

Predictive Factors Influencing the Outcomes of Double “J” Stent Placement in Stage IIIB Cervical Cancer Patients With Hydronephrosis Complication

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ABSTRACT

Objective: To determine the predictive factors that influence the outcome of Double “J” (DJ) stent placement in stage IIIB cervical cancer patients with hydronephrosis complications. **Methods:** An analytical observational study with a historical cohort was performed. Patients included in this study was patient with stage IIIB cervical cancer with hydronephrosis complication at Sanglah hospital. We analyzed the influence of time range since diagnosis until DJ stent placement, degree of hydronephrosis, and glomerular filtration rate on the outcomes of DJ stent placement namely: Lower urinary tract symptoms (LUTS), quality of life (QoL), and glomerular filtration rate changes (GFR). Data were tabulated and statistically analyzed using SPSS 25. **Results:** Of the 44 samples, the mean age of the patients was 51,93 (± 7.672) years. Late DJ stent placement increase the risk of severe LUTS (RR: 3.103; 95%CI: 1.319-7.301; $p < 0.001$) compared to patients with early DJ stent placement. We also found that a low glomerular filtration rate (bad renal function) is significantly associated with worse quality of life (RR: 1.917; 95%CI: 1.296-2.835; $p < 0.001$). **Conclusion:** Delayed DJ stent placement is associated with severe LUTS symptoms, and poor renal function resulted in a poor quality of life.

Keywords: cervical cancer stage IIIB, hydronephrosis, DJ stent, glomerular filtration rate, lower urinary tract symptoms.

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INTRODUCTION

Annually, estimated around 15.000 new cases of cervical cancer in Indonesia. In Bali, cervical cancer is one of the most common cancer in women, especially at productive ages. Sanglah Central Hospital in Bali recorded 69 cases of cervical cancer treated from 2016 to 2017 with more than 90% of them being in the late stage.¹

One of the problems faced by late-stage cervical cancer patients is hydronephrosis complication. This complication resulted from direct invasion of the tumor, pressure from retroperitoneal metastatic mass, or lymph mass pressure toward the ureter.² Neglected hydronephrosis may cause irreversible obstructive nephropathy that will affect

patients' quality of life and might give rise to many other symptoms.^{2,3} Double “J” stent placement is one of the options to manage this complication, and prevent obstructive uropathy in late-stage cervical cancer patients. The placement of the DJ stent hoped to manage the obstruction of the ureter, prevent the deterioration of renal function, improve quality of life, and prevent urinary tract symptoms in patients.³ Study from Shehab, et al shows the improvement of glomerular filtration rates (GFR) that used as the parameter of renal function.⁴ Some study by Al Marhoon, et al shows that 85.2% of patients with symptomatic hydronephrosis shows improvement of symptoms after DJ stent placement.⁵ Yet on the other hand DJ stent

placements are known to cause some urinary complications such as hematuria, urinary tract infection, and pain. This complication is known to cause disturbance in patients' quality of life (QoL).⁶

This study aims to observe the factors that might influence the outcomes of the DJ stent placements in cervical cancer stage IIIB patients with hydronephrosis complications. The factors observed in this study include the time range from the diagnosis of cervical cancer to the time of DJ stent placements, the initial glomerular filtration rate, and the degree of hydronephrosis. The outcomes of DJ placements that we studied include the severity of lower urinary tract symptoms (LUTS), patient quality of life (QoL), and changes in glomerular filtration rates.

METHODS

Design, time, and place of the study

This study was an analytic observational study with a historical cohort design. The aim is to assess the association of predictive factors with the severity of LUTS, GFR changes, and quality of life in cervical cancer stage IIIB with hydronephrosis complication. Data regarding patients' characteristics, staging, and time of DJ stent placement are obtained from patients' medical records, then we follow patients' history and collected the follow-up data of the GFR after DJ stent placements, LUTS, and Quality of life scores. The study was conducted at Sanglah General Hospital, Bali, Indonesia from 1st January 2018 until 31st December 2019.

Sample characteristics

We used total population sampling and obtained 44 samples. Patients included in this study are all cervical cancer patients stage IIIB with hydronephrosis complications that undergoing DJ stent placements in the Central Surgical Ward of Sanglah General Hospital during the period of the study. The diagnosis

of cervical cancer must be proven by pathological anatomy results, and hydronephrosis is diagnosed using ultrasound results. The exclusion criteria are incomplete medical record; patient with a history of chemo or radiotherapy; patient with severe comorbid outside of cervical cancer and hydronephrosis; history of urinary tract malignancy prior DJ stent placements, history of hemodialysis, and patient with a history of using medication that could alter renal function examination (e.g., long term analgetic).

