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Factors Affecting Renal Function on Ileostomy in Dr. Cipto Mangunkusumo General Hospital: a Cross-sectional Study

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Abstract

Introduction. Every year, about 30—60 ileostomy with various underlying diseases and indications were created in Dr. Cipto Mangunkusumo General Hospital (CMGH). There were a lot of complications attributable to these creations; one is the decline of renal function. The study goal was to find out factors influencing the renal function of ileostomy in CMGH.
Method. A cross-sectional study was conducted using medical records in April – May 2021. Samples were taken using the purposive sampling method. Inclusion criteria include male or female patients who underwent ileostomy closure in CMGH in the last four years with complete BMI, ileostomy creation and closure, serum creatinine, and estimated glomerular filtration rate (eGFR). Patients with underlying renal dysfunctions were excluded. The data were analyzed using univariate and bivariate analysis. Spearman's test was used to analyze the correlation.
Results. There were 55 subjects enrolled in the study. BMI ($p_{eGFR} = 0.044$; $p_{creatinine} = 0.015$), time of ileostomy closure ($p_{eGFR} = 0.014$; $p_{creatinine} = 0.012$), and high output ileostomy ($p_{eGFR} = 0.032$; $p_{creatinine} = 0.018$) were statistically significant as risk factor diminishing the renal function. The correlation analysis showed that time of ileostomy closure was significantly different for eGFR and serum creatinine values with $p = 0.039$ ($r = -0.279$) and $p = 0.021$($r = 0.310$), respectively.
Conclusion. In the study, factors that affect critical renal function in ileostomy were high output ileostomy, time of ileostomy closure, and body mass index. Hydration status, underlying disease, and age did not affect the diminished renal function.

Keywords: *Ileostomy, high output, dehydration, time of closure, renal function*

Introduction

Each year, about 40,000 patients undergo ileostomy creation in the United States, and to date, about 165,000–265,000 people live with an ileostomy.[1] In Dr. Cipto Mangunkusumo General Hospital (CMGH), about 30—60 ileostomies were indicated and created annually with various underlying diseases. Unfortunately, an ileostomy may be followed by complications that we should be aware of. Over 30% of ileostomy in CMGH was a high output ileostomy as one of the complications; the ileostomy production reached up to 1500 mL per day. Some studies showed that 34% of patients with high output ileostomy were dehydrated.[2,3] The risk is up to three times higher than those who didn't have high output ileostomy. In left untreated dehydration, the patient may have a decrease in renal function and further complications. In the United States, about 17% of patients were readmitted to the hospital due to decreased renal function attributable to dehydration. This diminished renal function increases serum creatinine and decreases the estimated glomerulus filtration rate (eGFR). These problems also occur in Australia, with 20% of patients being readmitted because of nutritional–, hemodynamic–, and serum electrolyte problems.[4–9]

To date, there were several factors known that may contribute to diminished renal function after ileostomy creation. These factors were underlying diseases, high output ileostomy, hydration status, and the timing of stoma closure. But these factors haven't been adequately studied in patients with an ileostomy. Besides, the relationship between these factors and renal function counted by changes in serum creatinine and estimated glomerular filtration rate (eGFR) have not been thoroughly defined. We conduct this study to find out which factors will influence the renal function of ileostomy in CMGH.

Method

A cross-sectional study enrolled all adult subjects with ileostomy from medical records at Dr. Cipto Mangunkusumo National Hospital (CMGH). Males and females who underwent ileostomy creation and closure at CMGH between January 2017 and December 2020 were included in the study, while those with underlying renal dysfunction were excluded. Demographical data recorded comprising gender, age, height, weight, body mass index, underlying disease as an indication for surgery, high output ileostomy status, time of ileostomy closure (weeks), hydration status, eGFR, and serum creatinine levels before creation and before ileostomy closure. Data were analyzed using IBM Statistical Package for the Social Sciences (SPSS) version 20. Numerical variables were expressed with mean (standard deviation, SD) or medians (interquartile ranges, IQRs). Categorical variables were presented as frequency (percentage). Independent variables were compared between changes in eGFR and changes in serum creatinine by non-parametrical analysis (Kruskal-Wallis and Mann-Whitney). Spearman's test analyzed the correlation between numerical variables. The Research Ethical Committee of Faculty of Medicine, Universitas Indonesia, reviewed and approved this study.

