

Stratified Outcome Evaluation of Peritonitis

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Abstract

Background: The heterogeneity of disease severity in peritonitis makes outcome prediction challenging. Risk evaluation in secondary peritonitis can direct treatment planning, predict outcomes and aid in the conduct of surgical audits. **Objective:** To determine the outcome of peritonitis in patients stratified according to disease severity at the Kenyatta National Hospital (KNH). **Design:** Prospective descriptive cross sectional survey. **Methods:** Seventy patients were consecutively enrolled within 24 hours of operation for peritonitis between December 2007 and April 2008. To stratify patients according to severity, Mannheim Peritonitis Index (MPI) scores were calculated using the following risk variables: age, sex, preoperative duration, organ failure, sepsis source, malignancy, character and extent of exudate. The main outcome on follow up was complications. Secondary outcomes were length of hospital stay and mortality for different MPI scores. **Results:** Fifty six males and 14 females

(M:F=4:1) were analysed. The mean age was 32.17 years (age range 13-59 years). Forty six (65.7%) had generalised peritonitis, 15(21.4%) had 2-3 quadrant peritonitis while 9(12.9%) had focal peritonitis. Common sources of peritonitis were perforations of appendicitis (31.4%), duodenal ulcer (22.9%) and ileum (18.6%). Patients who complicated had a mean MPI of 26.9 compared to those who did not (22.8) (p=0.018). Morbidity rates increased with rising MPI scores (31% for MPI <21, 54.2% MPI 21-29, 64% MPI >29). The risk of death was double for patients with an MPI ≥26. Hospital stay was 14 days for the whole group but 22 days for those who developed complications. ROC curve analysis showed a predictive power of 0.916 with a sensitivity of 88.9% and specificity of 85.2% at MPI of 29 points. **Conclusion:** MPI scores related with outcomes of peritonitis and can be used in prognosticating early outcome in patients with surgical peritonitis at KNH.

Key Words: Peritonitis, Outcome stratification, Mannheim peritonitis index

Introduction

Peritonitis is associated with higher morbidity and mortality rates when compared to outcome in other general surgical conditions (1, 2). The disease heterogeneity coupled with fairly uniform symptomatology compound to often make treatment planning problematic (3). This is underscored by the fact that the peritoneum responds fairly uniformly to irritation irrespective of the source. Surgical intervention does not guarantee a predictable recovery pattern owing to the differences in the severity of pathophysiological responses to the various irritants (4). Systemic complications may ensue and progress to multiorgan failure and adversely affect outcome (5, 6).

Scoring systems help surgeons in objective treatment planning, prognosticating outcome, and in communicating feedback to patients. Additionally, scoring systems assist in the conduct

of surgical audits by which care standards can be improved (7, 8).

In surgical peritonitis, surgery aims to eliminate foci of infection and restore peritoneal physiological and immunological functions to as near normal as possible (9). Early and definitive source control plus bacterial and toxins elimination reduces the need for re-operation and adverse outcomes (3,10) including surgical site infection, fistula formation, haemorrhage, prolonged ileus, organ failure and death.

Many factors are known to be associated with the adverse outcomes in peritonitis. These include the degree of contamination, age, immunodeficiency states and severity of patient's systemic response and physiologic compromise (11,12).

On their own, these factors do not prognosticate outcome in peritonitis. The MPI is an easily calculated score using eight patient and disease variables (8,11). The index takes into account the

patients age and gender, organ failure, malignancy as the source of contamination, preoperative duration of symptoms greater than 24 hours, origin of sepsis other than colonic, extent of spread and character of peritoneal fluid.

Methods

We carried out a prospective descriptive cross sectional survey at Kenyatta National Hospital between December 2007 and April 2008 and included patients admitted and operated for peritonitis in the general surgical wards. Excluded were patients with (i) no consent (ii) peritoneal signs due to haemoperitoneum (iii) primary peritonitis in the setting of renal or hepatic failure and (iv) those transferred in after laparotomy for peritonitis. The sample size was calculated using Fischer's formula which considered a peritonitis prevalence of 3% at the KNH wards and a precision estimate of 0.04.

Data on risk factors, intraoperative findings (appearance of the exudate; extent of exudate; source of sepsis) and definitive procedure done were extracted from the patients' files starting on the first post-operative day. Patient's age, sex, pre-operative data (duration of symptoms, presence or absence of ileus) were also recorded. Where applicable, histology of biopsies taken was used to rule in/out malignancy as the primary pathology.

