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EC EMERGENCY MEDICINE AND CRITICAL CARE
Research Article

The Clustering in Analyzing Effect of Jaundice, Malnutrition and Using of Immunosuppressive Therapy on the Occurrence of Dehiscence Laparotomy

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Received: June 29, 2019; **Published:** July 15, 2019

Abstract

The finish line of this study was to determine the influence of jaundice, malnutrition and using of immunosuppressive therapy on the occurrence of dehiscence laparotomy. The minimum sum of squares clustering method is new method applied in medicine. We first collect data of 989 patients in hospital in Serbia, taking into account 3 their attributes. Among 989 patients, 41 of them had the occurrence of dehiscence laparotomy. We analyze the risk of taking surgery based on clustering patient in groups, taking into account the influence of jaundice, malnutrition and using of immunosuppressive therapy on the occurrence of dehiscence laparotomy. Dehiscence of laparotomy occurred in 4.1% of patients. In patients with jaundice and indicative of hepatic dysfunction (serum bilirubin > 1.0 mg%), dehiscence of laparotomy is common. In patients with malnutrition with weight loss over 20% in last three months exist very significant correlation between dehiscence of laparotomy and this risk factor. In patients who using immunosuppressive therapy, dehiscence of laparotomy is not common. In this paper, for the first time, we present the minimum sum of squares clustering method in analyzing risk factors: the influence of jaundice, malnutrition and using of immunosuppressive therapy on the occurrence of dehiscence of laparotomy. We show that the minimum sum-square modeling group is well suited for this research. Some hypotheses can be performed automatically.

Keywords: *Clustering Method; Jaundice; Malnutrition; Immunosuppressive Therapy; Dehiscence Laparotomy*

Introduction

Complications related to postoperative wound healing up occur with varying frequency depending on the underlying disease, the patient's and surgeon's technical skills. Surgical site infections and wound and tissue dehiscence are well-known postoperative complications in gastrointestinal surgery, and general surgery as well. Evisceration is a complication associated with high morbidity, and high mortality as well, and the percentage in colorectal surgery still remains 2 - 3,5% [1,2]. The infection is certain in 5 - 10%. The rupture of the abdominal wall occurs in 1% of the cases, however with a high mortality rate (15 - 45%) [3]. The severity of these complications embraces mild cases needing local wound care and antibiotics to serious cases with multiple reoperations and a high mortality rate. In most cases, such complications prolong hospitalization, with a substantial increase in cost of care [4].

Extension of the age limit of surgical patients leads to the emergence of new problems related to the altered response of the organism (burdened by homeostasis disorders and the function of all age-old systems) on the surgical procedure. Far more important are the parameters that determine the biological age of the patient: the patient's general condition and ability to care for oneself (performance status), nutritional status (Seltzerov index), as well as the risk of anesthesia-estimated ASA score [5].

Microvascular disease, severe lung disease and weight loss are known to cause peripheral tissue hypoxia which increases the risk of wound infection and dehiscence.

Malnutrition with weight loss over 20% seen in surgical patients with concomitant hypoproteinemia, hypoalbuminemia, and a lack of amino acids (especially cysteine, arginine and methionine) leads to an extension of the inflammatory phase of the healing process, with the disruption of collagen synthesis.

Any patient with serum bilirubin up 1.0 mg% was considered as jaundiced and considered as indicative of hepatic dysfunction. Liver disease with coagulation disorder, decreased protein synthesis, and maturation of fibroblasts were also accompanied by difficult wound healing.

Methods

Statistical tests

Research is organized by type of prospective studies that have analyzed the following data as risk factors: the impact of jaundice (serum bilirubin > 1.0 mg%), malnutrition with weight loss over 20% in last three months and the using of immunosuppressive therapy (Imuran and Cell Cept) on the occurrence of dehiscence laparotomy of 989 operated patients at the Department of General Surgery in Nis in the period from 1st January 2018 to 31st May 2019. Complications-dehiscence of laparotomy was found in 41 patients. Statistical sample size is determined by the statistical methodology to meet the basic principle of representativeness. Was used to determine the optimal normogram sample. In this paper, results are presented in tables and graficly. The statistical analysis using the methods of descriptive statistics (mean, standard deviation), parametric tests (Student's t-test) and nonparametric Chi-square test. For statistical analysis we used the software package SPSS 14.0 and the imaging table and a Microsoft Office Word 2003.

