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Sensitivity and specificity of serum procalcitonin level compared to leucocyte count for diagnosis of surgical site infection on patients undergoing major surgery

Muhammad Sayuti[1]*, Supomo[2], Umi Sholekah Intansari[3]
[1]Study Program of Medical Doctor, Universitas Malikussaleh, Aceh, [2]Sub Division of Thorax Cardiovascular, Department of Surgery, [3] Department of Clinical Pathology, Faculty of Medicine, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia

ABSTRACT

Surgical site infection (SSI) is one of the most serious complications on sugical procedure. However, its diagnosis is still based on the clinical and laboratory examination that take more time and less sensitive and specific. Therefore, early diagnosis that is more accurate and precise is needed. Some biomarker such as serum procalcitonin (PCT) is promoted for diagnosis SSI. The aim of the study was to evaluate the sensitivity and specificity of serum PCT compared with leucocyte for diagnosis of SSI on patients undergoing major surgery. This was a descriptive analytical study with a prospective observational design. Patients who underwent a major surgery between October 30th and December 31st, 2011 and fulfilled the inclusion and exclusion criteria were recruited. Clinical and laboratory examinations including leucocyte count were conducted presurgery. On 3rd day postsurgery, blood sample was taken for PCT and leucocyte count measurement. A blood bacterial culture was performed on patients suffering from SSI according to Centers for Disease Control (CDC) criteria. Patients were then followed until 30 days postsurgery. A total of 49 patients consisting of 22 men and 27 women were involved in this study. Surgical site infection was found in 16 patients consisting of 8 (50%) patients with clean surgical wound, 3 (19%) patients with clean surgical contamination wound, 4 (25%) patients with surgical contamination wound and 1 (6%) patient with dirty surgical wound. Furthermore, laboratory examination found that 9 patients had abnormal leucocyte with 6 of them suffering from SSI, whereas from 15 patients with serum PCT abnormal, and 11 patients suffered from SSI. Diagnostic test showed that the sensitivity and specificity of serum PCT for diagnosis of SSI were 68.75 and 90.90%, respectively, whereas the sensitivity and specificity of leucocyte were 31.25 and 87.87%, respectively. In conclusion, serum PCT has better sensitivity and specificity compared with leucocyte for the diagnosis of SSI in patients with major surgery.

ABSTRAK

Infeksi luka operasi (ILO) merupakan salah satu komplikasi paling serius pada pembedahan. Namun demikian, diagnosis ILO masih bedasarkan pemeriksaan klinik dan laboratorium yang butuh waktu lama dan kurang sensitif maupun spesifik. Oleh karena itu, diagnosis dini yang lebih akurat dan tepat diperlukan. Beberapa biomarker seperti kadar prokalsitonin (PCT) dipromosikan untuk diagnosis SSI. Penelitian ini bertujuan untuk mengkaji sensitivitas dan spesifisitas PCT serum dibandingkan leukosit untuk diagnosis ILO pada pasien yang menjalani bedah mayor. Penelitian ini merupakan penelitian deskriptif analitik dengan rancangan observasional prospektif. Pasien yang menjalani bedah mayor antara 30 Oktober dan 31 Desember 2011 dan memenuhi kriteria inklusi dan eksklusi dilibatkan dalam penelitian. Hari ke 3 setelah

