PCT Level reached (mean \pm SD), ($54.6 \pm 8.8\text{ng/ml}$) in patients with complications, compared to ($9.1 \pm 9.3\text{ng/ml}$) in patients without complications. At the same time TLC and CRP could not differentiate between patients with infections from those without.^{20,21} Thus, it is advised to follow PCT level after 24h reading post-transplant.

In this study, TLC was higher in the positive culture group and statistically significant (P -value < 0.05) from day one till the fourth day postoperative. TLC cutoff value of $\geq 17.3/\text{mm}^3$ on day one; had the specificity of $> 90\%$. Therefore & according to our sample, both PCT & TLC can help early rapid diagnosis of infection till culture results will be available. While both CRP and band cells% were not differ in between the positive culture group and the negative one.

Although CRP results were high in both groups of culture results but were not statistically significant, this rise could be related to the surgery, underlying disease, or blood transfusion.

CRP level and leukocyte counts could not be able to differentiate between infectious and non-infectious complications at any time point.^{19,20}

Regarding outcome at PCT cutoff value of $\geq 9\text{ng/ml}$, ICU stay on day three was correlated with that cutoff & was statistically significant (P -value= 0.05). While hospital stay was not differ at either PCT cutoff value of $\geq 9\text{ng/ml}$ or $< 9\text{ng/ml}$ & it might be due to the small number of patients enrolled.

Study done for heart transplant recipients, found that increased PCT level to $> 10\text{ng/mL}$ was associated with poor outcomes.²²

While following the demographic, anesthetic and operative variables; the amount of blood loss and amount of blood transfused were correlated with the positive culture results and they were statistically

significant (P -value= 0.001 & 0.029 respectively). These results matches another study done where dominant elective abdominal surgeries were included and showed that the number of units of blood transfused was directly proportional to the incidence of complications and mortality; infectious complications represented the highest incidence 36.3%.²³

Therefore, the surgical and anaesthetic techniques that aid to limit blood loss and blood transfusion intraoperative will positively affect the incidence of postoperative infectious complications.

Conclusion:

In conclusion, according to the sample size in this study; following up both PCT level and TLC on day one is essential and will help to detect patients that have sepsis or multiple infections to guide the early antimicrobial initiation till culture results available.

According to the specificity of cutoff values of both PCT and TLC, we conclude that in low income countries and in the same population we can use TLC without PCT level on day one post LTx with a cutoff value $\geq 17.3/\text{mm}^3$ to help early diagnosis of infection and administration of antimicrobials.

Recommendations is for further researches with larger sample size in liver transplant recipients to investigate any difference in the cutoff value in comparison to this research and to search about the impact of using PCT on hospital stay, correlation with noninfectious complications, and mortality.

Abbreviations

NHTMR

National Hepatology & Tropical Medicine Research Institute, **ICU**:Intensive care unit, **LDLTRx**:Living donated liver transplant recipients, **LT**:Liver transplant, **TLC**:Total leukocyte count, **PCT**:Procalcitonin, **GRWR**:Graft recipient weight ratio, **SOFA**:Sequential organ failure assessment, **MAP**:Mean arterial pressure, **CVP**:Central venous pressure, **SaO₂**:Arterial oxygen saturation, **CRP**:C-reactive protein.

Declarations

Ethics approval and consent to participate:

The study file submitted for approval by NHTMRI IRB. Due to the retrospective nature of the research, the research participants' medical data were collected anonymously from patients' file by a third party. Reconstructing of patients will be difficult and will hinder research conduction, so we request the waiving of informed consent from the IRB. The study had the approval on February 2018.

This study was conducted in accordance with the declaration of Helsinki.

Consent for publication: Not applicable

Availability of data and materials: Not applicable.

Competing interests: None

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Authors' contributions:

Eman I. El-Desoki Mahmoud performed conceptualization, data gathering and writing the manuscript.

Maissa K. Noaman performed the statistical analysis.

Mohammad A. Algendy performed conceptualization.

Adel M. Al-Ansary supervised the project.

All authors read and approved the final manuscript.

