Prognostic Nutritional Index score is useful to predict post-operative mortality and morbidity in gastric cancer

Le score PNI permet de prédire la mortalité et la morbidité après chirurgie pour cancer de l'estomac

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RÉSUMÉ

Introduction : Le score PNI (prognostic nutritional index) est calculé à partir des valeurs de l'albuminémie et du taux de lymphocytes. Le but de ce travail était de valider le score PNI dans la prédiction de la mortalité et la morbidité après chirurgie pour cancer de l'estomac.

Méthodes : Il s'agissait d'une étude rétrospective ayant colligé les patients opérés pour un cancer de l'estomac au service de Chirurgie B de l'Hôpital Charles Nicolle de Tunis entre le 01/01/2008 et le 31/12/2012. Le critère de jugement principal était la mortalité post-opératoire (dans les 30 jours en post-opératoire). Le critère de jugement secondaire était la morbidité post-opératoire (dans les 30 jours en post-opératoire).
Nous avons réalisé une étude descriptive ainsi qu'une analyse univariée et multivariée avec régression logistique ainsi qu'une analyse à l'aide d'une courbe ROC.

Résultats : Nous avons colligé 14 femmes et 26 hommes, avec un sex ratio = 1.85. L'âge moyen des patients était de 63 ± 15 ans La mortalité post-opératoire était de 18%. La morbidité post-opératoire était de 28%. La courbe ROC nous a permis de valider le score PNI pour la mortalité post-opératoire dans le cancer de l'estomac avec une valeur seuil égale à 38 avec une sensibilité de 100% et une spécificité de 64%.
Le score PNI a également été validé pour la morbidité post-opératoire dans le cancer de l'estomac avec une valeur seuil égale à 38 avec une sensibilité de 82% et une spécificité de 66%.

Conclusion : Nous avons validé le score PNI pour prédire la mortalité et la morbidité après chirurgie pour cancer de l'estomac avec une valeur seuil égale à 38.

Mots-clés

Cancer de l'estomac, chirurgie, mortalité, morbidité, prognostic nutritional index.

SUMMARY

Background: The Prognostic Nutritional Index (PNI) score is based on the level of lymphocytes and albuminemia. The aim of this study was to validate the pre-operative PNI score for predicting post-operative mortality and morbidity of patients operated on for gastric cancer.

Methods: This retrospective study collected data from patients operated on for a gastric cancer at the surgical unit B of Charles Nicolle's hospital in Tunis between January 1st, 2008 and December 31, 2012. The main outcome measure was post-operative death within 30 days. The secondary outcome was post-operative morbidity (within 30 days). We have performed a descriptive analysis, a univariate and multivariate analysis with logistic regression and a ROC curve analysis.

Results: 14 women and 26 men were enrolled, with a sex ratio of 1,85. The mean age was 63 ± 15. Post-operative mortality and morbidity rate were respectively 18% and 28%. The ROC curve allowed us to validate the PNI for predicting post-operative mortality in gastric cancer with a threshold level of 38 with sensitivity 100% and specificity 64%. PNI was also validated for post-operative morbidity with a threshold level of 38 with sensitivity 82% and specificity 66%.

Conclusion: PNI was validated for predicting post-operative mortality and post-operative morbidity in gastric cancer.

Key-words

Gastric cancer, surgery, morbidity, mortality, prognostic nutritional index.

Evaluating post-operative morbidity and mortality in the surgery of digestive cancers is a real challenge for any surgeon. To do so, there are scores such as the ASA physical status score, the Charlson score, the POSSUM score and the PNI (prognostic nutritional index) score [1-8]. These scores, which assess the fitness of patients before surgery, allow to plan the therapeutic strategy and thus schedule surgery after a control of disorders (high blood pressure, diabetes, coronary syndrome), a transfusion (anemia), a high-calorie and /or high-protein diet (hypoalbuminemia). There is continuing interest in prognostic factors that allow more accurate patient stratification, improve clinical decision making, and that might contribute to more rational clinical trial design and analysis. Prediction of surgical risk and survival by evaluating preoperative immunological and nutritional status can be a useful mean to identify a strategy for preventing postoperative complications, death and improve overall survival.

