

**Research Article**

Innovative Biostatistic Processing End-Point Quantified Inferential Analysis-A Prognostic Value Indicator of Manheim Peritonitis Index (MPI) in Laparoscopic Surgery

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Abstract

Summary: Introduction: The Mannheim Peritonitis Index (MPI) is a useful tool for the evaluation for follow-up of patients who undergone surgical intervention for peritonitis. Generally, a high score is associated with increased mortality and it has not been yet sufficiently evaluated for laparoscopic interventions. A topic of interest is about the MPI benefits for classic surgery versus laparoscopic surgery. **Material and methods:** We performed a retrospective, observational, non-randomized study that included 109 subjects with peritonitis, with laparoscopic, emergency approach. As we did not record any deaths in our group, we resorted to innovative biostatistical processing and decided that the severity of the case should be quantified using the total duration of hospitalization, measured in days. Thus, the main “end-points” of the study were the duration of surgery and the total number of hospitalization days. The influence of MPI on the duration of hospitalization was investigated by logistic regression. In order to determine a possible association, we used a simple univariate linear regression model, with the variable dependent being the duration of hospitalization and the independent variable being the MPI. **Results:** The average recorded value of MPI was 11.04 and the maximum value was 20, and the distribution of the variable was close to the Gaussian distribution. A 1 value increase in the Mannheim score is associated with an approximately 1-day increase in hospital stay for patients operated laparoscopically for the diagnosis of peritonitis, the effect being statistically significant ($p <0.0001$). The box-plot did not reveal distributional outliers. **Conclusions:** In addition to its already committed role in the prognosis of mortality in patients with peritonitis operated by open surgery, MPI can also be considered more recently as an evolutionary prognostic factor in the laparoscopic treatment of this type of pathology. The outcome will help surgeons select the cases of peritonitis they intend to operate laparoscopically more carefully, with minimal risks for the patients. There are not enough studies on this topic in the literature, which is why we recommend further research.

Keywords: Peritonitis; Surgery; Laparoscopy; Prognosis; Severe

Introduction

The prognosis of peritonitis caused by organ perforations continues to be unfavourable, despite the most state-of-the-art diagnostic and treatment techniques. Therefore, early diagnosis of patients with severe peritonitis is crucial especially for selection of cases which require emergency surgical intervention [1-5].

The initial evaluation of the disease risk was performed in time by using several indices (Acute Physiology and Chronic Health Evaluation - **APACHE** II Score, Simplified Acute Physiology Score - **SAPS**, Sepsis Severity Score - **SSS**, Ranson Score, Imrite Score, Mannheim Peritonitis Index- **MPI**) [6-14].

Another index resulted from the history of the disease, the clinical examination, the intraoperative findings and the information about the physiological parameters, is the Peritonitis Index Altona (**PIA**). Qualitative variables are transformed into quantitative data and **PIA** was observed to have mainly a predictive value for exit us. The Mannheim Peritonitis Index (**MPI**) is a specific score, with high accuracy and offering a very easy way to manage clinical data, allowing the evaluation of the individual prognosis of patients with peritonitis [1,15-19]. **MPI** is an independent, disease specific, easier to calculate score with minimum basic investigations [20]. Well-established scoring systems do not consider intraoperative findings, such as the nature of exudate/contamination, and the source or level of perforation which alter the outcome of such cases. Thus, **MPI** can be applied with increased accuracy in smaller surgical services as well [21-23]. In such conditions, in the present study, for the early evaluation of the disease severity and the patient's follow-up, a group analysis was used according to the Mannheim Peritonitis Index (**MPI**) calculated perioperatively, in patients treated laparoscopically, a score that allows the estimation of the evolutive prognosis of the case. The laparoscopic surgical management that was applied was similar to the one used in classic surgery. Initial standard measures included fasting patient Nil Per Orally (NPO), intravenous fluid, antibiotics and analgesics, correction of electrolyte imbalance (if any), abdominal decompression using nasogastric tube and Foley's catheterisation. Patients who were prepared for surgery were managed by exploratory laparoscopy for peritoneal toileting and repair of perforation [24].

Purpose and objectives

The purpose of this study was to evaluate the indications and limitations that may be considered in laparoscopic treatment of peritonitis, a pathology that, due to its severity, challenges the entire intellectual and therapeutic surgical and anaesthetic arsenal. We investigated the benefits of extending the role of **MPI** from

open surgery to laparoscopic surgery. The literature reports lack of information about this association (**MPI** -laparoscopic surgery), but it is certain that more and more cases of peritonitis are nowadays operated laparoscopically. As a final objective, the study aims to prove that even severe case of peritonitis may be treated laparoscopically.