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References

1. Maartje AJ, van den Broek SWM, Olde Damink B, Winkens CE, Broelsch, et al. Procalcitonin as a Prognostic Marker for Infectious Complications in Liver Transplant Recipients in an Intensive Care Unit. *AASLD Liver Transpl.* 2010;16:402–10.
2. Garner JS, Jarvis WR, Emori TG, et al. CDC definitions for nosocomial infections. *Am J Infect Control.* 1988;16:128–40.
3. Levy MM, Fink MP, Marshall JC, et al (2003): International Sepsis Definitions Conference. *Crit Care Med* 31:1250–1256.
4. Sandkovsky U, Kalil AC, Florescu DF. The use and value of procalcitonin in solid organ transplantation. *Clin Transplant.* 2015;29:9689–696. DOI:10.1111/ctr.12568.
5. Erika D. Lease. (2015). Infections and sepsis after liver transplantation. *Contemporary Liver Transplantation* DOI 10.1007/978-3-319-05543-5\$419-1.
6. GILBERT DN. Use of plasma procalcitonin levels as an adjunct to clinical microbiology. *J Clin Microbiol.* 2010;48:2325.

7. FOUSHEE JA, HOPE NH, GRACE EE. Applying biomarkers to clinical practice: a guide for utilizing procalcitonin assays. *J Antimicrob Chemother.* 2012;67:2560.
8. ADAMIK B, KUBLER-KIELB J, GOLEBIEWSKA B, et al. Effect of sepsis and cardiac surgery with cardiopulmonary bypass on plasma level of nitric oxide metabolites, neopterin, and procalcitonin: correlation with mortality and postoperative complications. *Intensive Care Med.* 2000;26:1259.
9. ZAZULA R, PRUCHA M, TYLL T, et al. Induction of procalcitonin in liver transplant patients treated with anti-thymocyte globulin. *Crit Care.* 2007;11:R131.
10. Le moulllec JM, Jullienne A, Chenais J, et al. The complete sequence of pre-procalcitonin. *FEBS.* 1984;167:93–7.
11. Nylen ES, O'Neill W, Jordan MH, et al. Serum procalcitonin as an index of inhalation injury in burns. *Horm Melab Res.* 1992;24:439–42.
12. JARESOVA M, STRIZ I, CERMAKOVA J, et al. Serum procalcitonin concentrations in transplant patients with acute rejection and bacterial infections. *Immunol Lett.* 1999;69:355.
13. PERRAKIS A, YEDIBELA S, SCHELLERER V, et al. Procalcitonin in the setting of complicated postoperative course after liver transplantation. *Transplant Proc.* 2010;42:4187.
14. HAMMER C, FRAUNBERGER P, MEISER B, et al. Procalcitonin a new marker for diagnosis of acute rejection and nonviral infection of heart and lung transplant patients. *Transplant Proc.* 2001;33:2204.
15. CHEN J, WANG Y, SHEN Z, et al. Early diagnostic value of plasma PCT and BG assay for CRBSI after OLT. *Transplant Proc.* 2011;43:1777.
16. ZEGLEN S, WOJARSKI J, WOZNIAK-GRYGIEL E, et al. Procalcitonin serum concentration during *Pneumocystis jiroveci* colonization or *Pseudomonas aeruginosa* infection/colonization in lung transplant recipients. *Transplant Proc.* 2009;41:3225.
17. ZEGLEN S, SIOLA M, WOZNIAK-GRYGIEL E, et al. Procalcitonin serum concentration in lung transplant recipients during mold colonization or infection. *Transplant Proc.* 2011;43:3089.
18. KUNZ D, PROSS M, KONIG W, et al. Diagnostic relevance of procalcitonin, IL-6 and cellular immune status in the early phase after liver transplantation. *Transplant Proc.* 1998;30:2398.
19. PRIETO B, GONZALEZ-PINTO I LLORENTEE, et al. Plasma procalcitonin measured by time-resolved amplified cryptate emission (TRACE) in liver transplant patients. A prognosis marker of early infectious and non-infectious postoperative complications. *Clin Chem Lab Med.* 2008;46:660.
20. MADERSHAHIAN N, WITTEWERT T, STRAUCH J, et al. Kinetic of procalcitonin in the early postoperative course following heart transplantation. *J Card Surg.* 2008;23:468.
21. SUBERVIOLA B, CASTELLANOS-ORTEGA A, BALLESTEROS MA, et al. Early identification of infectious complications in lung transplant recipients using procalcitonin. *Transpl Infect Dis.* 2012;14:461.
22. STAEHLER M, HAMMER C, MEISER B, et al. Procalcitonin: a new marker for differential diagnosis of acute rejection and bacterial infection in heart transplantation. *Transplant Proc.* 1997;29:584.

23. João Manoel Silva Junior. Cezario TA, Toledo DO, et al (2008). Complications and Prognosis of Intraoperative Blood Transfusion. Rev Bras Anesthesiol ARTIGO CIENTÍFICO 58: 5: 447–61.

