

PROGNOSTIC FACTORS TOWARD BLADDER CANCER PATIENT RECOVERY AFTER RADICAL CYSTECTOMY SURGERY

¹Rendy Triyaka, ¹Ahmad Zulfan Hendri.

¹ Department of Urology, Faculty of Medicine/Gadjah Mada University, Sardjito General Hospital, Yogyakarta.

ABSTRACT

Objective: This study aimed to know independent prognostic factors to predict the recovery time of bladder cancer patients after radical cystectomy. So that it would be a consideration to determine patient feasibility before surgery and after surgery management. **Material & Methods:** This study was an observational analytical study with a retrospective approach to examine the relationship between pre-surgery variables of the bladder cancer patients and the duration of treatment post radical cystectomy. **Results:** From the results of this study, it is known that the average length of postoperative care for older patients (above 65 years) was lower when compared to patients under 65 years with averages of 17.08 and 18.03 days respectively p-value of this analysis was 0.781. Patients with low hemoglobin, albumin, and HALP scores had longer postoperative hospitalization periods but with P values of 0.384, 0.276, and 0.603, the ileal conduit has the longest hospitalization treatment period between the two other procedures, with a P-value of 0.904. It was found that the average length of postoperative care for underweight patients was 16.5 days and for patients with normal BMI was 19.59 days. The difference between these averages showed a p-value of 0.396 it is known that the average length of postoperative care for older patients (above 65 years) was lower when compared to patients under 65 years with averages of 17.08 and 18.03 days respectively. The p-value of this analysis was 0.781 it was found that patients with low hemoglobin, albumin, and HALP scores had longer postoperative treatment periods, p-value 0.384, 0.276, and 0.603. The average duration of postoperative care for patients who applied the ERAS protocol tended to be faster (15.67 days) compared to patients who did not apply the ERAS protocol (18.16 days). Nevertheless, the p-value of this difference was 0.518. **Conclusion:** This study concludes that there is no prognostic factor that can independently predict the duration of treatment of bladder cancer patients post-radical cystectomy. Therefore in-depth assessment of various factors is required before performing radical cystectomy to achieve the best postoperative recovery rates.

Keywords: Prognostic factors, bladder cancer, radical cystectomy surgery.

ABSTRAK

Tujuan: Tujuan dari studi ini adalah untuk mencari faktor prognostik independen dalam memprediksikan lama pemulihan pasien kanker kandung kemih paska radikal sistektomi, sehingga menjadi pertimbangan menentukan kelayakan pasien sebelum operasi dan manajemen pasca operasi. **Bahan & Cara:** Penelitian ini merupakan penelitian analisis observasional dengan pendekatan retrospektif untuk mengkaji hubungan antara beberapa variabel dari pasien penderita kanker kandung kemih sebelum operasi terhadap lama perawatan paska operasi radikal sistektomi. **Hasil:** Pasien dengan usia diatas 65 tahun memiliki rerata lama perawatan paska operasi radikal sistektomi lebih pendek jika dibandingkan dengan pasien usia dibawah 65 dengan rerata masing-masing 17.08 dan 18.03 hari, $p = 0.781$. Pasien dengan kadar rendah hemoglobin, albumin, dan HALP memiliki masa perawatan paska operasi yang lebih lama dengan $p = 0.384$, 0.276 , dan 0.603 , saluran ileum memiliki masa perawatan terlama di antara dua prosedur lainnya, dengan $p = 0.904$. Rerata lama perawatan paska operasi untuk pasien dengan berat badan kurang adalah 16.5 hari dan untuk pasien dengan IMT normal adalah 19.59 hari. Selisih rerata tersebut menunjukkan nilai p sebesar 0.396 yang diketahui bahwa rerata lama perawatan paska operasi pada pasien usia lanjut (diatas 65 tahun) lebih rendah jika dibandingkan dengan pasien dibawah 65 tahun dengan rerata masing-masing 17.08 dan 18.03 hari. Nilai p dari analisis ini adalah 0.781 , diketahui bahwa pasien dengan skor hemoglobin, albumin, dan HALP rendah memiliki periode perawatan paska operasi yang lebih lama, $p = 0.384$, 0.276 , dan 0.603 . Rerata lama perawatan paska operasi pasien yang menerapkan protocol ERAS cenderung lebih cepat (15.67 hari) dibandingkan pasien yang tidak menerapkan protocol ERAS (18.16 hari). Namun demikian, nilai p dari perbedaan ini adalah 0.518 . **Simpulan:** Tidak ada faktor prognostik yang secara independen dapat memprediksi lamanya pengobatan pasien kanker kandung kemih paska kistektomi radikal. Oleh karena itu, penelitian lebih lanjut terhadap berbagai faktor diperlukan sebelum melakukan kistektomi radikal untuk mencapai tingkat pemulihan paska operasi terbaik.