Laboratory parameters used to define organ failure were those of blood samples drawn within the first 24 hours of laparotomy. Organ failure was defined by the following parameters:

1. Kidney: creatinine $\geq 177\mu\text{mol/L}$ and urea $\geq 16.7\text{mmol/L}$, oliguria $< 20\text{ml/hour}$
2. Lungs: $\text{PCO}_2 \geq 50\text{mmHg}$ and $\text{PO}_2 \leq 50\text{mmHg}$
3. Shock: systolic BP $< 90\text{mmHg}$ recorded on admission
4. Intestinal: presence of ileus for > 24 hours

The sum of risk factors present (Table 1) was recorded for each patient and used to calculate the MPI score.

Table 1: The Mannheim Peritonitis Index

| Risk factor | Yes | No |
|------------------------------------|-----|----|
| Age > 50 years | 5 | 0 |
| Female gender | 5 | 0 |
| Organ failure | 7 | 0 |
| Malignancy | 4 | 0 |
| Preoperative duration > 24 hours | 4 | 0 |
| Origin of sepsis not colonic | 4 | 0 |
| Diffuse peritonitis | 6 | 0 |
| Exudates: Clear | 0 | 0 |
| Cloudy/purulent | 6 | 0 |
| Faecal | 12 | 0 |

Total patient MPI score was the sum total of all the positive risk factor scores. Outcome evaluations were conducted regularly every alternate day following the

initial visit until patient discharge or death. Morbidity during the follow up period was determined by duration of hospital stay and identification of one or more of the following complications; systemic (chest infection), local or gastrointestinal haemorrhage, wound sepsis, deep space infection, wound dehiscence, fistula formation or ileus lasting more than 5 days.

Source control was deemed to have been achieved at initial laparotomy in patients who henceforth showed no continuing peritoneal contamination from the previous site of origin of sepsis.

The study end point was reached at on patient discharge or death.

The data was analysed using SPSS v12 (SPSS Inc. Chicago, IL, USA). Individual patient MPI score and respective outcome was determined followed by stratification of the scores into 3 main groups of < 21 points, 21-29 points and > 29 points. A threshold score of 26 points was used to calculate morbidity and mortality relative risks, followed by evaluation of individual risk factors for significance. For statistical significance testing, Fisher's exact test, Mann Whitney U- test and Pearson correlation were applied as appropriate.

Morbidity and mortality rates for the stratified MPI scores (26 vs. 29 points) were calculated and the predictive power of the MPI, sensitivity and specificity derived from receiver-operator characteristic (ROC) curve analysis. The ROC curve essentially depicts the trade off between sensitivity and specificity of a particular test parameter (MPI in this case). The area under curve (AUC) of an ROC curve is a measure of accuracy or predictive value (power) of the test parameter. P values of less than 0.05 were taken as statistically significant and 95% confidence intervals applied as necessary.

Results

Patient Characteristics

Seventy patients were recruited of which 56 (80%) were males giving a gender ratio of 4:1. The mean age of presentation was $32.17 + 10.8$ years, the youngest being 13 years and the oldest 59 years (Figure 1). Most patients (74%, n 52) were aged between 20-40 years. The proportion of patients in the 10-19, 20-29, 30-39, 40-49 and 50-59 years was 7.1%, 40%, 30%, 15.8% and 7.1% respectively.

The mean preoperative duration of symptoms was $5.5 + 3.5$ days (range 1-14 days). Thirty nine (55.7%) patients had one or more organ dysfunction with ileus being the most frequent at 48.6%. Perforated appendicitis was the most common source of peritonitis (Table 2).

Table 2: Source of sepsis

| Source | Frequency | Percentage |
|----------------------|-----------|------------|
| Appendicitis | 22 | 31.4% |
| Duodenal perforation | 16 | 22.9% |
| Ileal | 13 | 18.6% |
| Colon | 9 | 12.9% |
| Pelvic | 5 | 7.1% |
| Gastric | 5 | 7.1% |
| Total | 70 | 100.0% |

The peritonitis was generalised, 2-3 quadrant and focal in 65.7%, 21.4% and 12.9% of cases respectively. Three patients had malignant bowel perforations (2 colon, 1 ileum).

Analysis of MPI Scores

The mean MPI was 24.7 + 7.4 points (range 10-42). Males had lower mean MPI of 23.7 points compared to females who scored a mean of 31 points (p<0.0001). Seventeen patients (24.3%) patients had an MPI >29 points, 24 (34.3%) MPI 21-29 while 29 (41.4%) had MPI < 21.

