Utility of base deficit, lactic acid, microalbuminuria, and C-reactive protein in the early detection of complications in the immediate postoperative evolution

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Abstract

Objective: To determine the utility of biochemical parameters such as lactic acid (LA), C-reactive protein (CRP), microalbuminuria (MAU), and base deficit (BD) as early markers of complications in the immediate postoperative evolution of elective open gastrointestinal surgeries.

Design and Methods: Sixty-two patients subject to elective open gastrointestinal surgery were evaluated during a period of 22 months.

Results: From the initial 62 patients, 2 were excluded, 29 (48.3%) evolved without complications, and 31 (51.6%) with complications. It was observed that the most significant areas under the ROC curve corresponded to BD in the preoperative period, LA on the first day, and CRP from the second to the seventh day after surgery. MAU was not a discriminating parameter since it did not reach a significant area under the curve (AUC) at any time.

Conclusions: The biochemical markers that best relate to the presence of complications are BD in the preoperative period, LA on the first day, and CRP from the second to the seventh day after surgery.

Keywords: Postoperative evolution; Biochemical markers

Introduction

It seems evident that the quality of the postoperative control is as important as the surgical procedure itself to obtain optimal results in surgery. This is even more relevant when the patient is monitored in general recovery rooms where the methods employed are of lower complexity than those at the intensive care unit. The implementation of follow-up studies with markers that can rapidly identify those patients with an abnormal course of evolution could allow diagnostic resources to be rapidly administered to this subgroup of patients.

The aim of the present work is to establish the utility of different biochemical parameters: lactic acid (LA), base deficit (BD), microalbuminuria (MAU), and C-reactive protein (CRP) as early markers of complications in the immediate postoperative evolution of elective open gastrointestinal surgery.

In the Systemic Inflammatory Response Syndrome (SIRS), these markers are frequently altered. An example of this is the alteration produced during a complicated postoperative period. The American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference Committee [1] proposed a set of definitions for the SIRS, sepsis, severe sepsis, and septic shock for the early detection of sepsis and the standardization of septic patients in clinical trials or research protocols. SIRS is defined as at least two of the following abnormalities: (a) leukocytosis or leukopenia; (b) tachypnea; (c) fever or hypothermia; (d) tachycardia. SIRS includes diverse clinical
conditions, infection, trauma, burn, acute pancreatitis, and postoperative. Previous studies [2,3] showed that SIRS is associated with the increased production of pro-inflammatory cytokines and the activation of a coagulation system. Evidence [2,3,4] supports the hypothesis that disruption of homeostasis by these mediators may result in the unnecessary auto-destruction of distant organs.

Abnormal levels of these markers and their persistence in time could serve as an early indicator of postsurgical complications, potentially more superior to clinical signs.

Materials and methods

Patients and sampling

Sixty-two patients were evaluated in a prospective way. They were subject to elective open gastrointestinal surgery between May 2000 and March 2002 at the “Servicio de Cirugía del Hospital de Agudos Dr. Cosme Argerich (GCABA).” The patients were 35 (56.4%) men and 27 (43.5%) women with an average age of 61 (maximum, 78 years of age; minimum, 21).

Regarding the initial pathology, 47 (75.8%) resulted malignant and 15 (24.1%) benign. The surgeries performed were the following: 23 pancreatoduodenectomies, 25 cholecotomies, 2 cystojejunoanastomoses, 1 distal pancreatectomy, 1 papillosphincteroplasty, 2 choledochoduodenostomoses, 3 transit restorations (following Hartmann’s operation), 1 presacral tumor resection, 1 hepaticojejunostomy, and 1 gastroenteroanastomosis.

The following exclusion criteria were established:
1. Patients with a case history of acute disease within 10 days before surgery.
2. Patients with acute or chronic hepatic and/or renal disease.
3. Presence of intraoperative shock. This is defined as a state when the mean arterial pressure (MAP) is less than or equal to 40 mm Hg for a period not shorter than 30 min, and/or if inotropic drugs are required to maintain normal hemodynamic parameters during surgery or immediately after it.

The variables taken into account were the following:
(a) Independent variables: plasmatic lactic acid (LA, mmol/l), C-reactive protein (CRP, mg/l), base deficit (BD), and microalbuminuria (MAU, mg/l) determined through the MAU/plasmatic creatinine ratio.
(b) Dependent variables: the postoperative evolution of the patients divided in two groups: with and without complications.