Kata Kunci: Faktor prognostic, kanker kandung kemih, operasi radikal sistektomi.

Correspondence: Rendy Triyaka; c/o: Department of Urology, Faculty of Medicine/Gadjah Mada University, Sardjito General Hospital, Jl. Kesehatan No. 1, Sinduadi, Sleman, Yogyakarta 55281, Indonesia. Phone: +62274631190. Email: rendy.triyaka@gmail.com.

INTRODUCTION

Bladder cancer is the highest prevalence of cancer in the urogenital system.¹ In 2017, it was estimated 79.030 new cases have been found in the united states, where bladder cancer on the 6th rank from all cancer and 4th rank as its prevalence on the man.² Radical Cystectomy is the first line of therapy on bladder cancer, especially for Muscle Invasive Bladder Cancer and High Risk-Non Muscle Invasive Bladder Cancer.³⁻⁴ Even though there is an advance in surgical technique and chemotherapy, the therapeutic outcome of bladder cancer still low, especially for patients who suffer from advance and metastatic bladder cancer.⁵

The outcome of the bladder was heterogeneous, with 5 years survival rate of 96.4% on in situ disease, 70.2% on the invasive tumor, and 3.0% and 5.4 % on the patient with the regional and far stadium.² Therefore it was very important to find prognostic factors that affect bladder cancer and decide optimum therapy and follow-up strategies.⁶

Besides the TNM, several prognostic factors would predict the patient with bladder cancer. Main prognostic factors that are known by the patient after radical cystectomy including tumor staging, degree, multifocality, metastatic process on lymph, vascular invasion, systemic spread out, performance status, systemic disease such cardiopulmonary disease, anemia, renal insufficiencies, genetic changes such mutations on tumor gene suppressor p53.⁷ Hematologic parameters including leukocyte count (neutrophil, lymphocytes, and monocyte), thrombocyte count and hemoglobin value. Albumin, C-Reactive protein, and fibrinogen were easy to assess and was a suitable indicator for after surgery prognostic factors. The combination from those indexes have better prediction ability, such neutrophil ratio toward lymphocyte (NLR), platelet ratio toward lymphocyte (PLR) and Lymphocyte to Monocyte ratio (LMR), HALP (Hemoglobin, Albumin, Lymphocyte, and platelet) were developed and shown as prognostic factors that significant for a patient with colorectal and gastric cancer.⁸⁻¹⁴

Knowing the prognostic factors affect the length of stay in the hospital after therapy, survival rate and life expectancy on invasive bladder cancer patients and complications observed after therapy and further therapeutic strategies.³⁻⁴

OBJECTIVE

In this study, the researcher wants to

evaluate the HALP as prognostic value and explore development indexes of new prognostic indexes for the patient with bladder ca especially after radical cystectomy that shown by the length of stay on the hospital after radical cystectomy and another indicator.

MATERIAL & METHODS

This study was an observational analytical study with a retrospective approach to examine the relationship between pre-surgery variables of the bladder cancer patients and the duration of treatment post radical cystectomy. The study is expected to find a variable that can act as an independent prognostic factor to estimate the recovery time of the patients, post radical cystectomy, assessed by the duration of postoperative care. The study was conducted in Sardjito General Hospital from January 2016 - December 2018. The target population is patients with bladder cancer at Sardjito General Hospital, who were planned to undergo radical cystectomy.