Results

Out of 125 patients, only 57 subjects (45.6%) met the criteria. Another 68 subjects (54.4%), their ileostomy was on or died before the closure and were excluded. Furthers, another two subjects were excluded as they had renal dysfunction before proceeding with ileostomy; thus, 55 subjects were subjected to analysis. Out of the 55 patients, 36 (6.5%) subjects were 40–65 years aged, and 3 (5.5%) subjects were above 65 years old (a subject aged 83 years). Half of the subjects (49.1%) were those with normal BMI, and 10 (18.2%) had lower BMI than normal.

Table 1. Subject characteristics

	Number of subjects n = 55	%
Age (Years)	46.75 (13.16)*	
18-40	16	29.1%
40-65	36	65.5%
>65	3	5.5%
Gender		
Male	29	52.7%
Female	26	47.3%
BMI (kg/m^2)	22.22 (4.45)**	
Underweight	10	18.2%
Normal	27	49.1%
Overweight	7	12.7%
Obese I	7	12.7%
Obese II	4	7.3%
Underlying diseases		
Gynecological problems	13	23.6%
Rectal malignancies	11	20.0%
Colon Malignancies	7	12.7%
Autoimmune	5	9.1%
Intestinal tuberculosis	4	7.3%
Trauma	3	5.5%
Typhoid perforation	2	3.6%
Diverticulitis of the colon	2	3.6%
Others	8	14.5%
High output ileostomy		
No	30	54.5%
Yes	25	45.5%
Time of ileostomy closure (Weeks after formation)	49.09 (32.16)*	
<12	9	16.4%
12—35	11	20.0%
>35	35	63.6%
Hydration status		
No dehydration	25	45.5%
Dehydrated	30	54.5%
Changes in eGFR (mL/min/1.73m^2)	-13.00 (35.00)**	
Changes in serum creatinine (mg/dL)	0.20 (0.49)**	

* Mean (SD) due to normally distributed data
** Median (*Interquartile Range*) due to irregular distribution of data

Of 10 underweight subjects, one had tuberculosis, four had malignancies, including gynecological and colorectal malignancies. Underlying diseases were grouped into gynecological problems (23.6%), rectal malignancies (20%), colon malignancies (12.7%), autoimmune problems (9.1%), intestinal tuberculosis (7.3%), trauma (5.5%), typhoid perforation (3.6%), colon diverticulitis (3.6%) and others (14.5%). Table 1 describes the subject characteristics.

Table 2. Relationships between factors that might affect eGFR and serum creatinine

	Changes in eGFR		Changes in serum creatinine	
	Median (IQR)	p	Median (IQR)	p
Age (years)$^{\#}$		0.987		0.779
18-40	-15.8 (42.7)		0.19 (0.40)	
40-65	-11.4 (34.5)		0.24 (0.50)	
>65	-15.2 (8.3)		0.20 (0.32)	
BMI (Kg/m^2)$^{\#}$		0.044*		0.015*
Underweight	-1.0 (28.65)		0.03 (0.30)	
Normal	-18.6 (33.0)		0.30 (0.41)	
Overweight	0.0 (23.1)		-0.01 (0.29)	
Obese I	-35.0 (19.0)		0.40 (0.30)	
Obese II	-13.6 (57.80)		0.19 (0.60)	
High output ileostomy†		0.032*		0.018*
No	-11.0 (21.1)		0.15 (0.32)	
Yes	-29.0 (35.6)		0.40 (0.40)	
Time of ileostomy closure $^{\#}$ (Weeks after formation)		0.014*		0.012*
<12	-6.0 (58.9)		0.10 (0.46)	
12—35	-2.0 (19.6)		0.06 (0.30)	
>35	-26.9 (30.5)		0.34 (0.40)	
Hydration status†		0.190		0.397
No dehydration	-11.0 (25.8)		0.19 (0.45)	
Dehydrated	-21.5 (44.9)		0.29 (0.50)	
Underlying diseases$^{\#}$		0.263		0.257
Malignancies	-15.2 (39.0)		0.20 (0.50)	
Autoimmune	-13.5 (31.8)		0.20 (0.56)	
Infection/Inflammation	0.7 (36.9)		-0.05 (1.09)	
Trauma	-29.0 (28.5)		0.40 (0.25)	
Others	-16.5 (60.5)		0.28 (0.62)	