Minimum sum-of-squares clustering

One of mostly used criterion for clustering is minimum sum-of-squares (MSS), where all entities are placed in n-dimensional Euclidean space and their dissimilarities calculated as squared distances in Rn. The number of clusters m is given in advance. The objective is to make groups of entities such that the total sum of squared distances within each group or cluster is minimum. It appears that minimizing the intragroup distances is equivalent to maximizing the square distances among entities from different groups [6]. This property makes MSS most popular criterion since it measures in the same time homogeneity and separation. Moreover, MMS may be equivalently presented as the problem of minimizing the square distances from each entity to its own cluster center or centroid [6].

Since MMS problem is NP-hard [6], there are many heuristics already appeared in the literature. The most popular heuristic is so-called k-means method. It alternatively solves allocation of entities to their closest centroid and finding the corresponding centroid of each cluster. Although being very popular due to its simplicity, the results obtained by k-means sometimes are very far from the global optimum [6]. That is the reason why there are many heuristics that are trying to improve precision of k-means algorithm. One among them is J-means and Variable neighborhood search (VNS) based heuristic [6].

In this paper we presented data of 989 patients in 3-dimensional space. As mentioned earlier, those three attributes (or risk factors) are: the influence of jaundice, malnutrition and taking of immunosuppressive therapy on the occurrence of dehiscence laparotomy. All three are considered as binary variables. In the next section we will analyze the results obtained by both k-means and VNS heuristics.

Results

Statistical tests

Dehiscence of laparotomy occurred in 4.1% of patients or 41 patients of the total 989 respondents. Of the total 41 patients with dehiscence of laparotomy, 27 patients were male or 65.8%, and 14 patients were female or 34.2%. Of the patients who did not have a dehiscence of laparotomy 555 patients were male or 58.5% and 393 patients without dehiscence of laparotomy were female or 41.5%.

Jaundice (indicative of hepatic dysfunction) was statistically significantly higher in the group of patients with dehiscence of laparotomy than in the second group of patients without dehiscence of laparotomy ($X^2 = 1.211$; $p < 0.05$). Jaundice in patients with dehiscence has 21 patients or 51.2% and in patients without dehiscence 416 patients had jaundice or 43.9% patients. Jaundice did not have 20 patients with dehiscence of laparotomy or 48.8% and 532 patients without dehiscence of laparotomy or 56.1% (Figure 1).

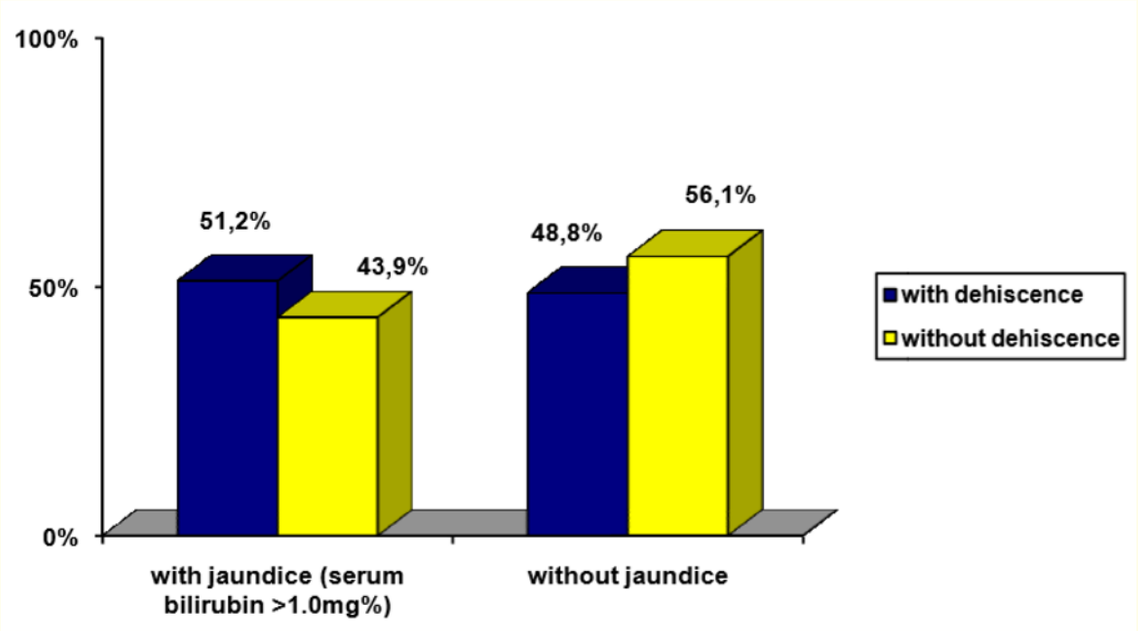

Figure 1: *The presence of jaundice on the occurrence of dehiscence of laparotomy.*

There is a statistically very significant relationship between dehiscence of laparotomy and malnutrition with weight loss ($X^2 = 19.988$; $p < 0.01$). Malnutrition with weight loss (>20% in last three months) was significantly more prevalent in patients with dehiscence of laparotomy. Of 41 patients with dehiscence of laparotomy them 35 or 85.4% had a weight loss, and of the 948 patients without dehiscence, weight loss had only 296 of them, or 31.2% (Figure 2).