The in-range population was patients with bladder cancer, planned to undergo radical cystectomy, at Sardjito General Hospital from January 2016 - December 2018. Subjects included all patients in-range population concordance to the inclusion and exclusion criteria. The data were collected from medical records of bladder cancer patients who underwent radical cystectomy from January 2016 - December 2018.

RESULTS

Of the 37 patients included in the study sample, 86.49% were male and 13.51% female. The number of patients included in the study group was 61 years (45-81 years) with a median of 62 years. Because this study aimed to look for independent prognostic factors that predict the recovery time of bladder cancer patients after radical cystectomy, patients who were deceased during the postoperative treatment period were excluded. A total of 3 patients died during postoperative care, by which only 34 patients were taken as research samples.

All radical cystectomy procedures were performed by a urologist at Sardjito General Hospital. The clinical characteristics of the patients are summarized in Table 3. The pathological staging of all patients included in this study was assessed according to the TNM system and according to the indications of radical cystectomy. Patients with non-

transitional cell carcinoma or urothelial carcinoma pathologies were not staged in this study and they were not included in statistical analysis (analysis related to pathological staging).

Most of the patients in this study were underweight (67.64%). Patients who were normal for the BMI category were 32.35%. This showed that the majority of patients with advanced-stage bladder cancer were underweight. From the analysis, it was found that the average length of postoperative care for underweight patients was 16.5 days and for patients with normal BMI was 19.59 days. The difference between these averages showed a p-value of 0.396 which meant that the difference was not statistically significant.

Morbidity was assessed from abnormalities or concomitant diseases owned by the patients during hospitalization including diabetes mellitus, hypertension, heart disease, old age/geriatrics, hydronephrosis, renal insufficiency, allergies, etc., which most of the patients (85.29%) had morbidity. From the results of the analysis, the average length of postoperative care of patients who had morbidity was 17.31 while for patients without morbidity was 18.6. The difference between these averages shows a p-value of 0.788 which means that the difference is not statistically significant.

Some parameters from clinical laboratory results were assessed in this study, including hemoglobin, albumin, and HALP scores (Hemoglobin, Albumin, Leukocytes, Platelets).⁷⁻¹⁰ Hemoglobin and albumin levels were assessed based on the adequacy of each of these values as indicated by the state of anemia and hypoalbuminemia. Based on the HALP score, these patients were divided into 2 groups. The cutoff of the two groups was obtained from the median HALP score of all patients, which was 20. Patients with anemia were 61.76% and those with hypoalbuminemia were 67.64%, whereas patients with low and high HALP scores were 52.94% and 47.05%, respectively. From all of the clinical laboratory parameters, it was found that patients with low hemoglobin, albumin, and HALP scores had longer postoperative treatment periods, p-value 0.384, 0.276, and 0.603, respectively, which meant that they were not statistically significant.

There were several types of urinary diversion which were performed after radical cystectomy in these patients, including neobladder, ileal conduit, and transureteroureterocutaneostomy (TUUC). Of all the urine diversion procedures, the ileal conduit was the most common procedure performed at Sardjito General Hospital (79.41%). Of

the whole procedure, the ileal conduit had the longest postoperative treatment period between the two other procedures. Nevertheless, the p-value of this analysis was 0.904 which meant that it was not statistically significant.

In terms of intraoperative, there were 2 factors assessed in this study which were the amount of bleeding during surgery and the duration of surgery. For intraoperative bleeding, a 300 cc cut-off was used to differentiate between 2 groups of patients with minimal bleeding (14.71%) and massive bleeding (85.29%). Whereas in terms of the duration of the operation, a cut-off of 5 hours was taken to divide patients into 2 different groups. Patients with minimal bleeding had an average postoperative duration of treatment of 21.10 days and patients with massive bleeding had an average postoperative duration of treatment of 16.88 days. Patients with a longer duration of surgery (above 5 hours) tended to have a longer postoperative period of treatment with an average of 18.27 days compared to 15 days in patients with a duration of surgery under 5 hours. However, the two mean differences were not statistically significant because the p values were 0.38 and 0.415, respectively.