Material and Method

We performed a retrospective, observational, non-randomized study, based on an analytical epidemiological investigation, on a sample of patients hospitalized and operated laparoscopically for the diagnosis of peritonitis, between 2009-2018, at the General Surgery Department of "Sf Ioan" Emergency Clinical Hospital of Bucharest, Romania. The surgical interventions were performed as immediate, emergencies or scheduled. The surgical teams were led by specialists with considerable experience in laparoscopic techniques, ensuring the premises for obtaining the most appropriate solutions for difficult cases and in various challenging intraoperative situations.

As an element of originality, we analysed the group of patients with peritonitis, according to the international codes of the Diagnostic Related Groups (**DRG**) Classification System, thus conducting the first national biostatistical study of cases with such pathologies, as reported to the Romanian National Health Insurance House, based on the Australian AR-DRG v.5 Classification System.

The inclusion criteria for the study were: the patient admitted in the hospital during the study period; the study documents had to mention emergency diagnoses such as acute surgical abdomen, peritonitis, acute appendicitis, perforated ulcer, intraperitoneal abscess, pelviperitonitis, etc.; emergency, delayed emergency or elective laparoscopic surgery; conversions of laparoscopic interventions for the mentioned diagnoses; intraperitoneal septic complications of classical or laparoscopic operations.

All cases who underwent emergency laparoscopic surgery (first 24 hours after admission), delayed emergency surgery (first 72 hours) or elective surgery (by appointment) for suspected or confirmed diagnosis of peritonitis or abdominal sepsis, were considered eligible. Given that not all surgeons have a high degree of training in laparoscopic surgery, it is recommended that patients admitted for acute abdomen should be treated laparoscopically or by open surgery, considering the presence of a well-trained surgical team and not being randomly assigned to a specific type of approach [25].

The exclusion criteria were as follows. Similar to other laparoscopy schools [25], since the beginning of our experience, we decided not to use laparoscopy in patients with: a complex abdominal surgical history (scarred abdomen, multiple operations, more than

two major surgeries), patients with significant air bowel distension (old peritonitis, bowel occlusions with old gastrointestinal tract perforations) and patients in critical general condition (patients in shock).

The diagnosis of peritonitis was obtained based on preoperative imaging investigations (ultrasonography, computed tomography) or by diagnostic laparoscopy, with the evidence of purulent fluid in the peritoneal cavity. Since mortality in our laparoscopic group was zero, we chose for a biostatistical processing solution and we decided that the severity of the cases has to be quantified using the total duration of hospitalization, measured in days.

The main “end-points” of the study were the duration of surgery and the total number of hospital days (although the number of postoperative hospital days is generally more important, but in the case of peritonitis, surgery is usually immediate and the number of hospital days postoperative period is substantially equal to that of total hospitalization days).

In the development of the MPI, 8 risk factors with prognostic relevance were included (age, sex, organ failure, cancer, duration of peritonitis, colon involvement, extent of peritonitis and nature of peritoneal fluid), which were identified from the patient records and operating protocols. The exact information to establish an estimate regarding the MPI was obtained during the laparoscopic surgical exploration. The clinical status, laboratory examinations, computer tomography (which confirmed the presence of intraperitoneal fluid and possible organ perforation) allowed us to early assess the severity of the disease using the MPI, with an estimate of the probability of survival of the respective patients. These patients benefited from curative laparoscopic surgery and not exploratory, as the etiological diagnosis of peritonitis was already known preoperatively. For the remaining patients with an uncertain preoperative etiological diagnosis of peritonitis, the

exploratory nature of the laparoscopic interventions helped us in establishing the exact MPI values.

Three sources of statistical data were used, originating from clinical observation records, surgical protocols and from the electronic personal records of the patients. The cases with extreme ages (>75 years old) were excluded, because the number was reduced and it represents a bias for the study.

The central trend indicators (mean and median), the dispersion indicators (**Standard Deviation-SD**), the Interquartile Range (**IQR**) and skewness were calculated and histograms, normal probability plots and box-plots were used; in the inferential statistics, in order to determine the power of association, simple univariate linear regression models were used for the continuous variables, calculating coefficients and Confidence Intervals [**IC**] 95% and the χ^2 test.

Results

The final group consisted of 109 patients operated exclusively laparoscopically. Among the 65 were women (59.63%) and 44 men (40.37%) who were treated laparoscopically, with an average age of 42.53 years (SD=15.70, (IQR) Median = 42.00, range 18–75 years), statistically significantly associated with the duration of surgery ($T=7.62$, $p<0.0001$, IC95% = 1.05) and with the postoperative evolution (total length of hospital stay - $T = 3.046$, $p = 0.0029$, IC95% = 0.07). The average duration of laparoscopic surgery was 67.71 minutes (AS = 15.02, IQR Median = 65.00-8.80, range 40.00–100.00), being statistically significant associated with the total length of hospital stay ($T = 3.275$, $p = 0.0014$, IC95% = 0.06).