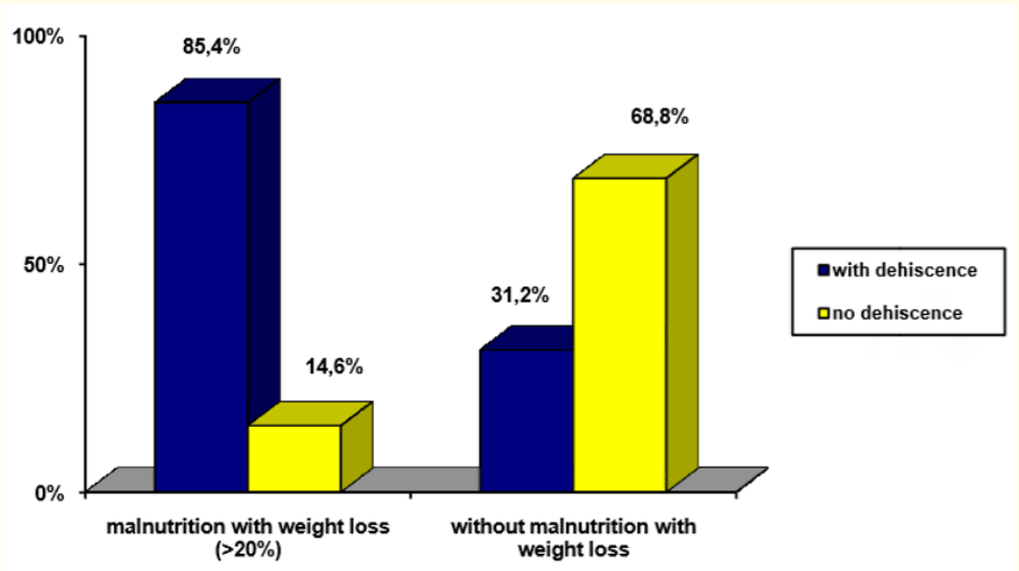

Figure 2: *Impact of malnutrition on the occurrence of dehiscence of laparotomy.*

Of the 989 patients examined, 78 took immunosuppressive therapy (Imuran and Cell Cept) or 7.9%. There is no statistically significant correlation between dehiscence of laparotomy and using of immunosuppressive therapy ($X^2 = 2.223$; $p > 0.05$). 3 patients who took immunosuppressive therapy, had dehiscence of laparotomy or 7.3% and 75 patients with immunosuppressive therapy did not have dehiscence of laparotomy or 7.9% (Figure 3).

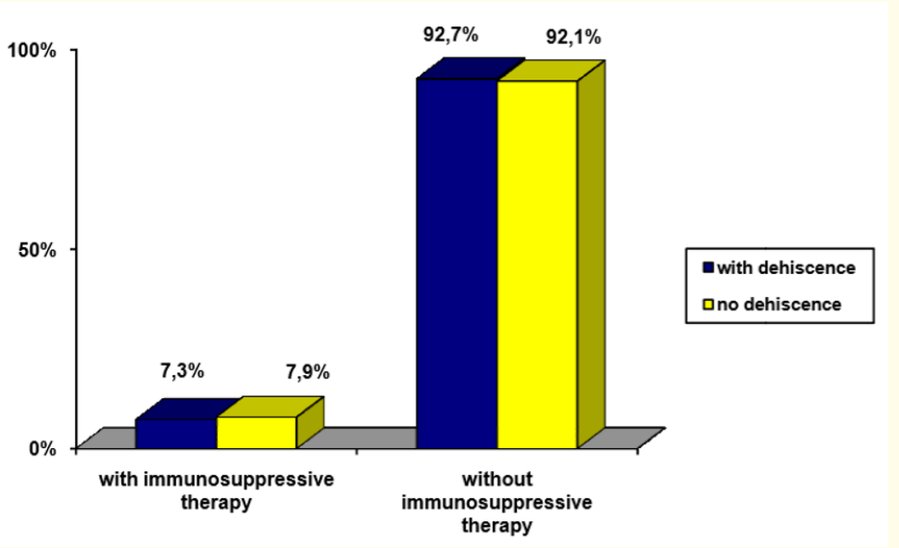

Figure 3: *The effect of using of immunosuppressive therapy on the occurrence of dehiscence of laparotomy.*