Regarding “surgical complication,” we have used the definition given by Clavien et al. [5]. Surgical complication can be defined, therefore, as the postoperative event that results from a surgical procedure inducing a deviation from the ideal course of evolution. This can lead to a deterioration of the patient’s conditions or to a delay in their recovery, forcing changes in the manipulation of the patient, subjecting it to additional diagnostic or therapeutic procedures.

Blood and urine samples were collected between 8:00 and 10:00 AM the day before surgery (X0) and then from days 1–7 after surgery (X1–X7).

If a patient was discharged from hospital before the seventh postoperative day, it was summoned daily to hospital to complete studies.

Biochemical determinations


These measurements were controlled with calibrators and controls (Roche Diagnostic GmbH, Germany) and were analyzed in an autoanalyzer, Hitachi 717 Boehringer Mannheim Diagnostic, USA. The laboratory is included in an External Quality Control Programme (Buenos Aires CEMIC).

White blood cell count (WBC): hematology cell counter. CELL-DYN 1400 (ABBOTT USA). Calibrators and controls: ABBOTT USA. The laboratory is included in an External Quality Control Programme (Buenos Aires CEMIC).


Statistical analysis

ROC curves were used to establish cutpoint values for the markers according to the evolution (with or without complications) for the preoperative day and for the 7 days after surgery.

The area under the curve (AUC) was determined for each of the variables during the 8 days. The cutpoint was determined if the AUC was greater than 0.6 according to the method by Vermont and Bosson.

Sensitivity (S), specificity (E), positive predictive value (PPV), and negative predictive value (NPV) were analyzed for the different cutpoints, while B (Bangdiwala) and Cohen’s K (Kappa) statistic coefficients were used to determine the level of agreement with evolution according to the guide established by Muñoz and Bangdiwala.

Results

Initially 62 patients were included in the present work, but 2 had to be excluded for not complying with the established protocol. Of the remaining 60 patients, 29 (48.3%) evolved without complications and 31 (51.6%)
presented postoperative complications. Five (8.3%) of these patients died. The cause of death was multiple organ dysfunction (MOD) related to sepsis, and it happened between days 8 and 12 after surgery.

Among the complications of the living patients there were: prolonged ileus (five), pneumopathy (five), urinary infection (two), pancreatic fistula (nine), prolonged febrile syndrome with positive hemocultures (two), colocutaneous fistula (one), bile-enteric fistula (one), intra-abdominal collection (one), suppurrating surgical wound (two). Ninety-five percent of the complications appeared after the fifth postoperative day and none of the patients presented failure of two or more organs.

Table 1
Sensitivity, specificity, positive predictive value, and negative predictive value of the cutoff points of the variables with AUC greater than 0.6 at different days

<table>
<thead>
<tr>
<th>Variable</th>
<th>Day</th>
<th>AUC</th>
<th>Cutpoint</th>
<th>S (%)</th>
<th>E (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactic acid (LA)</td>
<td>1</td>
<td>0.72</td>
<td>2.84</td>
<td>67</td>
<td>66</td>
<td>67</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.61</td>
<td>2.16</td>
<td>58</td>
<td>59</td>
<td>60</td>
<td>56</td>
</tr>
<tr>
<td>Base deficit (BD)</td>
<td>1</td>
<td>0.68</td>
<td>−2.9</td>
<td>62</td>
<td>63</td>
<td>64</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.60</td>
<td>−0.25</td>
<td>57</td>
<td>60</td>
<td>60</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.67</td>
<td>+0.25</td>
<td>60</td>
<td>65</td>
<td>64</td>
<td>60</td>
</tr>
<tr>
<td>C-Reactive protein</td>
<td>1</td>
<td>0.63</td>
<td>0.64</td>
<td>63</td>
<td>66</td>
<td>60</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.66</td>
<td>19.34</td>
<td>59</td>
<td>64</td>
<td>63</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.71</td>
<td>17.73</td>
<td>68</td>
<td>63</td>
<td>66</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.76</td>
<td>13.27</td>
<td>67</td>
<td>72</td>
<td>71</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.78</td>
<td>10.4</td>
<td>69</td>
<td>74</td>
<td>73</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>0.87</td>
<td>8.74</td>
<td>82</td>
<td>78</td>
<td>79</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.86</td>
<td>8.27</td>
<td>76</td>
<td>80</td>
<td>80</td>
<td>75</td>
</tr>
</tbody>
</table>

References: S = sensitivity; E = specificity; PPV = positive predictive value; NPV = negative predictive value; AUC = the area under the curve.