Normality tests using the Kolmogorov-Smirnov method show that all data excluding age and time of ileostomy closure were not normally distributed. The significant standard deviations of these variables might be responsible for this distribution.
The Mann-Whitney showed that ileostomy output was a significant factor that affected changes in eGFR (p = 0.02) and serum creatinine (p = 0.03). The hydration status that was grouped binary into the dehydrated– and not dehydrated groups showed no significant correlation between dehydration with changes in eGFR (p = 0.190) and serum creatinine (p = 0.397).

The Kruskal-Wallis's test for age, underlying diseases, BMI, and ileostomy closure time showed the following findings. Age showed no significant correlation with changes in eGFR (p = 0.987) and serum creatinine (p = 0.779). The underlying diseases were also showed no significant correlation with changes in eGFR (p = 0.263) and serum creatinine (p = 0.257). However, BMI and time of ileostomy closure show different findings where BMI and time of ileostomy closure is significantly correlated to changes in eGFR (p_{BMI} = 0.044; p_{time} = 0.014) and serum creatinine ($p_{BMI} = 0.015$; $p_{time} = 0.012$). Details are described in table 2.

The Spearman analysis was used to determine the correlation between the numeric – numeric variables including age, BMI, and time of ileostomy closure. Age and BMI showed no correlation to neither change in eGFR ($p_{age} = 0.848$; $p_{BMI} = 0.418$) and serum creatinine ($p_{age} = 0.749$; $p_{BMI} = 0.313$). Also, these variables showed a weak correlation with changes in eGFR ($r_{age} = -0.026$; $r_{BMI} = -0.111$) and serum creatinine ($r_{age} = 0.044$; $r_{BMI} = 0.139$). On the other hand, time of ileostomy closure shows different findings. Time of closure showed a correlation significantly with changes in both eGFR (p = 0.039) and serum creatinine (p = 0.021) and showed a weak correlation in eGFR (r = -0.279) and a moderate correlation in serum creatinine (r = 0.310). These findings are shown in table 3 and figure 1.

Table 3. Correlations between factors affecting changes of renal function in ileostomy

	Changes in eGFR		Changes in serum creatinine	
	r	p	r	p
Age (years)	-0.026	0.848	0.044	0.749
BMI (kg/m2)	-0.111	0.418	0.139	0.313
Time of ileostomy closure (Weeks after formation)	-0.279	0.039*	0.310	0.021*

*Significant difference (p <0,05)

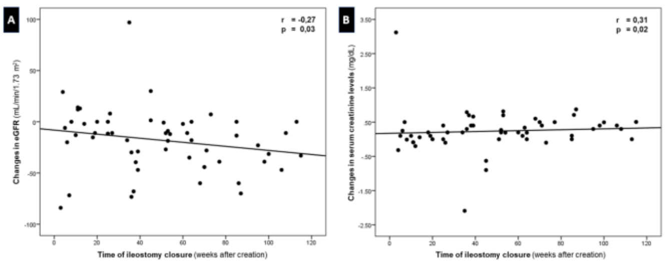

Figure 1. Scatter plot and correlation between time of ileostomy closure to (A) changes in eGFR (mL/min/1,73m^2) and (B) changes in serum creatinine