Clustering results

In table 1 we report results obtained by two heuristics for Minimum sum-of-squares clustering: *k*-means and VNS. The first the number of desired clusters are given. The second line gives the value of the objective function. In column 3 we report the number of entities in each cluster obtained by *k*-means. The next 3 columns report the same values given by VNS. It appears that both methods keep 41 patients with dehiscence laparotomy in the same cluster. The difference in results starts after $m = 6$, where the total sum of squares are 184.52 and 169.99 obtained by *k*-means and VNS respectively. Moreover, VNS keeps the 41 patients in the same cluster up to $m = 10$. This means that not only the clustering model is important but also the method used.

		K – means			VNS	
M	**f**	**# of entities**	**Time**	**f**	**# of entities**	**Time**
2	635.40	{41,948}	0.2	635.40	{41,948}	0.6
3	438.18	{41,334,614}	0.3	438.18	{41,419,529}	0.8
4	395.96	{41,123,211,614}	0.5	395.96	{41,192,227,529}	1.4
5	200.71	{41,119,127,284,418}	0.6	200.71	{41,97,109,213,529}	1.6
6	184.52	{19,22,108,135,287,418}	0.8	169.99	{41,73,78,81,187, 529}	1.9
7	129.77	{8,11,22,111,124,295,418}	0.9	88.80	{41,45,48,88,89,192,486}	2.1
8	82.30	{1,9,9,22,135,141,254,418}	1.0	63.63	{21,32,41,69,89,120,131,486}	2.4
9	60.20	{1,8,10,22,32,126,162,242,386}	1.2	43.81	{15,18,20,41,55,172,189,190,289}	2.6
10	33.86	{1,6,8,12,14,32,162,180,188,386}	1.5	24.19	{12,15,18,20,41,59,135,189,211,289}	2.8

Table 1: *Comparison of k-means and VNS heuristics in clustering n=989 patients into m groups.*

Some observations regarding results reported at table 1 are:

1. *Clustering models and methods may be successfully used in medicine in general and more particularly in Surgery in parallel with statistical tests;*
2. *Hypotheses may be automatically derived, e.g., the 41 patients with dehiscence of laparotomy are kept in the same group with up to 10 clusters;*
3. *Results obtained by clustering techniques are more rich in a sense that they provide more information to practitioners: relations between clusters, introduction of many patient's attributes in analysis, etc.;*
4. *The clustering method used may play a significant role in understanding the final results, i.e. VNS based heuristic outperform significantly k-means heuristic for number of clusters grater or equal to 6.*

Discussion

In this section we first discuss our results obtained by statistical tests and then comment on their relations with clustering.

Despite major advances in the understanding of the process of wound healing physiology, surgical techniques and the application of modern technologies and materials in surgery, the percentage of impaired healing laparotomy is still high. Dehiscence of laparotomy occurs in approximately 3% of patients. In a retrospective study by Rodriguez-Hermosa JI., *et al.* from Spain, in 57 patients or 0.45% of the total 12622 patients with laparotomy, there was dehiscence of laparotomy. There were 45 male patients and 12 female patients [7]. In India's study from Rajindra Hospital in Patiala male predominance (37/50) was observed, with ratio of male to female being 2.84:1 [8]. In our study compared to sex the patients of the total 41 patients with dehiscence of laparotomy, there were 27 males and 14 females. When it comes to full structure, our study does not show a statistically significant difference between sexes. The Cracow study Kenig J, Richter P, Zurawska S and associates with dehiscence of laparotomy occurred in 56 patients or 2.9% of their patients [9]. Our results show that dehiscence of laparotomy was present in 4.1% of patients or 41 patients of the total 989 respondents. Preoperative preparation is an important stage in the treatment of surgical patients and the adequacy of preoperative depends on result of the operation, the incidence of complications and mortality of patients. It is necessary that all the general condition of the patients preoperatively stabilized and carry a minimum of anesthesia and surgical preoperative whenever the patient's condition allows [10].

In a prospective study by Ramnesh G, Sheerin S., *et al.* jaundice (indicative hepatic dysfunction) had 16% of patients or 8 patients [8]. In our study jaundice in patients with dehiscence has 21 or 51.2% of patients. In our study exist a statistically significant relationship between dehiscence of laparotomy and jaundice ($X^2 = 1.211$; $p < 0.05$).