Table no.1 analyses the distribution of the MPI variable in the group of patients operated laparoscopically for peritonitis.

Mannheim peritonitis index Value						
Mannheim Score						
N (Patients group)	Average	Standard deviation	Median (IQR)	Minimum	Maximum	Skewness
109	11.04	4.74	11.00 (6.00)	0	20	0.1

Table 1: Analysis of the group of patients with peritonitis, according to the Manheim score value.

The average value of MPI recorded in the patients included in our group was 11.04; the distribution of the variable was similar to Gaussian distribution, as indicated by the following distribution plots (see chart no.1).

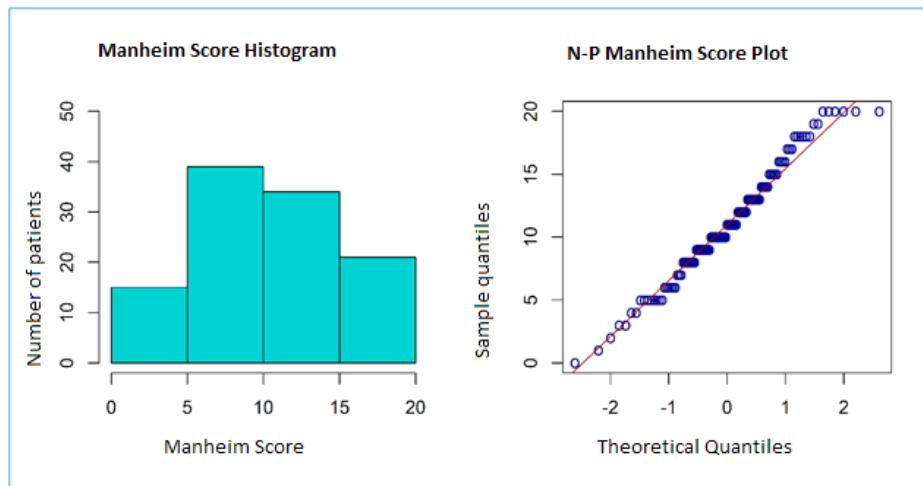


Chart 1: Distribution charts for the Manheim Peritonitis Index.

The boxplot type chart no.2 does not reveal distribution outliers.

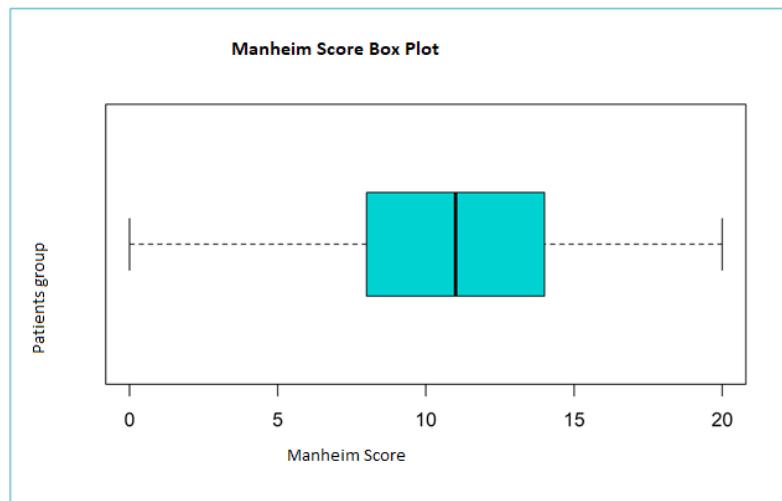


Chart 2: Boxplot type chart for the value of the Manheim Score.

The average length of hospitalization (table no. 2) in patients with peritonitis who benefited from laparoscopic surgical interventions (6.82 days) was comparable to the average annual length of hospitalization at the national level, in general surgery departments (5.5-6.5 days).

Number of hospitalization days						
N (Patients number)	Period(days)					
	Medie	Standard deviation	Median (IQR)	Minimum	Maximum	Skewness
4						

109	6.82	4.92	6.00 (4.00)	2	40	3.67
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Table 2: Period of hospitalization in patients operated laparoscopically for peritonitis.

The influence of MPI on the duration of hospitalization was investigated by logistic regression. To determine the possible association, we used a simple univariate linear regression model, with the dependent variable as the duration of hospitalization and the independent variable as the MPI (Table no.3).