It has been demonstrated that immunological and nutritional status of patients influences the post-operative course of patients operated on for malignant tumor of the digestive tract [9-14].The PNI score is based on the level of lymphocytes and albuminemia, described in 1983 by Buzby and modified by Onodera in 1984 [7-8].

The aim of this study was to validate the preoperative PNI score for predicting post-operative mortality and post-operative morbidity risks for patients operated on for a gastric cancer and assess the performance of this score.

METHODS

Patients:

This retrospective study collected data from patients aged more than 18 operated on for a gastric cancer at the surgical unit B of Charles Nicolle's hospital in Tunis between January 1st, 2008 and December 31, 2012. Were not included non operated patients suffering from a gastric cancer. Patients with no available albuminemia and/or full blood count were also excluded.

Collected variables:

The patient demographic and clinical characteristics were obtained retrospectively from the medical records. We also collected data from blood tests just before the operation, including the level of serum albumin, total lymphocyte count in peripheral blood. Then PNI was calculated using the following formula: 10 × serum albumin (g/dl) + 0.005 × total lymphocyte count in the peripheral blood (per mm3).

Outcome measure:

The main outcome measure was in-hospital post-operative death within 30 days. The secondary outcome was post-operative morbidity (within 30 days).

Statistical analysis:

We have performed a descriptive analysis. Qualitative variables were represented by percentage with 95% confidence interval. Quantitative variables were mentioned by mean with standard deviation when variable distribution was normal, otherwise, by median with ranges. We have performed a univariate and multivariate analysis with logistic regression. We have calculated the probability of post-operative morbidity and mortality according to PNI value. We have also performed a ROC curve analysis and calculated the cut-off point of the PNI with its sensitivity, specificity, and predictive values. Statistical significance was considered when $p < 0.05$, and 95% confidence intervals were also calculated. The statistical analyses were performed using the SPSS® software program, version 17.0 (SPSS, Chicago, IL)

RESULTS

Descriptive analysis

Were enrolled 14 women and 26 men, with a sex ratio of 1,85. The mean age was 63 ± 15 (range: 21-87 years). Three patients had diabetes mellitus, one patient had high blood pressure and seven patients had chemotherapy less than 6 months before intervention. 37 patients were operated on in a non-emergency condition and three patients on emergency. All patients were operated on by laparotomy. The mean body mass index was 21,9 ± 3,4 kg/m2 (range: 16,6 – 30 kg/m2).

The mean serum albumin value was 3,2 ± 0,6 g/dl (range: 1,5 – 4,5 g/dl). The median lymphocyte count in the peripheral blood was 1251 elts/mm3 (range: 250- 3700 elts/mm3). The mean value of PNI score was 37,5 ± 7 (range: 17- 49). Three patients received preoperative albumin: one patient during three days (PNI=22), one patient during five days (PNI=37,1) and one patient during 10 days (PNI=38,6). There were 35 digestive anastomosis, three patients have been transfused and the median operating duration was 260 ± 117 minutes (range: 60 - 480 min).

Seven patients died, mortality rate was 18%. Death was owing to a toxic shock in five cases, an acute pulmonary edema in one case and an acute myocardial infarction in one case. Four patients have been reoperated on (10%). We recorded 11 post-operative complications: morbidity rate was 28%. It was a parietal complication in two cases: a parietal abscess in one case and an evisceration in one case. We noted a deep abdominal post-operative complication in eight patients: a peritoneal abscess in four cases and an acute peritonitis in four cases. There were three extra site post-operative complications: a cerebro-vascular accident in one case, a superficial thrombophlebitis in one case and an acute myocardial infarction in one case. Median hospital stay was 24 ± 13 days (range: 3 - 58 days). Median follow-up was 6,5 months (range: 0-36 months).

Validation of PNI

The results of the univariate and multivariate analysis with logistic regression for post-operative morbidity and post-operative mortality are shown in tables n°1, 2 and 3.

