

## Research Paper

# Comparison Between Gemcitabine-Cisplatin Chemotherapy Outcome and Body Mass Index in Muscle Invasive Bladder Cancer Patients At Dr. Saiful Anwar General Hospital Malang, Indonesia

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## ARTICLE HISTORY

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**Abstract: Introduction:** Malignancy remain a worldwide challenge to overcome, one of the most common malignancy in men is bladder cancer, it represent the seventh most common cause of cancer in men worldwide. Over the past decade 6978 Indonesian were diagnosed with bladder cancer. In Dr. Saiful Anwar Hospital itself, 287 inpatient were hospitalized due to bladder cancer over the past 5 years. Bladder cancer therapy including, radical cystectomy, radiotherapy and chemotherapy depending on the tumor's stage. Patients requiring chemotherapy, are given six course of Gemcitabine-Cisplatin regiment. Body Mass Index (BMI) acclaimed to take part in cancer treatment outcome, therefore this study aimed to compared body mass index with bladder tumor outcome in bladder cancer patients receiving six course of Gemcitabine-Cisplatin chemotherapy.

**Method:** Fifteen bladder cancer patients with different BMI underwent (transurethral resection of bladder tumor) TURBT staging and received six course of Gemcitabine-Cisplatin Chemotherapy from 2016 to 2018 at Dr. Saiful Anwar General Hospital were recorded, we followed the patients during the six course of chemotherapy and evaluation were carried out using cystoscopy and bladder biopsy. The data then analysed using chi square and t-test to compared.

**Result:** Fifteen patients were eligible for this study, 10 were men and 5 were women. Mean age is 66.6 years old, body mass index (BMI) include normal weight (73.3%), underweight (6.67%), overweight(13.3%) and obese (6.67%). Pathology finding including Transitional Cell Carcinoma of high grade (46,7%) and low grade (53.3%). Tumor staging start from T2 (26.67%), T3 (6.67%) and T4 (66.66%). Three patients had metastatic tumor to the liver, liver and lung and rectum respectively. Lymph node involvement were N0 40%(6),N1 33.3% (5) N2 20%(3) and N3 6.7% (1) continuously.

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Out of fifteen patients who underwent Gemcitabine-Cisplatin chemotherapy for six series, tumor outcome after therapy was compared with the BMI. Tumor still remain in 11 patient (73.3%), while 4 (26.7%) patients were found to be tumor free after six course of Gemcitabine-Cisplatin chemotherapy. There is no statistically significant between body mass index and chemotherapy success rate ( $p=0.159$ ) in this study. Although, there were statistically significant found in the presence of tumor before and after Gemcitabine-Cisplatin chemotherapy ( $p=0.041$ ). There are no statistically significant between sex and age when compared to chemotherapy outcome with ( $p=0.446$ ) and ( $p=0.469$ ) respectively.

**Conclusion:** Body Mass Index has no relation in determining success rate of bladder cancer chemotherapy using Gemcitabine-Cisplatin.

**Keywords:** *BMI, Chemotherapy Outcome, Gemcitabine-Cisplatin*

## 1. INTRODUCTION

Malignancy remain a worldwide challenge to overcome, one of the most common malignancy in men is bladder cancer, it represent the seventh most common cause of cancer in men worldwide. Over the past decade 6978 Indonesian were diagnosed with bladder cancer. In Dr. Saiful Anwar Hospital itself, 287 inpatient were hospitalized due to bladder cancer over the past 5 years. Bladder cancer therapy including, radical cystectomy, radiotherapy and chemotherapy depending on the tumor's stage. Patients requiring chemotherapy, are given six course of Gemcitabine-Cisplatin regiment. Body Mass Index (BMI) acclaimed to take part in cancer treatment outcome, therefore this study aimed to compared body mass index with bladder tumor outcome in bladder cancer patients receiving six course of Gemcitabine-Cisplatin chemotherapy.

## 2. MATERIAL AND METHOD

Fifteen bladder cancer patients with different BMI underwent (transurethral resection of bladder tumor) TURBT staging and received six course of Gemcitabine-Cisplatin Chemotherapy from 2016 to 2018 at Dr. Saiful Anwar General Hospital were

recorded, we followed the patients during the six course of chemotherapy and evaluation were carried out using cystoscopy and bladder biopsy. The data then analysed using chi square and t-test to compared.

## 3. RESULT

Fifteen patients were eligible for this study, 10 were men and 5 were women. Mean age is 66.6 years old, body mass index (BMI) include normal weight (73.3%), underweight (6.67%), overweight(13.3%) and obese (6.67%). Pathology finding including, Transitional Cell Carcinoma of high grade (46,7%) and low grade (53.3%).

Tumor staging start from T2 (26.67%), T3 (6.67%) and T4 (66.66%). Three patients had metastatic tumor to the liver, liver and lung and rectum respectively. Lymph node involvement were N0 40%(6), N1 33.3%(5), N2 20%(3) and N3 6.7%(1) continuously. Out of fifteen patients who underwent Gemcitabine-Cisplatin chemotherapy for six series, tumor outcome after therapy was compared with the BMI. Tumor still remain in 11 patient (73.3%), while 4 (26.7%) patients were found to be tumor free after six course of Gemcitabine-Cisplatin chemotherapy.