* corresponding author: say_md@yahoo.com

pembedahan, sampel darah diambil untuk pemeriksaan kadar PCT dan leukosit. Pasien yang mengalami ILO menurut kriteria *Centers for Disease Control* (CDC), dilakukan kultur bakteri darah. Selanjutnya pasien diikuti kondisinya hingga 30 hari setelah pembedahan. Sebanyak 49 pasien terdiri dari 22 laki-laki dan 27 perempuan terlibat dalam penelitian. Infeksi luka operasi ditemukan pada 16 pasien yang terdiri dari 8 (50%) pasien denga luka operasi bersih, 3 (19%) pasien dengan luka operasi bersih kontaminasi, 4 (25%) pasien dengan luka operasi kontaminasi dan 1 (6%) pasien dengan luka operasi kotor. Pada pemeriksaan laboratorium ditemukan 9 pasien mempunyai leukosit abnormal dengan 6 diantaranya mengalami ILO, sedangkan diantara 15 pasien dengan PCT serum abnormal, 11 pasien mengalami ILO. Tes diagnosis menunjukkan sensitivitas dan spesifitas PCT serum untuk diagnsosi ILO berturut-turut adalah 68,75 dan 90,90%. Sedangkan sensitivitas dan spesifitas leukosit berturut-turut adalah 31,25 dan 87,87%. Dapat disimpulkan bahwa PCT serum mempunyai sensitivitas dan spesifitas lebih baik dibandingkan leukosit untuk diagnosis ILO pasien bedah mayor.

Keywords: procalcitonin serum - leucocyte - surgical site infection - diagnostic test - sensitivity - specificity

INTRODUCTION

Infection handling and prevention are now improving with an effective antibiotic discovery, complete immunization and modern sanitation. However, infection remains the most common cause of morbidity and mortality rate in many health care services in the world.[1] A prevalence survey conducted in 55 hospitals of 14 countries representing 4 WHO Regions namely Europe, Eastern Mediterranean, South-East Asia and Western Pacific showed that an average of 8.7% of hospital patients had nosocomial infections. At any time, over 1.4 million people worldwide suffer from infectious complications acquired in hospital.[2] Even in the developed countries where the medical services are well-developed, infection is also proclaimed as the highest cause of serious disease.[1] In USA, the Centers for Disease Control and Prevention (CDC) estimate roughly 1.7 million hospital-associated infections, from all types of bacteria combined, causing 99,000 deaths annually.[3]

One of the most often serious complications in surgical procedure is surgical site infection. Surgical site infection (SSI) is defined as the presence of liquid pus, abscess or cellulitis which extends on a wound within 30 days after surgery or within 1 year in case of implant.[4,5] Surgical site infection is diagnosed with clinical and laboratory examination. The diagnosis begins with an inspection to check any pus, abscess, inflammation reaction or cellulitis that extends on the surgical site. An open wound is also being checked, as well as pus liquid or abscess that leaks from organ or cavum. Pus or tissue specimen should be taken for culture examination and routine blood count for leucocyte count should be investigated.[4]

Procalcitonin (PCT) and leucocyte count are indicators of systemic infection. Procalcitonin is one of the applicable markers to detect bacterial infection in children and adults.[6] Plasma PCT level is comparable with specific response of bacterial infection, particularly for invasive or probably-invasive bacteria. High concentration of PCT indicates sepsis, severe sepsis or even septic shock condition. It may also represent another possibility and gives additional information towards conventional clinical data. Some studies state that procalcitonin is better, or at least has the same diagnosis potency with another infection marker such as CRP, leucocytosis and fever.[7]

A study conducted in a Pediatric Intensive Care Unit, Guy's Hospital, London shows that PCT level is better to be used as diagnostic marker than the leucocyte count in a critical patient. A procalcitonin concentration of 2 ng/

mL might be useful in differentiating severe bacterial disease in infants and children.[6] Another study conducted in Department of Anesthesiology and Critical Care, and Department of Pharmacy, Military Hospital, Tunis University, Tunis to compare the accuracy of PCT to diagnose postoperative infection after cardiac surgery and compare it with those of C-reactive protein, white blood cell count, and interleukins 6 and 8 concluded that PCT is a valuable marker of bacterial infections after cardiac surgery.[8]

This study was conducted to evaluate the sensitivity of PCT compared to leucocyte count in the diagnosis of bacterial infection after surgery in patients who underwent major surgery at Dr. Sardjito General Hospital, Yogyakarta.

MATERIALS AND METHODS

Subjects

This was a descriptive analytical study with a prospective observational design. Patient was observed since undergoing a major surgery until 30 days postsurgery. Samples were obtained by consecutive sampling technique with a maximum sample of 50 patients. Subjects in this study were surgical patients in Dr. Sardjito General Hospital Yogyakarta who underwent major surgery between October 30th and Desember 31st 2011.

