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# Correlation between the number of Interstitial cells of Cajal (ICC) and defecation pattern in patients with Hirschsprung's disease after Duhamel's surgery at General Hospital Dr. Soetomo



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#### ABSTRACT

**Background:** Hirschsprung is a congenital disorder of the distal bowel caused by the absence of a ganglion in the Aurbach and Meissner plexuses. Definitive treatment of the disorder is operative, namely by resection of the aganglionic segment of the intestine and performing a pull-through on the ganglionic segment. It cannot be denied that there are still disturbances in the pattern of defecation after definitive surgery, even though the pull-through segment has enough ganglion cells. Interstitial cells of Cajal (ICC) are the pacemaker in smooth muscle contraction in the intestine. In several studies, the number of these cells decreased in Hirschsprung's disease (HD), and it is not known with certainty the effect on the occurrence of defecation pattern disturbances.

Methods: Data were collected retrospectively from all patients with Hirschsprung's Disease (HD) who underwent Duhamel Procedure in Dr. Soetomo General Hospital, starting January 2016 – December 2021. Correlation analytic research with a cross sectional design was performed to analyze the correlation between the number of ICC and the defecation pattern of patients at Dr. Soetomo after Duhamel surgery.

**Results:** From this study, it was found a decrease in the number of ICC in the ganglionic segments of the resected specimens from pull-through surgery. From the results of the correlation test, it was found that the p-value was 0.49 for the defecation pattern of postoperative Duhamel patients at Dr. Soetomo for the period January 2016 – December 2021.

**Conclusion:** In this study, a significant correlation was found between the number of ICC and definitive pull-through postoperative defecation pattern.

**Keywords:** *defecation, hirschsprung's disease, interstitial cell of Cajal, Duhamel technique surgery.* **Cite This Article:** Honggowarsito, Y.S., Hariastawa, I.G.B.A., Matulatan, F., Rahniayu, A. 2023. Correlation between the number of Interstitial cells of Cajal (ICC) and defecation pattern in patients with Hirschsprung's disease after Duhamel's surgery at General Hospital Dr. Soetomo. *Bali Medical Journal* 12(1): 675-677. DOI: 10.15562/bmj.v12i1.4154

### **INTRODUCTION**

Hirschsprung's disease is a congenital disorder of the distal intestine caused by the absence of ganglions in the Aurbach and Meissner plexuses. This disorder has an incidence of up to 1:5,000 live births.¹ The prevalence among Asian people is around 1:3,847 live births.² There are no clear data about prevalence in Indonesia. The definitive treatment for this disorder is surgery, with resection of the aganglionic segment of the intestine and pull-through of the ganglionated segment. However, in some cases, bowel motility disorders still occur even though definitive surgery has been performed.³

It is undeniable that one of the postoperative complications of

Hirschsprung's disease is constipation, ranging from 30.8% of 161 patients who have undergone surgery.<sup>2</sup> From other studies, it was also found that 11% -35% of patients experienced constipation and soiling after a pull-through procedure. The exact cause for this condition is not yet known. This persistent defecation disorder illustrates that the intestinal segment that has sufficient ganglion alone does not give satisfactory results.<sup>4</sup>

Interstitial cells of Cajal are one of the factors for intestinal motility as smooth muscle pacemakers. If there is a decrease in the number of ICC, it can cause intestinal dysmotility, which causes constipation.<sup>5</sup> Several studies have shown that there is a disturbance in ICC distribution in

patients with Hirschsprung's disease.<sup>6,7</sup> In the resected intestinal segment, fewer Cajal interstitial cells were found than in the normal intestine and only formed sparse tissue. This is suspected as the cause of constipation in patients who have undergone definitive surgery. The presence of these factors can be assumed to be predictive of the occurrence of a disorder of defecation in patients who have had pull-through surgery.

The aim of this study was to find a correlation between impaired numbers of ICC from ganglionated bowel resection tissue in patients with Hirschsprung's disease who had undergone Duhamel pull-through surgery and impaired postoperative defecation patterns.