Discussion

In this study, there were 36 (65.5%) subjects in the 40—65 years old group and 3 (5.5%) patients in the >65 years old group. The correlation between the age group in serum creatinine levels changes and eGFR values showed no significant difference between age groups (p >0.05). This finding is contrary to some studies' findings showing that acute kidney injury is influenced by age. Increasing age is an independent risk of renal dysfunction. At various stages of chronic kidney diseases, subjects >50 years old have decreased renal function 5 to 30% of the normal population. The incidence did not differ between females and males.[10] Imai et al. found no difference in the decrease in glomerular filtration rate between age groups. Based on a longitudinal study in the 49—79 years old group in the Japanese population, the decrease in glomerular filtration rate occurred by 0.36 mL/min/1.73m^2/year.[11] Another study showed the rate of decrease was higher in the geriatric group, 0.39—0.42 mL/min/1.73m^2/year in the 70-79 years group in Japan and 0.75—1 mL/min/year in the geriatric population in the United States.[12,13] Study of Toyama et al. reported that the decrease in eGFR would slow down from the 70-79 years old group and over 80 years old group. However, in this study, there was also no significant difference in the decrease in eGFR values between age groups.[14]

In this study, BMI was correlated with changes in eGFR values and increased serum creatinine levels significantly (p <0.05). Various studies have found the correlation between obesity and a higher BMI to decrease eGFR and its impact on the progression of chronic renal disease. An increase in BMI is correlated with proteinuria even in patients without chronic kidney disease. Obese patients with high adipose reserves may lower adiponectin levels, increase leptin, resistin, and visfatin concentrations, increase insulin resistance, the renin-angiotensin-aldosterone system (RAAS) activation, trigger inflammation, oxidative stress, and abnormalities in lipid metabolism. The condition may lead to chronic kidney disease and exacerbate comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease.[15–18]

High output ileostomy and renal dysfunction

In this study, 25 (45.5%) of 55 subjects enfacing the problem of high output ileostomy. Six subjects underwent ileostomy closure before twelve weeks. The immediate ileostomy closure proceeded following a high output condition that could not be corrected by increasing water intake or medication. The condition may result in continuous dehydration, electrolyte imbalances, and hemodynamic problems. If the conditions are not treated, the problem remains irreversible. The number of high output subjects in this study reached up to half the number of subjects, higher than Gessler et al., who reported 46 (18%) of 250 patients having high output ileostomy. High output ileostomy is the most common complication of ileostomy, contributing to 49% of hospital readmission. Preventing the occurrence of high output ileostomy will be helpful to reduce hospital readmissions.[19]

In this study, high output ileostomy was significantly correlated to changes in eGFR values and serum creatinine levels (p = 0.018; p = 0.032). Vergara-Fernandez et al. found a significant correlation between high output ileostomy and renal failure (OR 3.3; 95%CI 1.18-9.37; p = 0.023), indicating that high output ileostomy will increase the risk of renal failure.[8] In this study, time of ileostomy closure in the high output group showed no difference significantly with changes in eGFR and serum creatinine compared to non-high output groups. This finding may be related to the number of samples for each group after stratification, which was small.

Time of ileostomy closure and renal dysfunction

In this study, renal function was assessed using serum creatinine levels and eGFR. Changes in serum creatinine levels showed significant moderate correlation to time of ileostomy closure (r = 0.31; p = 0.02). Changes in eGFR also showed significant correlation (r = -0.27; p = 0.03). This finding may explain that a longer period of ileostomy closure may increase serum creatinine level and decrease eGFR. Hence, this finding fulfilled the hypotheses of correlation between ileostomy closure and renal dysfunction.

Gessler et al. reported 308 subjects with significantly decreasing eGFR, increasing serum creatinine levels and an increasing number of subjects with renal impairment after ileostomy closure compared to the values before closure (7.5% vs. 21%).[31] Beck-Kaltenbach et al. emphasize the decreasing eGFR and increasing serum creatinine after ileostomy creation.[20,21] Yaegashi et al. reported that eGFR values remain to decrease up to 18 months after ileostomy creation. The decline of eGFR values is significant compared between ileostomy creation, the first month after creation, and six months after ileostomy closure.[33]

Another study by Yang et al. showed a significant increase in serum creatinine in patients with ileostomy compared to those without ileostomy. Measurements were carried out in the first month (p <0.05) and the third month (p <0.01) after ileostomy.[22] Meanwhile, decreased eGFR showed no significant difference between the first and third-month measurements compared to the baseline. However, eGFR showed a significant difference in the first and third months (p <0.01).[22]