Regressor	T Statistics	p Value	Coefficient [IC95%]
Mannheim Score	5.261	< 0.0001	1.04 [0.65 to 1.43]

Table 3: Influence of Mannheim Score on the total period of hospitalization in patients operated laparoscopically for peritonitis.

We observed that an increase of 1 in the Mannheim score is associated with an increase of approximately 1 day in the duration of hospitalization in patients operated laparoscopically for peritonitis, the effect being statistically significant ($p < 0.0001$) (chart no.3.)

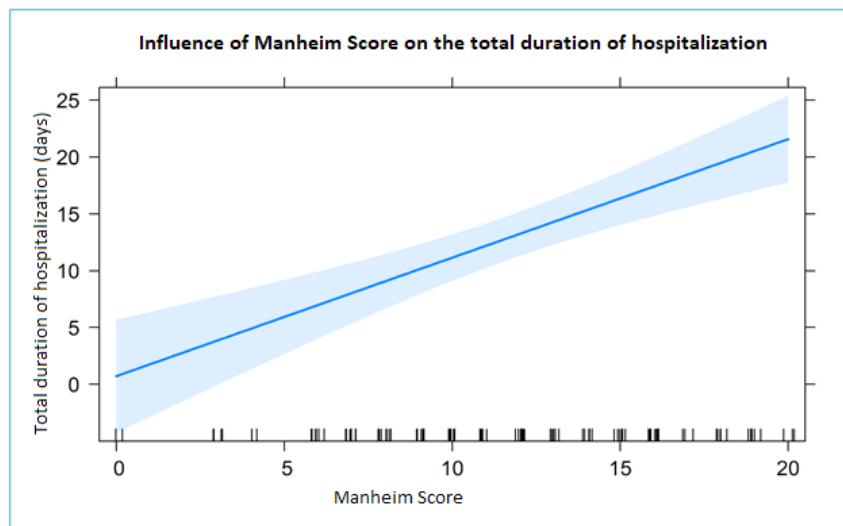
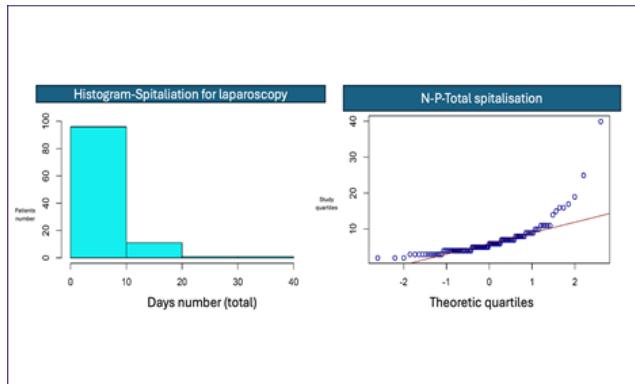


Chart no.3: Influence of Mannheim Peritonitis Index (MPI) on the duration of hospitalization, in patients operated laparoscopically for peritonitis.

The group is characterized by a great heterogeneity in terms of the duration of hospitalization - see graph no. 3. However, the majority of patients had a duration of hospitalization below the standard deviation, which suggests good therapeutic management of serious cases.



Graph no.3: Distribution of the group of patients with peritonitis, by duration of hospitalization - histogram and normal probability plot.

We observe that the distribution of the variable has a significant positive skewness (rightward deviation of the distribution) and is far from the normal distribution, having a negative exponential character.

Discussions

Although the aforementioned topic has been widely debated in the last decades, all previous studies have been about the treatment of peritonitis, individualized for different pathologies, using classical surgical techniques. The literature contains rather limited data on comparative studies between the classical and laparoscopic methods used in the surgical treatment of peritonitis. Even less information exists on the exclusively laparoscopic treatment of patients with peritonitis.

Elective laparoscopic surgery is now widely performed for both benign and malignant disease because it is less invasive than open surgery and postoperative recovery is more rapid [26-29]. Laparoscopy has been reported to be useful in various surgical procedures [26,30-33]. However, its usefulness in the emergency setting is still unclear. Laparoscopic surgery requires an experienced surgeon, a patient in stable condition, and appropriate equipment, not all of which are possible when emergency surgery is required [26,34-37].

Reproducible scoring systems that allow a surgeon to determine the severity of intra-abdominal infection are essential both for assessing the individual risk and for selecting patients who might benefit from a laparoscopic surgical approach.