Table 1: univariate analysis for post-operative morbidity

Variable	Post-operative Morbidity	No Post-operative Morbidity	p
Univariate		9/20	0,043
Drainage (no/yes)	0/11	29/0	0,004
Reintervention (no/yes)	7/4	5/24	0,042
Death (no/yes)	6/5	33,7 ± 8,7	0,028
PNI	39,4 ± 6,2		

Table 2: univariate analysis for post-operative mortality

Variable	Death	No Death	p
Univariate			
Emergency surgery (no/yes)	3/4	0/33	0,004
Deep abdominal complications (no/yes)	3/4	29/4	0,02
Reintervention (no/yes)	4/3	32/1	0,013
Age	75,9 ± 6,3	60,9 ± 16	0,02
Prothrombin ratio	76% ± 15%	91,6% ± 9,9%	0,001
PNI	29,1 ± 8,6	39,7 ± 5,6	0,000
Hospital stay	13 ± 6	28,6 ± 12	0,003

Table 3: multivariate analysis for post-operative morbidity and post-operative mortality

Post-operative Morbidity	Odds Ratio	CI 95%	p
PNI	0,895	0,803-0.997	0,044
Post-operative Mortality	Odds Ratio	CI 95%	p
PNI	0,794	0,670-0,941	0,008

We have also calculated the probability of post-operative morbidity and post-operative mortality according to PNI value (table n°4).

Table 4: probability of post-operative morbidity and mortality according to PNI value

PNI	Post-operative Morbidity	Post-operative Mortality
10	88,2%	99,8%
20	71%	87,9%
30	41%	47,3%
40	6,5%	22,8%
50	0,6%	8,1%

PNI was validated in gastric cancer for post-operative mortality with a threshold level of 38 (area under the curve = 0,874 with p<0,002, CI 95%: 0.756-0.993) with sensitivity 100%, specificity 64% [CI 95%: 47-80%], positive predictive value 37% [CI 95%: 15-59%] and negative predictive value 100% (figure n°1).

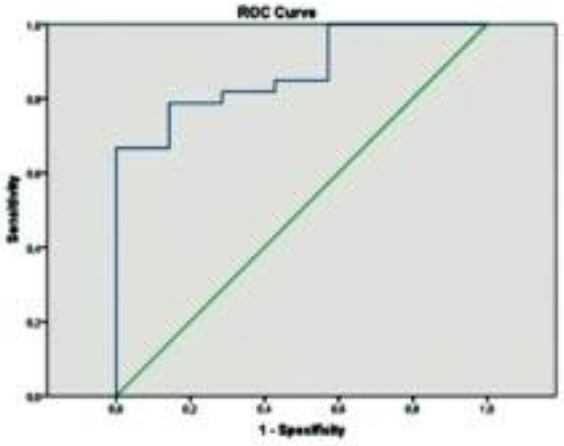

Figure 1 : ROC curve for post-operative mortality in gastric cancers

PNI was also validated in gastric cancer for post-operative morbidity with a threshold level of 38 (area under the curve = 0,730 with p<0,026, CI 95%: 0.549-0.912) with sensitivity 82% [CI 95%: 59-100%] , specificity 66% [CI 95%: 48-83%], positive predictive value 47% [CI 95%: 25-70%] and negative predictive value 90% [CI 95%: 78-100%] (figure n°2).

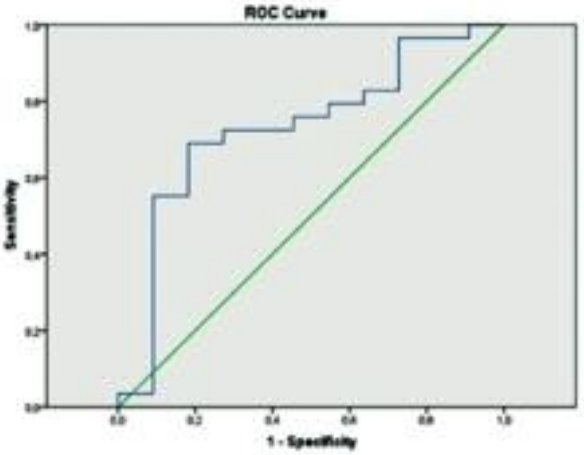

Figure 2 : ROC curve for post-operative morbidity in gastric cancers

DISCUSSION

This study validated PNI score for predicting post-operative mortality and post-operative morbidity in gastric cancer with a threshold level point of 38.