#### **METHODS**

This was an analytic observational study with cross sectional design. Data were collected retrospectively from medical records of all patients with Hirschsprung's Disease who underwent the Duhamel procedure in Dr. Soetomo General Hospital, starting from January 2016 – December 2021. We use total sampling to obtain the samples with inclusion criteria that the patients have the specimen which eligible for C-kit staining and the exclusion criteria if the specimens are not available for C-kit staining.

All data were entered into SPSS v26.0 for Windows. Shapiro – Wilk analysis was used for determining the distribution of the data, such as age and the number of ICC. The correlation between the ICC and Rintala scoring uses Spearman analysis.

#### **RESULTS**

In the Shapiro – Wilk normality test, it was found that the data were not normally distributed, then an analysis of the relationship test was carried out using the Spearman test. P=0.049, where P<0.05, so it can be concluded that there is a significant correlation between the Rintala score and the number of Cajal interstitial cells in the internal muscular layer. The value of r=0.369 was obtained, which indicated the strength of the correlation was 36.9%, which included weak criteria. The characteristic of the sex shown in Table 1.

The result of Rintala scoring is shown in Table 2, and the calculation number of ICC in the inner muscular layer and outer muscular layer is shown in Table 3. The Spearman analysis between Rintala scoring and the number of ICC in the inner muscular layer is shown in Table 4, and between Rintala scoring and the number of ICC in the outer muscular layer is shown in Table 5. The difference between a normal distribution and scattered C-kit positive ICC in the ganglionic intestine is shown in Figure 1.

#### **DISCUSSION**

Definitive pull-through is the only treatment for Hirschsprung's disease, with the removal of a ganglion segment of the intestine. While most patients did well after a one-stage pull-through operation, a small number of patients suffered from postoperative complications. Several studies have shown that the presence of residual bowel tissue containing abnormal ICCs, which have normal ganglion, can result in functional motility disorder and postoperative constipation in HD patients.<sup>8</sup>

In a study observing the long-term outcomes of patients with Hirschsprung's disease, out of 194 people, 20 people experienced soiling 42 people (21.7%) experienced constipation. A total of 48 people underwent definitive pull-through surgery using the Duhamel technique, and 8.3% were still constipated.9 From another study conducted in India, patients with Hirschsprung's disease who underwent surgery using the Duhamel technique, as many as 29.42% experienced soiling, 11.76%, strictures 11.76%, enterocolitis 11.76%, and 11.76% still experience postoperative constipation.<sup>10</sup> A study found that some HD patients had reduced numbers of ICCs in their proximal

ganglionic bowel. Therefore, insufficient resection of such bowel could be a cause of motility disturbances and recurrent constipation.<sup>11</sup> Another study shows the

Table 1. Characteristics of the patients.

Patientsi					
Sex	n	(%)			
Male	20	68.97			
Female	9	31.03			
	Age (year)				
Minimum	;	3			
Maximum	23				
Mean	9.24				
Median	8.00				
Mean ± SD	$9.24 \pm 4.86$				

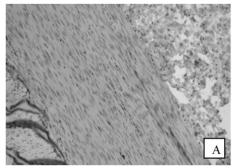
Table 2. Rintala scoring.

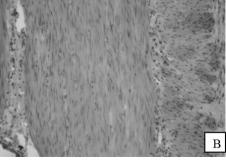
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Rintala	n	%
Poor	1	3.4
Fair	2	6.9
Good	12	41.4
Excellent	14	48.3

Table 3. Interstitial cells of Cajal.

	P value	
Inner Muscular Layer		0.00
Range	2 - 131	
Median	16.00	
Mean	21.03	
Mean ± SD	$21.03 \pm 24.2$	
Outer Muscular Layer		0.00
Range	1 - 89	
Median	12.00	
Mean	16.83	
Mean ± SD	$16.83 \pm 17.67$	

<sup>\*</sup>Normal distribution if P > 0.05





**Figure 1.** (A) Photomicrographic shows a normal distribution of C-kit positive ICCs in the ganglionic intestine (IHC x200). (B) Photomicrographic shows scattered distribution c-kit positive ICCs in the ganglionic intestine (IHC x200).