The early evaluation of the disease severity by using MPI will allow estimating the patient survival probability [4,17]. Patients are divided into three categories, depending on the MPI score: Score ≤ 21 ; score between 21 and 29; score ≥ 29 , with a maximum possible value of 47. In our practice, the diagnosis of peritonitis is not in principle a contraindication for laparoscopic surgery. However, we

draw attention to the fact that the choice of such an option must be made by surgeons with extended laparoscopic experience, and the decision to convert to open technique should be regarded more as a proof of full professional maturity, rather than the surgeon's failure to complete the minimally invasive surgery.

Because the maximum value recorded in our laparoscopic group (MPI_{Max} = 20) was at 42.55% of the maximum possible value (MPI_{Max} possible = 47), that proves once again the cautious attitude of surgeons in selecting cases of peritonitis intended for laparoscopy. In the laparoscopic group studied, the Mannheim peritonitis index (MPI) is a prognostic factor for the severe evolution of the cases, although the average value for the selected patients represented only 23.48% of the maximum possible value (MPI_{Average} of the study = 11.04, compared to MPI_{Max} possible = 47).

Our results are comparable to data provided by more extensive international studies.

It has already been proven that mortality increases at the same time with the increase of the MPI score. No deaths were recorded in our group among patients with peritonitis operated laparoscopically (MPI_{Max} = 20), the result being similar to the literature data [38] according to which the mortality rate was also 0% in patients with MPI Score < 21 .

A retrospective Asian study [39] comprising 131 cases operated for perforated ulcer (laparoscopic operations, n = 63 = 48.1%, compared to open operations, n = 68 = 51.9%), analyzed the two groups (laparoscopic vs open) based on the ASA score (American Society of Anesthesiologists) (p = 0.769), the Boey score 0/1 (p = 0.311), and the Mannheim peritonitis index > 27 (p = 0.528), proving eventually that there was no significant difference in the operative time (p=0.618), but the laparoscopic group had a significantly shorter average postoperative hospitalization duration (4.4 \pm 3.3 days vs 7.3 \pm 7.8 days, p = 0.008) than the open surgery

group. Other authors [40] reported an average length of hospital stay of 6.9 days (2–30 days range), at an average MPI index value = 22.45.

Numerous other international studies [41–45] outlined that the Mannheim Peritonitis Index (MPI) is a simple and useful prognostic index for assessing the severity of peritonitis, helping in an early and objective classification of the severity of peritonitis cases, as well as in selecting patients for surgery.

Therefore, the Mannheim peritonitis index (MPI) is a specific score, with very good accuracy, allowing the evaluation of the individual prognosis of patients with peritonitis [1].

In this study, we introduced the analysis of the laparoscopic group according to the value of the Mannheim Peritonitis Index (MPI) as an innovative element, relating it to the duration of hospitalization and not to mortality, as it was known, as a very specific score and with high accuracy, for the prognosis of death. This initiative was observed to be beneficial for the identification of MPI as an evolutionary prognostic factor in laparoscopically operated peritonitis cases.

We should consider the fact that, in addition to the advanced age of patients with severe peritonitis, there are a number of other causes that may limit the indication of laparoscopic approach and whose strength of association should be the subject of another research study (technical equipment, level of competence in laparoscopic techniques, intervention timing, availability of the anaesthesia-surgical team, therapeutic protocols, anaesthetic management, nursing techniques, etc.).

However, we must observe the limitations of the present study, considering the retrospective nature of the analysis of cases of peritonitis operated laparoscopically and the selection of patients with not very severe forms of the disease, for whom the laparoscopic surgical approach represented a safe treatment modality. Despite these limitations, laparoscopic surgery in the treatment of peritonitis proved to be feasible and reproducible. For a correct evaluation of the impact that laparoscopic surgery has on the therapeutic management of peritonitis cases, extensive epidemiological investigations with prospective multicentre studies and meta-analyses are needed, meant to implement laparoscopic protocols for this severe pathology.

Conclusions

According to the inferential analysis quantified by innovative “end-points” of biostatistical processing, MPI is currently gaining significant prognostic value in the laparoscopic treatment of peritonitis. These results prove us that all those cases of peritonitis with low-medium severity, whose Mannheim Peritonitis Index (MPI) does not far exceed the value of 20, can be approached

laparoscopically, by experienced surgeons and in impeccable technical conditions.

As there is a lack of information in the literature regarding the association of MPI as a prognosis factor in laparoscopic surgery, we consider that more extensive future studies are required. The beneficial impact of the results of the current study will allow future generations of surgeons to decide on the optimal treatment approaches for such a severe pathology, based on fully documented, relevant and indisputable scientific arguments.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, but no ethical committee was necessary, being a retrospective study.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

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Conflicts of Interest

The authors declare no conflicts of interest.

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