Data analysis

Data obtained from the medical records are tabulated using SPSS version 25. Sample characteristics are presented as continuous and categorical data. Continuous data are presented as mean and standard deviation (SD), and categorical data are presented in frequency and percentages. For analytical data, we categorized data into two groups. For Independent variables, the time range variables are grouped into Late DJ stent placements (≥ 2 months), and early DJ stent placement (< 2 months). Degree of hydronephrosis are grouped into severe and mild-to-moderate, Glomerular filtration rate calculated by estimated glomerular filtration rate using Cockcroft-Gault formula, and grouped into good GFR (≥ 60 mL/minutes/1.73 m²) and bad GFR (< 60 mL/minutes/1.73 m²). Dependent variables consist of LUTS, GFR changes, and QoL. LUTS was measured by International Prostate Symptom Score (IPSS) and grouped into mild-to-moderate symptoms (IPSS ≤ 19) and severe symptoms (IPSS > 19). QoL is measured by The European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ C-30) that has already been translated and validated in Bahasa Indonesia. Grouped into good QoL (Total score > 500), and bad QoL (total score

≤ 500). GFR changes are the difference of GFR before DJ stent placement and 2 months after DJ stent placements. It is grouped into increased GFR and decreased GFR.

We then conduct bivariate analysis using crosstabs between each independent variable as a predictive factor, and each dependent variable as an outcome. The statistical tests are conducted using the Chi-Square test. We also calculated the relative risk (RR) and 95% confidence interval (95%CI) for each crosstab.

RESULTS

Characteristics of the study

As many as 105 patients registered to undergo DJ stent placements during the study period. 80 of those patients are patients with cervical cancer stage IIIB, with 60 patients

conducting DJ stent placement on one side of the ureter. Of 60 patients that satisfy inclusion criteria, 16 of them were excluded from the study due to incomplete medical records. 44 patients are included and analyzed in this study without any loss to follow-up.

The mean ages of the patients are 51.93 (SD: 7.672) years old. From the independent variables, patients divided into severe (n:11) and mild to moderate (n:33) hydronephrosis; Late (n:29) and early (n:15) time span; and also good renal function (n:23), and bad renal function (n:21). We found that 28 patients (63.3%) developed severe LUTS, 34 (77.3%) patients have decreased GFR, and 33 patients (75%) have bad QoL. The full characteristics of the samples can be seen in **Table 1**.

Table 1. Sample Characteristics

Variables	N: 44 (Mean \pm SD)
Age (years)	51.93 \pm 7.672
Parity (n)	2.02 \pm .549
Haemoglobin levels (mg/dL)	10.1239 \pm 2.05875
Time span (months)	1.95 \pm .914
GFR before DJ stent (mL/minutes/1.73 m ²)	64.2500 \pm 26.66687
GFR after DJ stent (mL/minutes/1.73 m ²)	43.3182 \pm 30.83020
GFR Difference after DJ stent (mL/minutes/1.73 m ²)	-20.9318 \pm 26.54123
Hydronephrosis degree	n(%)
Severe	11 (25.0)
Mild-to-moderate	33 (75.0)
Quality of Life (%)	
Bad	33 (75.0)
Good	11 (25.0)
LUTS (%)	
Severe	28 (63.6)
Mild-to-moderate	16 (36.4)
Time range (%)	
Late	29 (65.9)
Early	15 (34.1)
GFR Difference (%)	
Decreased	34 (77.3)
Increased	10 (22.7)
Initial GFR (%)	
Bad renal function	21 (47.7)
Good renal function	23 (52.3)

The association of the predictive factors with the severity of LUTS

We conducted the bivariate analysis using crosstabs and Chi-Square statistical analysis to assess the association of several predictive factors to the risk of developing severe LUTS. We found that late DJ stent placements (DJ

stent placed after more than 2 months) are associated with an increased risk of Severe LUTS (RR: 3.103; 95%CI: 1.319-7.301; $p < 0.001$). However the degree of hydronephrosis and initial GFR did not have a significant association with the severity of LUTS (**Table 2**).

Table 2. The distribution and association of various predictive factors to the severity of LUTS after DJ stent placements

Variables	Severe LUTS	Mild-to-moderate LUTS	RR	95% CI	p
Time range					
Late DJ stent	24 (82.8%)	5 (17.2%)	3.103	1.319-7.301	< 0.001*
Early DJ stent	4 (26.7%)	11 (73.3%)			
Hydronephrosis degree					
Severe	7 (63.6%)	4 (36.4%)	1.235	0.708-2.154	0.484
Mild-to-moderate	17 (51.5%)	16 (48.5%)			
GFR					
Bad renal function	10 (47.6%)	11 (52.4)	0.782	0.449-1.363	0.378
Good renal function	14 (60.9%)	9 (39.1%)			

*Statistically significant (Chi-square test)

The association of the predictive factors with the GFR changes

We found that none of the predictive factors have a significant association with DJ stent placements outcomes (**Table 3**). Late DJ stents have a higher frequency of having decreased GFR (79.3%) compared with early

DJ stent placements (73.3%), however, the difference is not statistically significant. The same result was also found for hydronephrosis degree and initial GFR that indicate the difference is small and not significant that can be attributed to chance only (null hypothesis).