**Tab. (1).** Interaction of molecular flavonoid with active side of COX-2. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

Characteristic Distribution	N	%	Significant
<b>Age</b>			P>0.05
40-49	1	6.7	
50-59	3	20	
60-69	7	46.7	
70-79	2	13.3	
>80	2	13.3	
<b>Sex</b>			P?0.05
Male	10	66.7	
Female	5	33.3	
<b>Body Mass Index</b>			P<0.05
Normal	11	73.3	
Underweight	1	6.67	
Overweight	2	13.3	
Obese	1	6.67	
<b>Tumor Pathology</b>			P<0.05
TCC High Grade	8	53.3	
TCC Low Grade	7	46.7	

**Tab. (2).** Bladder tumor characteristic at Dr. Saiful Anwar General Hospital Malang before and post chemotherapy evaluation by cystoscopy biopsy of the bladder.

Staging	Pathology Anatomy	Tumor Post Chemotherapy
Bladder Cancer T2bN2M1 Liver	Low Grade TCC	+
Bladder Cancer T2a N0 M0	High Grade TCC	-
Bladder Cancer T4a N0 M0	High Grade TCC	+
Bladder Cancer T4a N1 M0	Low Grade TCC	+
Bladder Cancer T4a N1 M0	High Grade TCC	+
Bladder Cancer T2b N1 M0	Low Grade TCC	-
Bladder Cancer T4b N2 M1 Rectum	High Grade TCC	+
Bladder Cancer T4a N0 M0	High Grade TCC	+
Bladder Cancer T4a N0 M0	High Grade TCC	+
Bladder Cancer T3 N1 M0	Low Grade TCC	+
Bladder Cancer T4 N1 M0	Low Grade TCC	+
Bladder Cancer T4 N0 M0	Low Grade TCC	+
Bladder Cancer T4a N3 M1 Liver + Lung	High Grade TCC	+
Bladder Cancer T2a N0 M0	Low Grade TCC	-
Bladder Cancer T2b N2 M1 Liver	High Grade TCC	-

#### 4. DISCUSSION

Bladder cancer represents the fourth most common cause of cancer in men in the United States and the seventh most common

cause of cancer in men worldwide, with a much lower incidence in women, with ratio of 3;1. Similar to this study, male to female ratio was 2:1 Bladder cancer effect patient at

their sixties, but also by chance can affect younger patients. More than 90% of bladder cancer represent urothelial carcinomas, which can be subdivided by grade, stage, and subtype (1). Similar to this study, male to female ratio was 2:1 this condition mostly due to smoking, whereas according to Zeegers et al. it is concluded that current cigarette smokers have an approximately threefold higher risk of bladder cancer than non-smokers. Mean age of 66 years and pathology results revealed transitional cell carcinoma, whereas epithelial lining of the urinary tract is transitional (2).

In this study, tumor stage was found mostly as muscle invasive bladder cancer whereas starting from T2 stage, tumor had already invade muscle layer. Pathologic staging is based on the presence or absence of invasion and, in the case of invasive tumors, on the extent of invasion into the bladder wall, with the layers of the bladder wall and adjacent organs serving as staging landmarks. In general, progressive invasion into the bladder wall by microscopic level increases stage, including involvement of the lamina propria (pT1), superficial or deep muscularis propria (pT2a and pT2b, respectively), perivesical fat either microscopically (pT3a) or macroscopically (pT3b), and adjacent organs (pT4a) or the pelvic/abdominal wall (pT4b). However, on TUR specimens, only invasion up to the pT2 stage can be diagnosed with certainty; involvement of fibroadipose tissue on small (non-cystectomy) specimens may be misleading, as fibroadipose tissue can frequently be identified in the lamina propria and may lead to an erroneous diagnosis of perivesical fat involvement. In addition, pT4 diagnosis at pathology may be made only in the presence of a full resection, in which transmural invasion through the bladder wall and into the prostate can be identified with certainty using appropriate orientation.

Invasion into the detrusor muscle (muscularis propria; pT2 disease) will lead to a consideration for a cystectomy depending on a variety of clinical factors such as the patient's comorbidity (1) (3). High staging tumor also due to patient delayed to seek for medical advice and patient refuse to undergo radical surgery when tumor is still operable.

According to Westhoff et al. high BMI and certain dietary factors have also been hypothesized to be associated with bladder cancer prognosis. Excess body fat is associated with increased circulating concentrations of insulin and insulin-like growth factor-1, as well as systemic inflammation, all of which may be related to worse bladder cancer outcomes (4). In this study BMI does not affect the outcome of tumor remission after therapy, shown by  $p=0.159$ , although there were still statistically significant in tumor outcome before and after given Gemcitabine-Cisplatin therapy with  $p=0.041$ . This condition might be due to dosing of Gemcitabine-Cisplatin according to body surface area, whereas there won't be under dose or overdose to give an effect to the tumor.

Meanwhile there were statistically significant in the presence of tumor before and after Gemcitabine-Cisplatin therapy. This condition is due to mechanism of action of Gemcitabine-Cisplatin together. Cisplatin induces release of the T cell activating cytokine IFN- $\gamma$  by APCs enhancing T cell activation (5). Meanwhile gemcitabine is phosphorylated to its active diphosphate (dFdCDP) and triphosphate (dFdCTP) metabolites, which inhibit RR and DNA synthesis of cancer cell, respectively (6).

Study by Westhoff et al. show an increased recurrence risk in overweight or obese NMIBC patients may be explained by

systemic and local changes induced by obesity, such as altered levels of insulin, insulin-like growth factor-1, leptin, adiponectin, steroid hormones, and cytokines. In NMIBC patients, markers of systemic inflammatory response have indeed been associated with increased risk of recurrence and progression [44]. Also, potential difficulties in performing a high quality (complete) transurethral resection of the bladder may play a role, particularly for obese patients. For NMIBC patients it therefore seems advisable to attain or maintain a healthy body weight (4).

## CONCLUSION

Body Mass Index has no relation in determining success rate of bladder cancer chemotherapy using Gemcitabine-Cisplatin.

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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