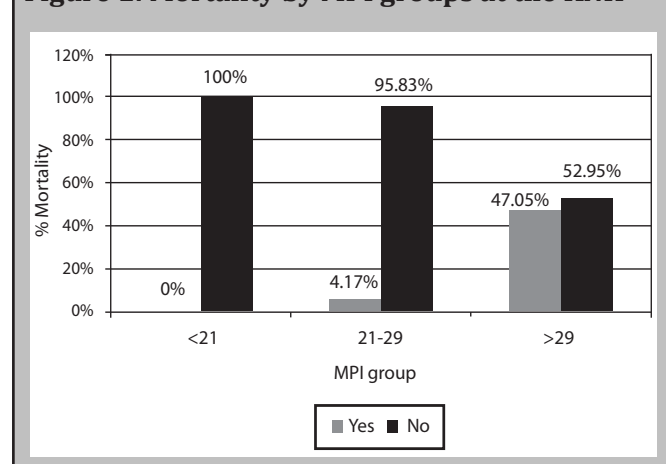
Outcomes

The overall morbidity rate was 47.1%. The most common complications were superficial wound sepsis (45.7%), dehiscence (18.6%), fistula formation (12.9%) and deep space abscess (8.6%). Two patients developed chest infections that were successfully treated with antibiotics while another two developed gastrointestinal haemorrhage following fistula formation and eventually succumbed. Three patients were admitted to the ICU postoperatively for mechanical ventilation out of which one succumbed.

Patients with morbidity had a significantly higher mean MPI of 26.9 points compared to those without who scored a mean MPI of 22.8 points (p=0.018). Morbidity rate increased from 31% for MPI < 21 to 54.2% for MPI 21-29 and 64.7% for MPI > 29.

Nine patients (six males and three females) died giving a 12.9% overall mortality rate. Mortality by gender was 10.7% for males and 21.4% for females. The mean MPI for non survivors was 33.8 points compared to 23.4 points for survivors (p<0.0001). Of all the non survivors, only one patient (4.2%) had an MPI of <29 points (27 points). Figure 1 depicts mortality trends across the MPI groups.

Figure 1: Mortality by MPI groups at the KNH



All the nine patients in whom source control was not achieved after initial laparotomy had an MPI of ≥27 points. The overall mean hospital stay was 14±10.4 days (range 1-45 days) but significantly higher with morbidity at 22 days compared to 7 days with no morbidity (p=0.01). There was no significant difference in duration of hospital stay between survivors and non survivors.

Risk Evaluation

An MPI score of ≥26 points doubled the risk of hospital death (95% CI 1.62-2.4) and increased the risk of complications by 1.54 times (table 3). Age >50 years, presence of organ dysfunction, character and extent of exudate were significantly associated with an MPI score of ≥26.

Prolonged hospital stay strongly correlated with an MPI of ≥26 points (11.3 + 7 days for MPI < 26 versus 17.7 + 11.8 days for MPI > 26, p=0.016) (Table 3).

Table 3: Hospital stay in days vs MPI

| MPI GROUP | Mean | N | Std. Deviation | Median | Minimum | Maximum |
|-----------|---------|----|----------------|---------|---------|---------|
| <26 | 11.2813 | 32 | 7.04014 | 8.5000 | 5.00 | 36.00 |
| ≥26 | 17.7105 | 38 | 11.82966 | 14.0000 | 1.00 | 45.00 |
| Total | 14.7714 | 70 | 10.37859 | 10.0000 | 1.00 | 45.00 |

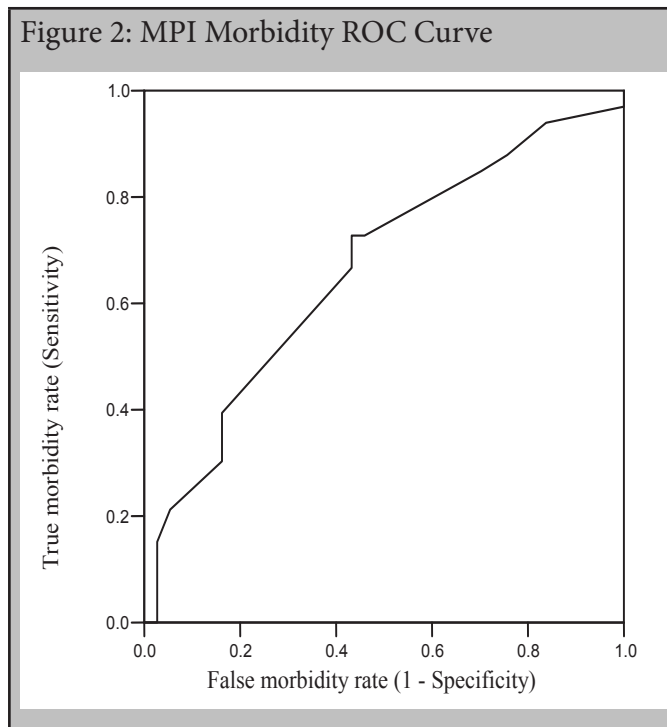
Mann Whitney U-test, Z=-2.417: P<0.05 (0.016)

Roc Curves For Morbidity And Mortality

Thirteen (76.5%) out of 17 patients with an MPI ≥ 29 had adverse outcomes.