Many tools have been developed to examine the biological behavior of malignant tumors such as tumor markers. Among these methods, the nutritional condition of the patient is an important factor in determining postoperative morbidity and survival in patients with gastric carcinoma [9-13]. The PNI was initially designed by Buzby to assess the immunological and nutritional

aspects of patients who underwent surgical treatment for diseases of the gastro-intestinal tract [7]. However, the value could be calculated based on the measurement of many different parameters. Thereafter, Onodera proposed the modified PNI that was calculated by two factors the serum albumin concentration and the lymphocyte [8].

The preoperative immunological and nutritional statuses have been demonstrated to be associated not only with postoperative complications, but also with the long-term outcomes of patients with malignant tumors [13-17]. Several authors reported that PNI was a good prognostic marker for oesophageal, gastric, colorectal, pancreatic and hepatocellular cancer [9-23]. These studies have reported an impact of the PNI on the long-term outcomes in several malignancies, and various cutoff values for the PNI were used in those studies [9-23]. The cutoff value was usually set at 45, because a PNI<45 is defined as moderate to severe malnutrition. In fact, most authors validated PNI with a cut-off of 45 whereas in our study, the cut-off was 38. We could explain this difference by saying that in our country, patients with gastric cancer consult late, in bad general condition, malnourished and in advanced cancer state. However, the optimal cutoff value of the PNI to predict the post-operative course and long-term outcomes remains unclear.

In the present study, we performed a ROC curve analysis, and the optimal cutoff value for the PNI in gastric cancer was determined to be 38. When the PNI was less than 38, the sensitivity and specificity for the post-operative mortality and morbidity were 100% and 67% respectively. A meta-analysis found that PNI was an independent prognostic factor for overall survival, post-operative complications, depth of invasion and lymph node metastasis in gastric cancer [9]. Sun et al [10] found that PNI was associated with the overall survival of gastric cancer patients in univariate analysis, but only PNI was an independent prognostic factor in multivariate analysis before and after propensity score adjustment. In the same study Sun et al [10] evaluated the Canton score which is based on PNI, neutrophil-lymphocyte ratio and platelet-lymphocyte ratio. Canton score is more complicated to calculate and was also validated in gastric cancer for overall survival, whereas in our study, we validated PNI in gastric cancer for post-operative morbidity and post-operative mortality.

Watanabe et al [11] determined that PNI might be a predictor of both postoperative complications and hospital mortality in the elderly (age > 75 years old). Nozoe et al [12] demonstrated with a multivariate analysis that a lower value of PNI (threshold level=49,7) was independently associated with a more unfavorable prognosis of patients with gastric carcinoma . Migita et al [13] concluded that PNI influenced the overall 5-year survival and relapse free 5-year survival when inferior to threshold level of 48 [13].

The limitations of our study were its retrospective and single-center design. This study did not include all consecutive patients because of missing data due to incomplete serum albumin or peripheral blood lymphocyte count data. Nevertheless, the results of the present study suggested that the presence of a systemic inflammatory response, as indicated by PNI, is a simple and useful tool in the assessment of post-operative mortality and morbidity in patients with gastric cancer.

PNI was validated for post-operative mortality and post-operative morbidity in gastric cancer with a threshold level of 38. We recommend to calculate PNI for patients with gastric cancer to identify a sample of patients with a high risk of post-operative morbidity and mortality. Thus, PNI should be included in the routine assessment of gastric cancer patients before surgery and physicians should pay attention to peri-operative care for patients with a low PNI value. We need a prospective study with a large sample size to confirm these results.

CONCLUSION

PNI was validated for post-operative mortality and post-operative morbidity in gastric cancer with a threshold level of 38.

PNI is a simple and useful predictive factor of post-operative mortality and morbidity, which can allow us to adapt the therapeutic strategy. Thus PNI should be included in the routine assessment of gastric cancers to achieve nutritional and immunological levels that optimize the PNI, and then perform surgery at the optimal time.

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