Tables

Table 1. Demographic variables & Co-morbidities.

| | Positive culture (N=17) | | Negative culture (N=43) | | P-value |
|-----------------------------|----------------------------|------|-------------------------|------|---------|
| | N | % | N | % | |
| Gender (Row%) | | | | | |
| Male | 13 | 27.7 | 34 | 72.3 | 0.826 |
| Female | 4 | 30.8 | 9 | 69.2 | |
| Co-morbidities | | | | | |
| Diabetes mellitus | 2 | 11.8 | 7 | 16.3 | |
| Hypertension | 1 | 5.9 | 2 | 4.7 | |
| Autoimmune | 0 | 0.0 | 1 | 2.3 | |
| Overlap syndrome | 1 | 5.9 | 0 | 0.0 | |
| Smoking status | | | | | |
| Non-smoker | 13 | 76.4 | 38 | 88.4 | |
| Ex-smoker | 2 | 11.8 | 3 | 7.0 | |
| Current smoker | 2 | 11.8 | 2 | 4.6 | |
| Child-Pugh score | | | | | |
| A5 | 0 | 0.0 | 4 | 9.3 | |
| A6 | 0 | 0.0 | 4 | 9.3 | |
| B8 | 1 | 5.9 | 2 | 4.6 | |
| B9 | 2 | 11.8 | 8 | 18.6 | |
| C10 | 8 | 47.0 | 11 | 25.6 | |
| C11 | 4 | 23.5 | 10 | 23.3 | |
| C12 | 1 | 5.9 | 3 | 7.0 | |
| C13 | 1 | 5.9 | 1 | 2.3 | |
| Cause of transplant* | | | | | |
| Viral | 14 | 82.4 | 28 | 65.1 | |
| HCC | 4 | 23.5 | 16 | 37.2 | |
| Others** | 3 | 17.6 | 8 | 18.6 | |

*The same patient may have more than one cause for transplant.

**Others include; autoimmune, cryptogenic and congenital.

The comparison could not be performed due to either large number of groups or small number of patients per group.

Table 2. Anesthetic and operative variables.

| | Positive culture | Negative culture | P-value |
|--|-------------------------|-------------------------|----------------|
| | Mean ±SD | Mean ±SD | |
| | Median (Min-Max) | Median (Min-Max) | |
| Hours of surgery | | | |
| | 11.8±1.2 | 12.0±1.0 | 0.528 |
| | 12.0 (8.3-14.0) | 12.0 (9.0-16.0) | |
| Amount of blood loss intraoperative (ml) | | | |
| | 2550.0±1008.0 | 1493.0±931.4 | 0.001 |
| | 2700.0 (800.0-4000.0) | 1100.0 (200.0-4000.0) | |
| Amount of blood given intraoperative (ml) | | | |
| | 1253.3±632.6 | 868.8±588.9 | 0.029 |
| | 1050.0 (350.0-2350.0) | 700.0 (8.0-2350.0) | |
| FFP* given intraoperative (ml) | | | |
| | 777.0±307.3 | 696.6±300.4 | 0.552 |
| | 600.0 (450.0-1500.0) | 600.0 (6.0-1650.0) | |
| Platelets given intraoperative (ml) | | | |
| | 466.7±231.0 | 760.0±288.1 | 0.393 |
| | 600.0 (200.0-600.0) | 600.0 (500.0-1200.0) | |
| Cryo given intraoperative (ml) | | | |
| | 111.7±35.9 | 107.5±48.8 | 0.526 |
| | 100.0 (40.0-170.0) | 100.0 (12.0-280.0) | |
| Warm ischemic time (min.) | | | |
| | 50.1±15.3 | 53.6±25.0 | 0.921 |
| | 45.0 (30.0-100.0) | 45.0 (2.0-120.0) | |
| Cold ischemic time (min.) | | | |
| | 76.2±40.6 | 81.6±43.8 | 0.639 |
| | 70.0 (25.0-180.0) | 75.0 (24.0-205.0) | |
| GRWR | | | |

| | | | |
|--|---------------|---------------|-------|
| | 0.9±0.2 | 1.0±0.2 | 0.221 |
| | 0.8 (0.6-1.4) | 0.9 (0.7-2.0) | |

*FFP= fresh frozen plasma.

From the previous table, only the amount of blood loss & blood transfused intraoperative had the association with positive culture results and they were statistically significant (*P-value* <0.05).