Table 3. The distribution and association of various predictive factors to the GFR changes after DJ stent placements

Variables	Decreased GFR	Increased GFR	RR	95% CI	p
Time range					
Late DJ stent	23 (79.3%)	6 (20.7%)	1.082	0.757-1.546	0.714
Early DJ stent	11 (73.3%)	4 (26.7%)			
Hydronephrosis degree					
Severe	8 (72.7%)	3 (27.3%)	0.923	0.617-1.381	0.692
Mild-to-moderate	26 (78.8%)	7 (21.2%)			
GFR					
Bad renal function	15 (71.4%)	6 (28.6%)	0.865	0.622-1.202	0.481
Good renal function	19 (82.6%)	4 (17.4%)			

*Statistically significant (Chi-square test)

The association of the predictive factors with the quality of life

For the quality of life outcomes, we found that all patients with bad renal function (GFR \leq 60) have bad quality of life (EORTC QLQ C-30

score \leq 500), with bad initial GFR, is associated with increased risk of having a bad quality of life (RR: 1.917; 95%CI: 1.296-2.835; $p < 0.001$) (Table 4).

Table 4. The distribution and association of various predictive factors to the patient's quality of life after DJ stent placements

Variables	Bad QoL	Good QoL	RR	95% CI	p
Time range					
Late DJ stent	20 (69.0%)	9 (31.0%)	0.796	0.581-1.090	0.282
Early DJ stent	13 (86.7%)	2 (13.3%)			
Hydronephrosis degree					
Severe	9 (81.8%)	2 (18.2%)	1.125	0.794-1.594	0.701
Mild-to-moderate	24 (72.7%)	9 (27.3%)			
GFR					
Bad renal function	21 (100.0%)	0 (0.0%)	1.917	1.296-2.835	$< 0.001^*$
Good renal function	12 (52.2%)	11 (47.8%)			

*Statistically significant (Chi-square test)

DISCUSSION

Ureteral obstruction caused by the advancement of cervical cancer might cause further complications if it happened over a long time. Obstructive uropathy might cause abnormality of renal tissue structure and function. Most of the abnormalities are asymptomatic until they reach severe destruction of renal tissues that leads to deterioration of renal function. This can give rise to various symptoms such as uremia, disturbance of fluid and electrolytes balances, urinary tract infections, anemia, and renal failure that leads to morbidity and mortality.⁶ This shows the importance of ureter de-obstruction to prevent irreversible loss of renal function.

DJ stent placement is one of the methods to deobstruct the ureter in patients with cervical cancer stage IIIB. This study aimed to observe the factors associated with the improvements of outcomes for the patients who underwent DJ stent placements. We observe three factors in this study which are the time range from the diagnosis of cervical cancer to the DJ stent

placements; initial GFR, and degree of hydronephrosis. Of the 44 samples that we obtained, we found that late DJ stent placement (DJ stent placements conducted in more than 2 months after cervical cancer diagnosis) increased the risk of severe LUTS after DJ stent placements by 3.103 times compared to a patient with early DJ stent placement (RR: 3.103; 95%CI: 1.319-7.301; $p < 0.001$). We also found that a low glomerular filtration rate (GFR < 60) is significantly associated with worse quality of life compared to good initial GFR (≥ 60) (RR: 1.917; 95%CI: 1.296-2.835; $p < 0.001$). We found no statistically significant association for other variables that we assess.

Irreversible deterioration of renal function in pigs happened after 6 weeks of obstruction. Microscopic findings that may cause the decrease of renal function are the collapse of the glomerulus, atrophy of renal tubules, and interstitial fibrosis.⁷ Our study did not find a significant association between the time range to DJ stent placement and the GFR improvements. However, our study does show

that late DJ stent placements indicating prolonged renal obstruction do increase the risk of severe LUTS after DJ stent placements.

The study also observes the association of hydronephrosis severity with the outcomes of DJ stent placements. We found there is no significant association between the degrees of hydronephrosis and all of the DJ stent outcomes observed in the study. This finding is in line with the study by Gumilar, et al that also did not find any association of hydronephrosis degree with the success of DJ stent placements in cervical cancer patients.⁸

Quality of life is also one of the important outcomes that shows the actual improvements that can be felt by the patients after DJ stent placements. Our study found that although late DJ stent placements increase the risk of severe LUTS, it is not significantly associated with worse quality of life compared to early DJ stent placements. This may happen because the patients with cervical cancer already have other symptoms that reduced their quality of life and such as cancer pain, disturbance of daily activity, etc, even without LUTS. This might result in similar QoL in patients with severe LUTS and mild-to-moderate LUTS. Our study however found that initial renal function is associated with worse quality of life. None of the patients with bad GFR have a good QoL. Bad GFR is associated with an increased risk of bad QoL compared to patients with good GFR (RR: 1.917, 95% CI 1.296-2.835, P<0.001).

Our study has several limitations. A small sample size might reduce the power of our study to detect the difference in the result statistically. Our historical cohort design also might cause biased data caused by excluding patients with incomplete medical history. Uncontrolled confounding variables also might bias our results, since lack of methods to control the confounding variables.

CONCLUSION

Delayed DJ stent placement is associated with severe LUTS symptoms, and poor renal function glomerular filtration rate resulting in a poor quality of life. This study can be used as a preliminary study to further study and improve patients with cervical cancer treatments to improve patients' quality of life and prevent complications.

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DISCLOSURE

The authors declared no conflict of interest exists regarding this research.

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