The inclusion criteria were the patient who underwent major surgery, was more than 18 years old, and willing to participate the study by signing an informed consent. Major surgeries included in this study were cranitotomy, laminectomy, laparotomy, cholecystectomy, thoracotomy, cardiac surgery, costae clipping, mastectomy, soft tissue tumor surgery, cavum oris tumor surgery, ORIF (open reduction internal fixation), extremity amputation, open prostatectomy, orchidectomy/orchidopexy, ureterolithotomy, and pyelolithotomy. Exclusion criteria in this study were those who had been diagnosed by infection clinically before undergoing surgery, those who had major surgery due to trauma, pancreatitis, combustion or chemical substance exposure, and those who had kidney failure, HIV/AIDS, or in immunocompromised state. The study has been approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta.

Experimental procedures

On admission to Department of Surgery to undergo major surgery, clinical examinations were conducted before surgery and blood samples were taken for routine laboratory investigations including leucocyte count. An explanation concerning the background, objectives, benefits of the study was informed. Patients who fulfilled the inclusion and exclusion criteria were given an informed consent to be signed. After major surgery, SSI of patients was observed. Surgical site infection was defined as the presence of pus liquid, abscess or cellulitis that extends on the surgical site within 30 days post surgery or 1 year in case of implant according to CDC criteria. Furthermore, blood samples were then taken again for routine laboratory investigations including leucocyte counts and for PCT measurement as well as blood culture. Leucocyte counts were measured by the hospital haematology laboratory. Leucocyte count value of 4.800-10.800/mm^3 was considered as normal value. Serum PCT level was measured by immunoluminometric assay (BRAHMS Diagnostika). Serum PCT level of < 0.5 ng/mL was considered as normal value. Blood culture was conducted in an aerobic and anaerobic condition using BACTEC (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD, USA) 9240 automatic blood culture analyzer system.

Statistical analysis

Bivariate analysis using Chi-square (χ^2) was used to evaluate the relationship between leucocyte counts or PCT and SSI. Odds ratio

(OR) with 95% confidence intervals (95% CI) was calculated to assess the risk factors of SSI due to leucocyte count or PCT. A p value of less than 0.05 was considered to be significant.

RESULTS

During a period from October 30th until December 31st 2011, 51 patients who fulfilled inclusion and exclusion criteria were obtained. However, two patients could not continue this study due to loss of laboratory data. Therefore, only 49 patients could finish this study. The ages of subjects were between 22 until 77 years old with an average of 48.2 years old. Among 49 patients involved in this study, 16 patients suffered from SSI. The characteristics of patients are presented in TABLE 1, whereas the characteristics of patients suffering from SSI are presented in TABLE 2.

TABLE 1. Characteristics of patients

Characteristics	n (%)
Gender	
• Male	22 (44.8)
• Female	27 (55.1)
Surgery subdevision	
• Plastic	6 (12)
• Urologic	6 (12)
• Oncologic	11 (23)
• Digestive	17 (35)
• Neurologic	4 (8)
• Thoracis	3 (6)
• Orthopedic	2 (4)
Surgical wound	
• Clean surgical	23 (47)
• Clean surgical contamination wound	17 (35)
• Surgical contamination wound	7 (14)
• Dirty surgical wound	2 (4)
Surgical site infection	
• Yes	16 (33)
• No	33 (67)

TABLE 2. Characteristics of patients suffering from SSI

Characteristics	n (%)
Age (years)	
• 21-40 years	1 (6)
• 41-60 years	12 (75)
• >60 years	3 (19)
Gender	
• Male	5 (31)
• Female	11 (68)
Surgical wound	
• Clean surgical	8 (50)
• Clean surgical contamination wound	3 (19)
• Surgical contamination wound	4 (25)
• Dirty surgical wound	1 (6)