Table 3. Laboratory variables, TLCs, band cells% and CRP.

| | Positive culture | Negative culture | P-value |
|-------------------------------|-------------------------|-------------------------|----------------|
| | Mean \pm SD | Mean \pm SD | |
| | Median (Min-Max) | Median (Min-Max) | |
| TLC1 (/mm³) | | | |
| | 16.7 \pm 6.8 | 11.3 \pm 5.1 | 0.003 |
| | 15.3 (5.7 -34.5) | 10.1 (4.1-29.0) | |
| TLC2 | | | |
| | 18.9 \pm 10.3 | 12.4 \pm 8.2 | 0.010 |
| | 16.4 (5.7-38.0) | 10.0 (2.8-37.7) | |
| TLC3 | | | |
| | 16.6 \pm 9.4 | 10.2 \pm 6.8 | 0.015 |
| | 13.9 (3.2-33.0) | 8.3 (0.5-26.3) | |
| TLC4 | | | |
| | 17.8 \pm 18.8 | 8.3 \pm 4.7 | 0.002 |
| | 13.9 (2.2-85.9) | 7.7 (1.1-19.7) | |
| TLC5 | | | |
| | 13.6 \pm 10.8 | 7.6 \pm 3.6 | 0.071 |
| | 10.9 (1.9-41.7) | 7.2 (1.4-15.7) | |
| Band 1 (%) | | | |
| | 13.9 \pm 5.3 | 15.9 \pm 7.5 | 0.421 |
| | 14.0 (5.0-28.0) | 14.0 (1.0-37.0) | |
| Band 2 | | | |
| | 15.8 \pm 7.5 | 16.2 \pm 5.4 | 0.430 |
| | 13.0 (5.0-33.0) | 16.5 (6.0-27.0) | |
| Band 3 | | | |
| | 13.9 \pm 5.5 | 14.3 \pm 5.3 | 0.732 |
| | 13.0 (7.0- 22.0) | 14.0 (4.0-25.0) | |
| Band 4 | | | |

| | | | |
|----------------------|-------------------------------|-------------------------------|-------|
| | 14.7±7.9 14.0 (4.0-35.0) | 12.1±5.6 11.0 (3.0-27.0) | 0.257 |
| Band 5 | | | |
| | 9.8±4.8 10.0 (1.0-18.0) | 9.8±5.7 8.0 (3.0-28.0) | 0.529 |
| CRP 1 (mg/dl) | | | |
| | 27.8±23.7 24.0 (2.5-72.3) | 23.1±18.2 16.1 (5.8-98.4) | 0.863 |
| CRP 3 | | | |
| | 44.9±28.3 39.4 (6.0-116.0) | 32.2±20.2 25.1 (6.0-105.8) | 0.094 |
| CRP 5 | | | |
| | 22.3±17.3 18.2 (5.9-76.0) | 24.3±20.8 14.0 (5.8-79.0) | 0.844 |

Regarding the laboratory variables used to help diagnosing infection; only total leukocyte count (TLC) was elevated in the positive culture group in comparison to the negative culture one & was statistically significant (P -value <0.05) till the fourth day postoperative. While band cells% & CRP was not statistically significant in both groups.

Table 4. PCT value in association with the culture result.

| | Positive culture | Negative culture | P-value |
|---------------------|-------------------------|-------------------------|----------------|
| | Mean ±SD | Mean ±SD | |
| | Median (Min-Max) | Median (Min-Max) | |
| PCT1 (ng/ml) | | | |
| | 16.5±15.4 | 5.8±4.9 | 0.002 |
| | 9.4(1.9-60.0) | 4.5(0.5-25.9) | |
| PCT3 | | | |
| | 15.1±17.3 | 4.5±5.3 | 0.007 |
| | 6.2(1.0-52.3) | 3.0(0.2-24.7) | |
| PCT5 | | | |
| | 9.5±11.1 | 3.5±5.2 | 0.033 |
| | 4.7(0.4-34.0) | 1.8(0.03-25.0) | |

Procalcitonin assessed in both groups & was higher in the positive culture group than in the negative one on days 1, 3, and 5 postoperative & was statistically significant (P -value <0.05).

Table 5. PCT at cutoff value \geq 9ng/ml.

| | PCT 1 | PCT 3 | PCT 5 |
|---------------------------|--------------|--------------|--------------|
| Sensitivity % | 52.9 | 47.1 | 41.2 |
| Specificity % | 83.7 | 90.7 | 88.4 |
| PPV % | 56.3 | 66.7 | 58.3 |
| NPV % | 81.8 | 81.3 | 79.2 |
| Overall accuracy % | 75 | 75 | 75 |

The cutoff value of PCT in day one postoperative was ≥ 9 ng/ml, it had the sensitivity of 52.9% while the specificity of 83.7%. The positive predictive value (PPV) was 56.3%, the negative predictive value (NPV) was 81.8%, and the overall accuracy of the test was 75%.

Supplementary Files

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