Table 4. Correlation of ICC on the inner muscular layer with Rintala scoring.

Rintala N		Inner muscular layer				Р-	
Kilitala	IN	Range	Median	Mean	Mean +SD	value	r
Poor	1	22-22	22	22		0.049	0.369
Fair	2	2-40	21	21	21 + 26.87		
Good	12	2-40	10	14.58	14.58 + 11.996		
Excellent	14	4-131	16.50	26.50	26.50 + 31.843		

<sup>\*</sup>Significant if P < 0.05

Table 5. Correlation of ICC on the outer muscular layer with Rintala scoring.

Dintala N		Outer muscular layer				P-	
Rintala N	Range	Median	Mean	Mean +SD	value	r	
Poor	1	11-11	11	11		0.064	0.348
Fair	2	7-24	15.50	15.50	15.50 + 12.02		
Good	12	2-42	9.50	11.42	11.42 + 11.23		
Excellent	14	1-89	12.50	22.07	22.07 + 22.24		

<sup>\*</sup>Significant if P < 0.05

correlation between colonic motility disorders, manometric findings, and the expression of ICCs. <sup>12</sup> In this study, ICCs are defective not only in the ganglionic bowels of HD disease but also in specimens from chronic intestinal pseudo-obstruction and idiopathic intractable constipation patients. <sup>12</sup> Not only the reduction in ICCs in the ganglionic part of the HD bowel but the ICCs also present formed only a sparse network around the ganglia of the myenteric plexus compared to normal controls. <sup>8</sup>

We assessed the patient's defecation patterns using the Rintala score to determine the defecation problem of the patients and categorized them into 4 categories: excellent, good, fair, and poor. 13 In our study, we analyze the ganglionic segment with C-kit positive for ICC. There's a significant correlation between the number of ICC in the inner muscular layer and disturbance of defecation pattern. The more it has ICC, and the patient has better defecation pattern according to the Rintala score. Another study also describes a few cases suffering from severe constipation or enterocolitis resulting in patient death after a definitive operation for Hirschsprung's disease, even though the normoganglionic intestine had been successfully pulled through. A decrease in ICCs distribution using c-kit immunostaining in the normoganglionic segment is probably the cause of this problem.<sup>14</sup> The limitation of this study was

that our design study couldn't rule out the dietary problem of the defecation pattern.

#### **CONCLUSION**

We conclude from this study that a decrease of ICC in the normoganglionic bowel can affect the outcome of patients after definitive pull-through surgery.

#### **ETHICAL CONSIDERATIONS**

This study was approved by The Research Ethics Committee of Dr. Soetomo General Academic Hospital (Ref No. 0461/KEPK/VIII/2022).

#### **CONFLICT OF INTEREST**

No conflict of interest.

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### **AUTHOR CONTRIBUTION**

YSH: Concept, methodology, preparation of the manuscript. AH: Supervision and guidance. FM: Supervision and guidance. AR: consultant of Anatomical Pathology.

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#### 0461/KEPK/VIII/2022

KOMITE ETIK RSUD Dr. SOETOMO SURABAYA TELAH MEMPELAJARI SECARA SEKSAMA RANCANGAN PENELITIAN YANG DIUSULKAN, MAKA DENGAN INI MENYATAKAN BAHWA PENELITIAN DENGAN JUDUL:

"HUBUNGAN ANTARA JUMLAH SEL INTERSISIAL CAJAL DENGAN POLA DEFEKASI PADA PASIEN DENGAN HIRSCHSPRUNG'S DISEASE PASKA TINDAKAN OPERASI DUHAMEL DI RSUD DR. SOETOMO "

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Berlaku dari : 04/08/2022 s.d 04/08/2023

Surabaya, 4 Agustus 2022

KETUA

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NIP. 19610817 201601 6 101

\*) Sertifikat ini dinyatakan sah apabila telah mendapatkan stempel asli dari Komite Etik Penelitian Kesehatan