No less important in terms of post-operation, the use of the ERAS protocol was one thing to be reckoned with. From the samples of this study, 26.47% of patients applied the ERAS protocol during postoperative care while 73.53% did not. The average duration of postoperative care for patients who applied the ERAS protocol tended to be faster (15.67 days) compared to patients who did not apply the ERAS protocol (18.16 days). Nevertheless, the p-value of this difference was 0.518 which meant that it was not significant.

From the results of this study, it is known that the average length of postoperative care for older patients (above 65 years) was lower when compared to patients under 65 years with averages of 17.08 and 18.03 days respectively. The p-value of this analysis was 0.781 which meant that it was insignificant. Whereas when viewed from the T staging of the TNM system, it was found that patients with smaller T staging had longer average postoperative care duration, 16 days for pT2, 14.33 days for pT3, and 10.77 days for pT4. The p-value was 0.269 which meant that it was not significant.

From all of the clinical laboratory parameters, it was found that patients with low hemoglobin, albumin, and HALP scores had longer postoperative hospitalization periods but with P values of 0.384, 0.276, and 0.603, respectively,

which meant not significant.

There are several types of urinary diversion that can be performed after radical cystectomy in these patients, including neobladder, ileal conduit, and transureteroureterocutaneostomy (TUUC). Of all the urine diversion procedures, the ileal conduit is the most common procedure performed at Sardjito General Hospital (79.41%). Of the whole procedure, the ileal conduit has the longest hospitalization treatment period between the two other procedures, with a P-value of 0.904 which means it is not significant.

From the intraoperative side, there are 2 factors monitored in this study; the amount of bleeding during surgery, and the duration of surgery. For intraoperative bleeding, 300 cc was used as the cut-off to differentiate between patients with minimal operative bleeding (14.71%) and major operative bleeding (85.29%). In terms of the duration of the operation, 5 hours was used as the cutoff to separate patients into 2 different groups. Patients with minimal bleeding had a mean postoperative hospitalization of 21.10 days, compared with patients with bleeding above 300 cc which amounted to 16.88 days. Whereas patients with longer surgery duration above 5 hours tend to have longer postoperative hospitalization with an average of 18.27 days compared to 15 days in patients with surgery duration under 5 hours. However, the two mean differences are not statistically significant with P-values of 0.38 and 0.415, respectively.

No less important, in terms of the postoperative side, the use of ERAS protocol is one thing to be reckoned with. From all data collected from the study sample, ERAS protocol was applied on 26.47% of patients during postoperative care while 73.53% was not. The mean duration of postoperative hospitalization for patients in which ERAS protocol was applied tended to be faster (15.67 days) compared to a patient who didn't follow the ERAS protocol (18.16 days). Where the P-value of this difference is 0.518 which means it is not significant.

From the results of this study, it was found that the average length of postoperative hospitalization period in geriatric patients (over 65 years) was lower when compared to non-geriatric patients (under 65 years) with averages of 17.08 and 18.03 days, respectively, with a P-value of 0.781 which means no significant. When viewed from the T-staging of the TNM system, it was found that patients with lower T-staging had a longer mean postoperative hospitalization period of 16 days for

pT2, 14.33 for pT3, and 10.77 for pT4, with P-values of 0.269 which means not significant.

DISCUSSION

Bladder cancer is a disease with a high incidence rate in the population over 50 years, with a peak incidence in the sixth and seventh decades of life. The average age found in this study was 61 years and is similar to other studies published to date.¹⁵ In this study, it was found that patients over 65 years of age had a shorter postoperative hospitalization period after radical cystectomy compared with patients under 65 years of age, even though the difference was not statistically significant ($p = 0.781$). In contrast to this study which assessed the length of postoperative hospitalization, previous studies generally assessed the morbidity and mortality from surgery by comparing age at the time of surgery. Where patients with advanced age will have higher morbidity and mortality rate. But on the contrary, this study showed that the average postoperative hospitalization period in elderly patients is shorter.