In our study exist a statistically very significant relationship between dehiscence of laparotomy and malnutrition with weight loss ($X^2 = 19.988$; $p < 0.01$). Malnutrition with weight loss (> 20% in last three months) was significantly more prevalent in patients with dehiscence of laparotomy, 35 operated patients with dehiscence of laparotomy or 85.4% had a malnutrition with weight loss.

Our research has confirmed numerous studies showing that there is statistically very significant association between dehiscence of laparotomy and malnutrition with hypoproteinemia. According to literature data, 89.25% of patients with dehiscence of laparotomy have hypoproteinemia [7] and in our study the incidence of hypoproteinemia in 85.4% of patients with dehiscence of laparotomy. Malnutrition is statistically significantly more prevalent in people with dehiscence of laparotomy. Patients with dehiscence of laparotomy have a statistically significantly lower average value of total proteins and albumins. It is important to note the importance of preoperative treatment measures using substitution therapy and nutrient replacement in undernourished patients, because malnutrition with a body weight loss of over 20%, seen in surgical patients with associated hypoproteinemia, hypoalbuminemia and a lack of amino acids (especially cysteine, arginine and methionine) leads to the prolongation of the inflammatory phase of the wound healing process, along with the disorder of collagen synthesis [10].

In the study of Akkus A, Avdinuraz K and a colleague at the Kirikkale University Medical School in Turkey, proven that long-term use of corticosteroid therapy leads to a change in enzymes involved in the glycolysis process during wound healing. The study covered three groups. In Group A, eight patients received metilprednisolone seven days before surgery and after surgery to complete healing of the wound. In Group B, twelve patients received methylprednisolone seven days before laparotomy. After surgery, methylprednisolone injections continued, but immunosuppressive treatment with carnitine was also introduced to complete wound healing. In Group C, eight patients received no treatment. In half of the patients examined, wounds were healed within seven days after laparotomy. The remaining wounds were healed up to the fourteenth day after surgery. Tension on the wound line and the content of hydroxyproline are parameters whose values are monitored in all three investigated groups. The study found that there was no statistically significant difference in both parameters in all three groups on the seventh day after laparotomy. On the fourteenth day, both parameters showed a statistically significant difference between the group in which methylprednisolone and control groups were administered ($p < 0.05$). Tension values

on the wavy line were lower in the group where carnitine was administered compared to the group where methylprednisolone was administered ($p > 0.05$). The use of carnitine led to an increase in the level of hydroxyproline in wounds in a group of patients receiving methylprednisolone and carnitine compared to the control group of patients ($p < 0.05$). The use of carnitine leads to a decrease in tension on the wound line in relation to the tension of the wound where only methylprednisolone is applied [11].

In the work of Akkus A, Avdinuras K and associates, it has been found that the administration of carnitine helps to restore energy deficiency and create collagen during healing of the wound. There is no statistically significant difference between the group of patients administered by immunosuppressive therapy with carnitine and the control group in wound healing ($p > 0.05$) [11]. Our prospective study confirms the positive impact of immunosuppressive therapy on wound healing. There is no statistically significant difference between the group of patients with dehiscence of laparotomy who are on immunosuppressive therapy and the control group of patients with deficiency of laparotomy who were not on immunosuppressive therapy ($X^2 = 2.223$; $p > 0.05$).

Comparing the results with the results of international studies in this paper we come to the conclusion that our results are not worse than the results of the world's health task.

Conclusion

Dehiscence of laparotomy occurred in 4.1% of operated patients. In patients with malnutrition with weight loss over 20% in last three months exist very significant correlation between dehiscence of laparotomy and malnutrition with weight loss. In patients with jaundice, dehiscence of laparotomy is common. In patients who used immunosuppressive therapy dehiscence of laparotomy is rarity. By analyzing these three risk factors, the surgeon can identify patients with high risk. Therefore, it is important to identify them early and treat those patients with care.

Further, development of clinical pathways would prove valuable if the absolute risk of each patient could be estimated when planning surgery to specifically optimize the patient's preoperative condition to reduce the risk of complications.

Good preoperative preparation reduce postoperative wound complications.

In this paper, for the first time, we present the minimum sum of squares clustering method in analyzing risk factors: the effect of jaundice, malnutrition with weight loss over 20% in last three months and using of immunosuppressive therapy on the occurrence of dehiscence of laparotomy. The minimum sum-square modeling group is well suited for this research. Some hypotheses can be performed automatically. The researchers in future work may use different clustering methods for the analysis of various risk factors in medicine in general.

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Volume 3 Issue 8 August 2019