The predictive power of the MPI for morbidity in this study was 0.663 with a sensitivity of 33.3% and specificity of 83.8% at a score of 29 points (Figure 2).

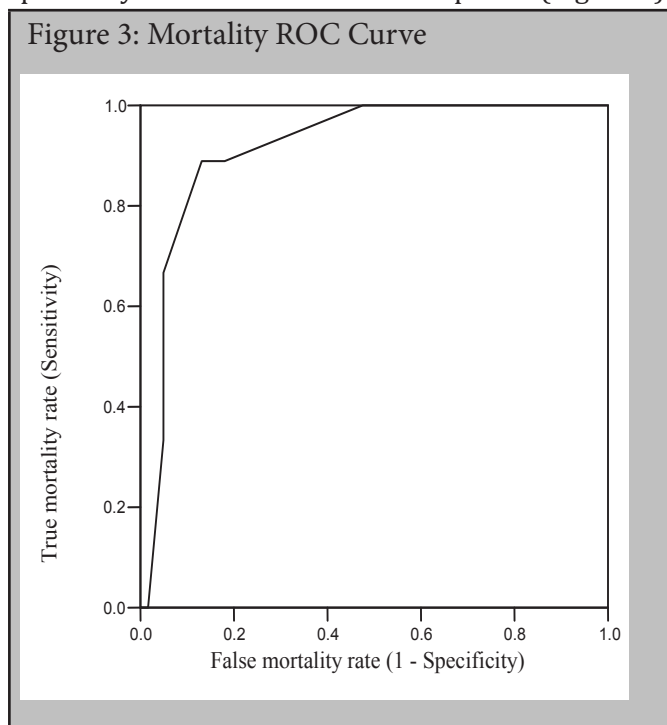
Figure 2: MPI Morbidity ROC Curve



Mortality ROC Curve

The ROC curve for mortality showed a predictive power of 0.916 with a sensitivity of 88.9% and specificity of 85.2% at an MPI of 29 points (Figure 3).

Figure 3: Mortality ROC Curve



Discussion

This study set out to stratify the severity of peritonitis and predict outcome using the MPI at KNH. Of the seventy patients recruited, an unequal sex distribution was observed giving a male to female ratio of 4:1. This pattern of male preponderance in laparotomy for general surgical pathology has been previously reported at this institution (1, 2) but contrasts studies from the developed countries which show even gender distribution or a slight preponderance of either sex (3,6,7,10,13). A comprehensive explanation for this observation is uncertain from our data but could be a result of variations in the predominant aetiologies of secondary peritonitis in our setting compared to the West.

The majority of our patients were young with a mean age of 32.17 ± 10.8 years and 74% of the study group falling in the 20-40 years age category. Melero in Mexico reported a similar distribution with a mean of 34.6 years but studies from Europe show a much older age group with a range of 44-64.8 years even in centres where source spectrum closely resembles our findings (3, 6, 7, 13-15).

Our study which included patients with focal peritonitis shows that perforated appendicitis (31.4%) is the commonest source of peritoneal sepsis at KNH. However, considering that most patients with focal peritonitis had a diagnosis of appendicitis, perforated gastro duodenal peptic ulcers (30%) remain the commonest cause of generalized peritonitis at KNH followed by ileal perforation at 18.6% in keeping with the above findings (1). Studies from Europe show a different picture with colonic perforation due to diverticular disease and cancer (16-70%) the leading causes followed by gastro duodenal peptic ulcer perforation (16%) and perforated appendicitis (8%) (3,6,13).

The mean MPI of 24.7 ± 7.4 points in this study compares well with previous studies by Sailer in generalised peritonitis, Bielecki in large bowel perforation and Pacelli in peritonitis of varied sources (3,6,15). In our study, the mean male MPI score of 23.7 points was close to the overall study mean compared to females whose mean of 31 points stratified them into a high risk group for both morbidity and mortality. Outcomes in females were worse compared to male counterparts recording higher gender morbidity (65%) and mortality (21.4%) rates. Although female sex is one of the risk factors in the MPI, we did not find previous studies that compared differences in gender mean MPI scores.