Note: SSI=surgical site infection

Clinical manisfestation of patients suffering from SSI according to CDC criteria is presented in TABLE 3. Among 16 patients suffering from SSI, 7 patients (43.7%) had a

TABLE 3. Clinical manisfestation of patients suffering SSI according to CDC critetia

Characteristics	n (%)
Skin redness	
• Yes	13 (81)
• No	3 (19)
Pain on the surgical site	
• Yes	12 (75)
• No	4 (25)
Liquid leakage	
• Yes	10 (63)
• No	6 (37)
Purulent leakage	
• Yes	10 (63)
• No	6 (37)
Superficial SSI	
• Yes	12 (75)
• No	4 (25)
Clean surgical wound	
• Yes	8 (50)
• No	8 (50)

Note: SSI=surgical site infection; CDC=centers for disease control

positive culture with causative micro-organisms. There were *Pseudomonas aeruginosa* in 4 patients (57.1%), *Escheria coli* in 1 patient (14.2%), *Staphylococcus aureos* in 1 patient (14.2%), and in 1 case there was co-infection between *P. aeruginosa* and *S. aureos*. Nine patients did not undergo culture examination.

Relationship between leucocyte count or PCT and SSI is presented in TABLE 4. No significant relationship between leucocyte count and SSI was observed. However, OR analysis showed that patients having abnormal leucocyte had SSI risk of 3.295 times higher than the normal one. In contrast, significant relationship between PCT and SSI was observed. Moreover, OR analysis showed patients having abnormal PCT had SSI risk of 22.000 higher than the normal one.

TABLE 4. Relationship between leucocyte count or PCT and SSI

Independent variables		SSI		p	OR	95% CI
		Yes	No			
		n (%)	n (%)			
Leucocyte count	Abnormal	5 (55.56)	4 (44.44)	0.105	3.295	(0.745-14.547)
	Normal	11 (27.50)	29 (72.50)			
PCT	Abnormal	11 (78.57)	3 (21.43)	0.000	22.000	(4.489-107.813)
	Normal	5 (14.29)	30 (85.71)			

Note: PCT=procalcitonin; SSI=surgical site infection

Comparison of sensitivity and specificity from serum PCT level and leucocyte count to diagnose SSI is presented in TABLE 5. The sensitivity and specificity of leucocyte count were 31.25% and 87.87%, respectively, whereas, the sensitivity and specificity of serum PCT level were 68.75% and 90.9%, respectively.

TABLE 5. Leucocyte count result towards SSI case

Variables		SSI		Amount	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)
		Yes	No					
Leucocyte count	Abnormal	5	4	9	31.25	87.87	55.55	72.50
	Normal	11	29	40				
	Total	16	33	49				
PCT	Abnormal	11	3	14	68.75	90.90	78.57	85.71
	Normal	5	30	35				
	Total	16	33	49				

Note: PCT=procalcitonin; SSI=surgical site infection; Sens.=sensitivity; Spec.=specificity; PPV=postive predictive value; NPV=negative predictive value

DISCUSSION

A study of SSI among adult patients after surgey has been previously conducted in Dr. Sardjito General Hospital. The result showed that the occurrence of SSI was 5.6% consisting of 3.5% patients with surgical contamination wound and 2.3% patients with dirty surgical wound.[9] Another study conducted in Dr. WZ Yohanes Distric Hospital, Kupang, Nusa Tenggara among patients who underwent caesarean section found that the occurrence of SSI was 16.7% consisting of 75% patients with superficial type, 25% patients with deep incisional type and 25% patients with reoperated case due to deheciency.[10] A study conducted in Jinnah Postgraduate Medical Center (JPMC), Karachi, Pakistan reported that the SSI was present as much as 7.3% (82 patients) in 1120 patients. As much as 65.9% of them came from an emergency procedure while the rest 34.1% came from an elective procedure. According to the surgical wound type, this research reported that there was 1.5% case of SSI of clean surgical wound, 2.5% of clean surgical contamination wound, 6.5% of surgical contamination wound, and 21.4% of dirty surgical wound. According to the age, SSI most often occurred in the group of 41-60 years old (75%).[11]