Good pre-operative nutrition should be achieved to lower the risk of postoperative morbidity and mortality. Based on research conducted by Johnson et al., poor pre-operative nutritional status can predict an increase in the number of complications after radical cystectomy.¹⁶ In addition to BMI, nutritional status can also be shown from the pre-operative serum albumin. In this study, the results showed that patients with a low BMI tend to have a shorter hospitalization period when compared with a normal BMI ($p = 0.396$). This is contrary to the other study that showed a better average survival rate in patients with better nutritional status after radical cystectomy. However, from nutritional status analysis based on preoperative serum albumin level, patients with pre-operative hypoalbuminemia tend to have a longer postoperative hospitalization period compared with patients with normal albumin levels ($p = 0.276$).

Based on previous research, staging is one of the best prognostic factors to assess the morbidity and mortality of patients with bladder cancer after radical cystectomy. The staging value commonly used is the T (tumor) value. A study conducted by Gardiner, 2014 showed that patients with high T staging would have higher postoperative morbidity and mortality rates.¹⁷ But in our study, patients with lower T staging had a longer postoperative hospitalization period ($p = 0.269$). This difference is

most likely due to the small number of samples in this study and the unequal comparison between groups. Another possibility is that the speed of recovery of patients after radical cystectomy is not directly proportional to the survival rate. In a previous study, it was mentioned that local pathological staging and lymph node metastases were a predictive factor for the patient's survival in bladder cancer.¹⁷

Hospitalized bladder cancer patients generally don't come with bladder cancer as a single condition, but are accompanied by several other diseases both directly caused by cancer or other accompanying diseases. In addition, because the majority of patients with bladder cancer come with advanced age, the likelihood of other comorbidities is increased. Some of the accompanying diseases that generally accompany patients with bladder cancer are renal insufficiency, chronic kidney failure, diabetes mellitus, hypertension, heart failure, allergies, and other malignancy or metastatic disease. In this study, it was mentioned that patients with morbidity had a slightly shorter treatment period compared to patients who had morbidity ($p = 0.788$). Those with morbidity had a slightly shorter treatment period compared to patients who had morbidity ($p = 0.788$).

Clinical laboratory results are the main basic consideration of an operation, including radical cystectomy. In this study, the researcher tried to analyze several laboratory parameters to predict the survival rate of a disease or procedure, especially malignancy, namely hemoglobin, albumin, and HALP scores (Hemoglobin, Albumin, Lymphocytes, and Platelets). The HALP score is a medical novelty, its usage as a prognostic factor is still very limited. In some case studies, this score had been a predictive factor in survival rates for post-radical cystectomy patients. In this study, the HALP score was used to predict the recovery time of post-radical cystectomy patients. HALP score is obtained by the formula of Hemoglobin (g/L) x Albumin (g/L) x Lymphocytes (count/L)/Platelet (count/L). All HALP scores in the patients were divided into 2 groups, low and high HALP scores, where the cutoff is the median. By the analysis, with a median score of 20, patients with lower HALP scores had a longer recovery time after surgery ($p = 0.603$). Although insignificant, this can be a trigger for other researchers to develop the HALP score advantages. The results of this study are in line with the previous studies, stating the patients with low HALP scores

tend to have lower survival rates post-radical cystectomy.¹⁸

From the analysis of both hemoglobin and albumin levels, it showed the patients with preoperative anemia had a longer recovery time, similar to patients who had preoperative hypoalbuminemia when compared to patients with normal albumin serum level. This is certainly in line with the previous literature, where the patients with good clinical laboratory parameters also have better recovery rates, although in this study the difference was not significant.⁸⁻¹⁴

