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Neutrophil CD64 as a Marker for Postoperative Infection: A Pilot Study

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Abstract The aim of this pilot study was to evaluate the clinical utility of quantitative CD64 measurements to differentiate between systemic inflammation in response to surgical trauma and postoperative bacterial infection.

In a consecutive series of 153 patients undergoing elective vascular surgery, peripheral venous blood samples were taken preoperatively on admission and postoperatively during the first 24 h. The samples were analysed for C-reactive protein (CRP), total leucocyte counts (white blood cell (WBC)), serum procalcitonin (PCT) and neutrophil CD64 expression.

Of the 153 patients, the focus is on those with (1) postoperative infection alone (group 1; $n = 1$ 4); (2) pre- and postoperative infection (group 2; $n = 6$); and (3) postoperative fever with no other signs of infection (group 3; $n = 29$).

In group 1, all four markers were significantly increased in the 24 h after surgery: CD64 ($p = 0.001$), CRP ($p = 0.001$), WBC ($p = 0.002$) and PCT ($p = 0.012$); in group 2, there was no significant difference in the CD64 ($p = 0.116$), WBC ($p = 0.249$) and PCT ($p = 0.138$) values, whereas a marginal significance was shown for CRP ($p = 0.046$); and the results for group 3 were similar to those of group 1.

This pilot study suggests that the role of neutrophil CD64 measurements in facilitating the diagnosis of early postoperative infection merits further investigation.

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Postoperative infections are relatively common complications with potentially grave consequences. This problem is further accentuated in vascular surgery owing to the use of prosthetic materials. Deep infections in vascular patients are often caused by low-virulence bacteria which lead to a protracted and belated debut of clinical symptoms, even several years after surgery.

The neutrophil CD64 (cluster of differentiation 64) receptor, also known as FcγRI, is a 72-kDa glycoprotein that binds monomeric immunoglobulin G (IgG)-type antibodies with high affinity.[1,2] CD64 is a potent cytotoxic trigger expressed exclusively on mononuclear phagocytes and activated polymorphonuclear (PMN) leucocytes.[3] PMN CD64 analysis has been shown to have a high sensitivity and specificity for the early detection of bacterial infection.[4] The aim of this pilot study was to evaluate the clinical utility of quantitative CD64 measurements to differentiate between the inflammation in response to surgical trauma and postoperative bacterial infection.

Patients and Methods

A consecutive series of 153 patients undergoing elective vascular surgery was analysed in an ongoing prospective cohort study. In accordance with the normal practice at our institution, all patients received intravenously administered prophylactic antibiotics perioperatively (Cefalotin 2 g × 1 preoperatively and 2 g × 2 postoperatively). All the patients included had given their informed, written consent.

Peripheral venous blood samples were taken preoperatively on admission and postoperatively during the first 24 h. The samples were analysed for C-reactive protein (CRP), total leucocyte counts, serum procalcitonin and neutrophil CD64 expression. CRP ($mg\,l^{-1}$), leucocyte counts ($\times 10^9\,l^{-1}$) and serum procalcitonin ($\mu g\,l^{-1}$) were measured with the Cell Dyn Sapphire Hematology Analyzer®. CD64 expression was measured using the LK64-H-Assay™ kit produced by Trillium Diagnostics, LLC, on the Cell Dyn Sapphire Hematology Analyzer®. In addition to the laboratory tests, clinical parameters including body temperature, heart rate, blood pressure and signs of local infection were observed and recorded. Blood and urine cultures were taken on the clinical suspicion of infection.

Statistical analysis

The paired Student's *t*-test was used for intra-group analyses, the Mann—Whitney *U* test for inter-group comparisons and the receiver operating characteristic (ROC) curve analysis for establishing cut-off points, sensitivity and specificity for CRP, procalcitonin and CD64. The software program 'SPSS for Windows 13.0' (SPSS Inc. (2004), IL, USA) was used for statistical computations.

Results

Of the 153 patients, the focus is on those with (1) postoperative infection alone (group 1; $n = 14$); (2) pre- and postoperative infection (group 2, $n = 6$); and (3) postoperative fever with no other signs of infection (group 3; $n = 29$). In group 1, the infectious agent was successfully identified in blood and/or urine cultures in five of the 14 cases. For the other nine cases, no infectious agent was isolated; however, there was a clinical suspicion of infection and all patients, except for one, responded to antibiotics: the non-responder was diagnosed with ischaemic colitis at laparotomy.

In group 1, only all four markers were significantly increased in the 24 h after surgery: CD64 ($p = 0.001$); CRP ($p = 0.001$); WBC ($p = 0.002$); and PCT ($p = 0.012$). The results for those with postoperative fever only (group 3) were similar. CD64 values were significantly higher, both pre- and postoperatively, than for the patients with no pre- or postoperative infection (Table 1). Postoperative values of serum procalcitonin also were higher than for patients with no infection detected (Table 1).

In group 2, the group with pre- and postoperative infection, there was no significant difference in the CD64 ($p = 0.116$), WBC ($p = 0.249$) and PCT ($p = 0.138$) values, whereas a marginal significance was shown for CRP ($p = 0.046$). The postoperative CD64 values were lower than the corresponding preoperative values in two cases in this group; nevertheless, they were higher than for patients with no pre- or postoperative infection detected.

Discussion

The aim of this pilot study was to evaluate the possibility of using CD64 measurements to diagnose bacterial infections postoperatively. The analysis of the pre- and postoperative values of CD64 in the three groups revealed some interesting relationships. In the group with postoperative infection ($n = 14$), which included five proven cases of infection based on culture results and nine cases based on clinical signs, there was a suggestion of higher preoperative CD64 values. In the small group of patients ($n = 6$), with clinical signs of infection both pre- and postoperatively, there were high CD64 values both pre- and postoperatively. To show the extent of the effect of trauma on CD64 postoperatively, we can highlight the results for two patients in this group with proven preoperative bacterial infection — one with gangrene in one foot and the other with an infected prosthetic graft. The patients were managed by the amputation and excision of the infected graft, respectively. The postoperative values of CD64 were lower than the preoperative values. This anecdotal evidence indicates that surgical trauma may not always influence the CD64 levels; nonetheless, removing the source of infection results in a reduced CD64 level. However, the group with postoperative fever ($n = 29$), but no signs of infection, had low preoperative CD64 values but relatively high postoperative values, possibly indicative of the inflammatory response to surgical trauma. Neutrophil CD64 measurement may offer the possibility of the early diagnosis of postoperative infection; however, a much larger study with more aggressive searches for infective organisms would be necessary to investigate this hypothesis.