The main causative microorganism of SSI found in this study was *P. aeruginosa* followed by *E. coli* and *S. aureus.* These findings were not different with the previous study conducted in Dr. Sardjito General Hospital reporting that *P. aeruginosa* was the most common cause of SSI accounted for 33.3% of cases.[9] Furthermore, *P. aeruginosa* was reported as the common pathogen found in both inpatient and outpatient installation at the hospital, while *P. aeruginosa* and *S. negative coagulase* were reported as the most common pathogen found in the surgical ward and ICU of the hospital.[12] A multi center study conducted in Thailand reported that the three most common pathogens isolated were *E. coli*, *S. aureus*, and *P. aeruginosa*, with 15.3%, 8.5%, and 6.8% cases of infection, respectively.[13] The variables associated with the risk of SSI were duration of antibiotic prophylaxis, age, elevated American Association of Anaesthetists (ASA) score, prolonged preoperative hospital stay, duration of operation, emergency surgery, and sex.[14-16]

Bivariate analysis between leucocyte count and SSI showed that leucocyte count had no significant relationship with SSI. An abnormal leucocyte count had the possibility of 3.295 times higher than the normal one. However, it was not statistically significant (OR=3.295; 95%CI=0.745-14.574; p=0.105). In contrast, serum PCT level had a significant relationship with SSI. An abnormal serum PCT level had the possibility of 22 times higher than the normal one (OR= 22.000; 95%CI=4.489-107.813; p= 0.000). It was demonstrated that serum PCT level could be a better predictor of SSI compared to leucocyte count. This result was consistent with previous study which also reported that serum PCT level was a better predictor of SSI.[13] Another study reported that serum PCT level could be used as an infection marker in a febris patient who underwent orthopedic surgery. Moreover, serum PCT level was proclaimed as a significant predictor for postoperative infection.[17,18]

Diagnostic test showed that the sensitivity and specificity of serum PCT level in detecting SSI was higher than those of leucocyte count in this study. This result is in line with previous studies reported by some authors. Study conducted in Tunisia on 100 patients who underwent elective procedure of cardio-pulmonary bypass reported that serum PCT level was better than leucocyte count as the biomarker of a bacterial infection after surgery.[19]

Moreover, a systemic review concluded that serum PCT level is important in identifying patients with infectious complications after cardiac surgery. The serum PCT level is useful in differentiating acute graft rejection after heart and/or lung transplantation from bacterial and fungal infections.[20] Another study also reported that serum PCT level is more accurate to diagnosis of bacterial infection due to high sensitivity and specificity.[21] Furthermore, the serum PCT level can be used to support clinical and microbiological examination to decide whether the fever post orthopedic surgery is caused by infection or non-infection factors. Serum PCT level is also significantly higher in infected patients on day 0, 1, and 3 of fever while it does not happen with the leucocyte count. This finding underlines the potential function of serum PCT level as a predictor of infection after surgery on day 0, 1, and 3 of fever.[18] Serum PCT level also had diagnostic value to diagnose infection and bacteremia. Serum PCT level showed a better predictor than leucocyte count to detect an infection caused by *S. negative-coagulase growth.*[22]

Although many studies reported that serum PCT level had a high predictive value in detecting infection after surgery,[18-22] however, a study conducted in patients who underwent elective spinal urgery gave different result, as serum PCT level in general remained at <0.25 ng/mL during the postoperative course. Moreover, serum PCT level did not correlate with age, sex, DM, hypertension, BMI, operation time, operation site, or use of instrumentation.[23]

CONCLUSION

Serum PCT level is more sensitive and specific than leucocyte count to diagnose SSI in patients who underwent major surgery. The sensitivity and specificity of serum PCT level are 68.75% and 90.9%, respectively, whereas the sensitivity and specificity for the leucocyte count are 31.25% and 87.87%, respectively.

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