The urinary diversion performed on patients after radical cystectomy is thought to have an important role in predicting the recovery of the patients after surgery.¹⁹⁻²⁰ Previous studies have never directly assessed the duration of postoperative recovery for each type of diversion, especially the length of stay in the hospital after surgery. The study conducted by Ziouziou, 2018 showed that from the results of a meta-analysis in non-randomized studies, patients with ileal conduit type urinary diversion have a better quality of life when compared with the neobladder. Research from Lee, 2014, showed that ileal conduit is the fastest and easiest type of diversion with tolerable complications after radical cystectomy, so ileal conduit is the most common type of urinary diversion performed. This study indicated the patients treated with ileal conduit type of urine diversion have a slightly longer duration of treatment than the other two types of diversion namely neobladder and TUUC.

Intraoperative factors, such as the volume of bleeding and the duration of the surgery, are thought to be one of the prognostic factors in the patients' recovery post-radical cystectomy.¹⁵ More blood loss generally increases the number of postoperative complications and increases the amount of blood transfusion required. Concordance with bleeding, longer surgery duration can also cause an increased risk of anesthesia and the possibility of further postoperative complications.²¹ This study founded that patients with minimal bleeding had a longer treatment time compared to the bleeding volume above 300 ml. While for patients with a longer duration of surgery, the mean duration of/postoperative care is also longer, concordance with the existing literature and theory.

One variable measured in this study is the usage of the ERAS protocol in the treatment of radical cystectomy after surgery. The ERAS protocol has been studied for more than 20 years in various

surgical procedures, mostly in colorectal surgery.²² The concept of improving patient care and reducing postoperative complications is applied to major urologic operations and especially radical cystectomy procedures. This procedure is technically challenging, due to large surgical resections and a high rate of postoperative complications, reaching 65%. The ERAS protocol was formed after several clinical pathways or protocols were introduced to improve perioperative management and reduce the length of stay.

CONCLUSION

In this study, several factors were found to be in line with previously published studies and literature. However, they were not statistically significant. This study concludes that there is no prognostic factor that can independently predict the duration of treatment of bladder cancer patients post-radical cystectomy. Therefore in-depth assessment of various factors is required before performing radical cystectomy to achieve the best postoperative recovery rates.

This study is expected to be a preliminary study for subsequent researchers. The shortcomings in this study, the sample size and the inhomogeneity of the data, are expected to be improved in future studies, so better results can be achieved and benefit the clinician.