The mean MPI for morbidity in this study was 26.9 points (22.8 for no morbidity) with group morbidity rates rising progressively from 33% at MPI 21 points to 65% at MPI >29 points. Based on disease severity stratification, this would be the expected pattern although previous studies only stratified scores for mortality rates.

The overall mortality rate of 12.9% falls within but on the lower side of rates from referenced studies. Rates from European studies range from 6% to 42% (3, 6, 7, 10, 13). Locally, a rate of 22% in patients with generalized peritonitis due to jejunoileal perforations has been reported (1). The mean MPI for non survivors was 33.8 points (23.4 points in survivors) and compares favourably with other studies that give a range of 26.37-32.7 points (3, 6, 13).

In a meta-analysis of results from 7 centres involving 2003 patients, Billing reported an average group mortality rate of 2.3% for MPI <21 points, 22.5% at MPI of 21-29 points and 59% with MPI of >29 points. Our group mortality rate albeit lower appear to follow this pattern as no mortality occurred at MPI <21 points, was 4% with MPI 21-29 points and was 47% with MPI >29 points. Differences in patient demographics, sepsis source and co morbidities between our study population and international reports already alluded to above may be responsible for the lower mortality rates observed in this study.

Morbidity increased hospital stay significantly to a mean of 22 days a finding that was in keeping with other studies (6, 8, 13). Higher mean MPI scores correlate with increased morbidity rates and by extrapolation imply prolonged hospital stay.

Patients who scored at least 26 points in this study had twice as much risk of in hospital death compared to their counterparts who scored fewer points. Sailer, Bielecki, and Qureshi in their separate studies had already shown that patients who scored ≥ 26 points had a significantly higher mortality rate than their counterparts scoring <26 points (3,6,16).

The most significant predictive factors for morbidity/mortality in this study were female gender, age above 50 years, presence and number of organ dysfunction, character of and exudate extent. Melero found a similar pattern but notes that gender was not a significant factor (7). Malignancy, preoperative duration, and source of sepsis had no significant influence on eventual MPI score in this study unlike in other studies (17). Sailer whose study focussed on generalized peritonitis reports similar findings only that he found preoperative duration to significantly

influence eventual mean MPI from 23.2 to 29 points (3). That our study included patients with focal peritonitis coupled by large numbers of late presenters may explain lack of statistical significance. Studies by Anaya, Notash and Billing showed that peritonitis of appendicular or colonic origin carries a lesser risk than those from other sources (10,11,14). Correlation between sepsis source and eventual MPI score in our study did not attain statistical significance.

This study attained a morbidity predictive power of 0.663 by ROC curve analysis. Although low, it did attain statistical significance albeit with a low sensitivity of 33% but good specificity of 83.3% at a score of 29 points. A recent study from Kigali has reported a higher predictive power of 0.896 with a sensitivity of 66.7% and specificity of 99.04% at a similar score (17). The reason for this disparity in rates is unclear. Possibly, the fact that 60% of all patients with morbidity had an MPI ≤ 29 points may explain.

In analysis of ROC curve for mortality, Biondo reported a predictive power of 0.725 at an MPI score of 26 points, while Notash found a predictive power of 0.972 with 79% sensitivity and 96% specificity at an MPI of 29 points (13, 14). Billing in a meta analysis of 2003 patients reported a mean sensitivity of 86% (54%-98%) and specificity of 74% (58%-97%) at a score of 26 points (11). In the Kigali paper, ROC curve for mortality showed a predictive power of 0.903 with sensitivity of 88.2% and specificity of 74.8% at MPI 29 (17). Our study attained a mortality predictive power of 0.916 with a sensitivity of 88.9% and specificity of 85.2% at an MPI of 29 points showing consistency with the published literature.

Studies evaluating the usefulness of the MPI in outcome prediction in comparison with other risk stratification studies have shown that it compares well with most of them, if not superior. Validation studies comparing its strength in outcome prediction with established scoring systems like APACHE II have shown that the two are accurate predictors of early outcome in peritonitis (8,11,13). Overall, our results validate its usefulness in risk stratification and outcome prediction.

This study had its own limitations. Being an observational study, we assumed that all patients received standard and adequate therapy commensurate with the diagnosis. Inadequate therapy contributing to either morbidity or mortality could be confounding factors. The exclusion of children less than 13 years also renders the results inapplicable to this group of patients.

Conclusion

The MPI score is a useful disease severity stratification tool and can be used to prognosticate early outcome in patients managed for secondary peritonitis at KNH.

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