The finding indicated that a patient with an ileostomy has a higher risk of renal dysfunction. Fielding et al. also showed that patients with an ileostomy showed a decrease in eGFR (p <0.0001) compared to those without ileostomy. Even after a more extended period, eGFR remained to decrease significantly (p <0.0001).[23] This study and studies abroad conclude that the longer time of ileostomy closure may increase serum creatinine levels and decrease eGFR.[24]

Hydration status and renal function

In present study, 30 (54.5%) subjects were dehydrated, indicating that ileostomy led to more than 50% dehydration. This study also discovered that hydration status couldn't be used as a predictor of renal function. The analysis in the study shows that hydration status was not significantly correlated to neither change in eGFR (p = 0.190) nor changes in serum creatinine (p = 0.397). It means that ileostomy with dehydration might not have a decrease in renal function in CMGH.

Previously, dehydration was a risk factor for decreased renal function, though this process takes time. Patients with dehydration typically will have hydration therapy to prevent an early decreased renal function.[7,25] The procedure proceeded in CMGH to ileostomy patients, hence what we found in the analysis. Out of 25 subjects with high output ileostomy, 15 (60%) subjects were dehydrated. About 40% of subjects who were not dehydrated had good preoperative and postoperative care.

However, not all dehydrated subjects were caused by high output ileostomy. Of 30 dehydrated subjects, 15 (50%) were not subjected to high output ileostomy. In these cases, dehydration is thought to be associated with the lack of fluid and electrolyte intake. Adequate fluid and electrolyte and nutritional intake and medicals such as loperamide and codeine are essential and should be carried out in conjunction with each other.[26] According to Migdanis et al., a significant decrease in sodium and an increase in serum creatinine were found in 20 days following ileostomy. Migdanis et al. concluded that patients with an ileostomy are at risk for dehydration and electrolyte imbalance showed by a decrease in sodium and an increase in serum creatinine. Hence, oral rehydration is vital to prevent electrolyte and fluid imbalance. Adequate oral hydration is proven to be significant in preventing readmission due to dehydration.[27]

Underlying diseases and renal dysfunction

This study shows that underlying diseases showed no correlation to changes in eGFR (p = 0.263) and serum creatinine (p = 0.257). Rhemouga et al. found that out of 151 patients in their study, underlying diseases including diabetes, hypertension, chronic obstructive pulmonary disease (COPD), and malignancies categorized into adjuvant and non-adjuvant chemotherapy have no significant correlation to changes in eGFR and serum creatinine (p >0.05). Their study also enrolled rectal cancer referred to the 2nd highest underlying disease out of the 55 patients.[28]

Fielding et al. show a different finding where the severity of underlying diseases scored using guidelines from the American Society of Anesthesiologists (ASA) shows a significant correlation with changes in eGFR (p = 0.03). Their study revealed that when compared to ASA 1, ASA 2 and 3 will decrease eGFR by 3.18 times and 4.38 times, respectively. On the contrary, ASA 4 will increase eGFR by 0.74 times when compared to ASA 1. Fielding et al. also deduced that the degree of malignancies is not significantly correlated with decreasing renal function (p = 0.06). Their finding may explain this study finding where most subjects (31 or 56%) have malignancy.[23]

No protocol of ideal time for ileostomy closure,[29] studies show that ileostomy is preferably be closed in 8–12 weeks following creation or when the necessity for closure is met.[30] Closing an ileostomy at the right time may improve the overall quality of life and physical and social function.[31]

The study enfacing limitations. Although the hypothesis is proven with intended 55 samples, the power of a study was less than 80%. Hence, the findings referred to a preliminary study.

Conclusion

In present study, some factors affecting decreased renal function in patients with an ileostomy were high output ileostomy, time of ileostomy closure, and body mass index. Other factors, i.e., hydration status, underlying disease, and patient's age, are affecting. In preventing renal dysfunction, early closure is preferable if no contraindication and the criteria for closure are met.

Disclosure

The authors disclose no conflict of interest

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