Table 2
Level of agreement between the variables discretized by their cutoff point and evolution according to $K$ and $B$ coefficients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Day</th>
<th>Cutoff</th>
<th>$B$</th>
<th>$K$</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>1</td>
<td>2.84</td>
<td>0.38</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>2.16</td>
<td>0.38</td>
<td>0.23</td>
</tr>
<tr>
<td>BD preoperative</td>
<td>+0.1</td>
<td>0.15</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td></td>
<td>−2.9</td>
<td>0.13</td>
<td>−0.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>−0.25</td>
<td>0.20</td>
<td>−0.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>+0.25</td>
<td>0.11</td>
<td>−0.33</td>
<td></td>
</tr>
<tr>
<td>CRP preoperative</td>
<td>0.64</td>
<td>0.20</td>
<td>−0.09</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.9</td>
<td>0.34</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17.23</td>
<td>0.47</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td></td>
<td>13.27</td>
<td>0.49</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.4</td>
<td>0.59</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.74</td>
<td>0.59</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.27</td>
<td>0.59</td>
<td>0.54</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. ROC curves of C-reactive protein. Plasma concentration of C-reactive protein at preoperative day ($\Delta$) and at third (●), fifth (×), sixth (○), and seventh (●) postoperative days. The y axis shows sensitivity, and the x axis shows (1 − specificity).

References:

- A still controversial topic is the one regarding follow-up studies during the immediate postoperative period (POP) using parameters that help differentiate at an early stage those patients with an abnormal course of evolution.
- The work by Haga et al. [6] makes important contributions. The presence of two or more Systemic Inflammatory Response Syndrome (SIRS) criteria during the first 3 days after gastrointestinal surgeries would not be related to the presence of postoperative complications. Actually, it would be related to the type of surgery, its duration and to the relationship between blood loss during surgery and weight loss.

It is the reappearance of SIRS criteria or their persistence beyond the third day and during two consecutive days that...
relates to postoperative morbidity of infectious and noninfectious origin.

In our work, we observed the behavior pattern of some biochemical parameters in the immediate preoperative period and during the first 7 days after surgery (POP). We looked for a cutpoint for each parameter that would enable us to differentiate patients with and without complications in their evolution at an early stage. Thus, we have selected

1. BD and LA as indicators of hidden hypoperfusion, whose persistence is related to the appearance of infectious or respiratory complication and MOD among others, as demonstrated in trauma [7,8,9].

2. MAU as an indicator of increased capillary leak resulting from endothelial damage that is observed as consequence of the systemic inflammatory response [10,11]. As Zkria and Boscom [12] and Gosling et al. [13] have pointed out, the persistence and increase of capillary permeability following traumatic or postoperative SIRS lead to a decrease in the release of oxygen in tissues. This is in turn accompanied by a higher percentage of complication, especially respiratory distress and MOD.

3. CRP: acute phase protein used as marker of inflammatory response [14] with a very good correlation with the level of SIRS in POP as demonstrated by Haga et al. [6] in his work already mentioned.

According to these results, we can conclude that

(A) During the preoperative period, BD is the most relevant marker for postoperative evolution (cutpoint: +0.1). This is of great importance for the correct preoperative preparation of the patient, regarding especially its internal environment, and its subsequent postoperative evolution.

(B) LA is the best parameter for the first day after surgery. With a cutpoint of 2.84 mmol/l, it reflects the relationship between the quality of the intro and immediate postoperative resuscitation instituted to the patient and its evolution.

(C) CRP is the best indicator of evolution between days 2 and 7 after surgery, with different cutpoints each day (mg/l): 19.34, 17.73, 13.27, 10.40, 8.47, and 8.27, respectively. In this way, it becomes a good marker to differentiate the inflammatory response characteristic of the postoperative period, from the pathological one produced during an abnormal course of evolution.

(D) MAU did not result as a good indicator of evolution for any of the studied days.

The aim of the present paper was not to determine predictive parameters of the evolution postoperative period of base disease, the work based in proceeding gastrointestinal surgical technique.

It will be interesting in a future investigative work, looking the anormal results, to evaluate the predictive value of this markers in each one of the different subgroup of patients.

In this work, the number of patients in the different subgroups is small and unequal to correlate the parameters with different diseases.

Acknowledgment

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References