REFERENCES

1. Clark PE, Agarwal N, Biagioli MC, Eisenberger MA, Greenberg RE, Herr HW, et al. Bladder cancer: Clinical practice guidelines in oncology. *JNCCN J Natl Compr Cancer Netw*. 2013; 11(4): 446-75.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. *CA Cancer J Clin*. 2017; 67(1): 7-30.
3. Babjuk M, Böhle A, Burger M, Capoun O, Cohen D, Compérat EM, et al. EAU Guidelines on Non-Muscle-invasive Urothelial Carcinoma of the Bladder: Update 2016. *Eur Urol*. 2017; 71(3): 447-61.
4. Alfred Witjes J, Lebre T, Compérat EM, Cowan NC, De Santis M, Bruins HM, et al. Updated 2016 EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer. *Eur Urol*. 2017; 71(3): 462-75.
5. Chang SS, Boorjian SA, Chou R, Clark PE, Daneshmand S, Konety BR, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. *J Urol*. 2016; 196(4): 1021-9.
6. DeSantis CE, Lin CC, Mariotto AB, Siegel RL, Stein KD, Kramer JL, et al. Cancer treatment and survivorship statistics, 2014. *CA Cancer J Clin*. 2014; 64(4): 252-71.
7. Alfred Witjes J, Lebre T, Compérat EM, Cowan NC, De Santis M, Bruins HM, et al. The impact of preoperative anemia on oncologic outcome in patients undergoing radical cystectomy for urothelial carcinoma of the bladder. *CA Cancer J Clin*. 2016; 71(4): 489-94.
8. Moschini M, Suardi N, Pellucchi F, Rocchini L, La Croce G, Capitanio U, et al. Impact of preoperative thrombocytosis on pathological outcomes and survival in patients treated with radical cystectomy for bladder carcinoma. *Anticancer Res*. 2014; 34(6): 3225-30.
9. Klinga G, Sherif A. A retrospective evaluation of preoperative anemia in patients undergoing radical cystectomy for muscle-invasive urothelial urinary bladder cancer, with or without neoadjuvant chemotherapy. *Springerplus*. 2016; 5(1): 1167.
10. Eggers H, Seidel C, Schrader AJ, Lehmann R, Wegener G, Kuczyk MA, et al. Serum C-reactive protein: A prognostic factor in metastatic urothelial cancer of the bladder. *Med Oncol*. 2013; 30(4).
11. Lambert JW, Ingham M, Gibbs BB, Given RW, Lance RS, Riggs SB. Using preoperative albumin levels as a surrogate marker for outcomes after radical cystectomy for bladder cancer. *Urology*. 2013; 81(3): 587-92.
12. Temraz S, Mukherji D, Farhat ZAA, Nasr R, Charafeddine M, Shahait M, et al. Preoperative lymphocyte-to-monocyte ratio predicts clinical outcome in patients undergoing radical cystectomy for transitional cell carcinoma of the bladder: A retrospective analysis. *BMC Urol*. 2014; 14(1): 1-6.
13. Ma C, Lu B, Diao C, Zhao K, Wang X, Ma B, et al. Preoperative neutrophil-lymphocyte ratio and fibrinogen level in patients distinguish between muscle-invasive bladder cancer and non-muscle-invasive bladder cancer. *Onco Targets Ther*. 2016; 9: 4917-22.
14. Zhang GM, Zhu Y, Luo L, Wan FN, Zhu YP, Sun LJ, et al. Preoperative lymphocyte-monocyte and platelet-lymphocyte ratios as predictors of overall survival in patients with bladder cancer undergoing radical cystectomy. *Tumor Biol*. 2015; 36(11): 8537-43.
15. Stein JP, Lieskovsky G, Cote R, Groshen S, Feng AC, Boyd S, et al. Radical cystectomy in the treatment of invasive bladder cancer: Long-term results in 1,054 patients. *J Clin Oncol*. 2001; 19(3): 666-75.
16. Johnson DC, Riggs SB, Nielsen ME, Matthews JE, Woods ME, Wallen EM, et al. Nutritional predictors of complications following radical cystectomy. *World J Urol*. 2015; 33(8): 1129-37.
17. Monzó Gardiner JI, Amo FH, Díez Cordero JM, Benavente RC, Moyano AS, Fernández CH. Factores pronósticos en la supervivencia de los pacientes con carcinoma transicional de vejiga tratados con cistectomía radical. *Actas Urol Esp*. 2009; 33(3): 249-57.
18. Peng D, Zhang CJ, Gong YQ, Hao H, Guan B, Li XS,

- et al. Prognostic significance of HALP (hemoglobin, albumin, lymphocyte, and platelet) in patients with bladder cancer after radical cystectomy. *Sci Rep*. 2018; 8(1): 1-9.
19. Ziouziou I, Irani J, Wei JT, Karmouni T, El Khader K, Koutani A, et al. Bricker vs néovessie de substitution?: laquelle offre la meilleure qualité de vie après cystectomie radicale? Une revue systématique de littérature et méta-analyse. *Prog en Urol*. 2018; 28(5): 241-50.
20. Lee RK, Abol-Enein H, Artibani W, Bochner B, Dalbagni G, Daneshmand S, et al. Urinary diversion after radical cystectomy for bladder cancer: Options, patient selection, and outcomes. *BJU Int*. 2014; 113(1): 11-23.
21. Terry WJ, Bueschen AJ. Complications of radical cystectomy and correlation with nutritional assessment. *Urology*. 1986; 27(3): 229-32.
22. Vukovic N, Dinic L. Enhanced recovery after surgery protocols in major urologic surgery. *Front Med*. 2018; 5: 1-10.