Neonatal intestinal volvulus. Review of our experience over the last 20 years

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Research Article

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Abstract

Background: There are two types of volvulus: midgut (MGV) and segmental (SV). Patients with different types of volvulus are often included in the same case series, which may affect the perception of how severe "intestinal volvuli" are. We aimed to create a predictive model of death and intestinal failure (IF) in neonatal intestinal volvulus.

Methods: Retrospective cohort study including all patients with MGV and SV up to 60 days of life admitted to a tertiary hospital in Spain over a 20-year-period (1999-2019). A comparison between groups and a logistic regression model for mortality and IF were done.

Results: We identified 39 patients: 28 MGV and 11 SV. Prenatal diagnosis, intestinal atresia, meconial conditions, cystic fibrosis, and intestinal resection were significantly more frequent in SV. Need of inotropic durgs, birth weight (BW) 1500-2499g, BW 1000-1499g and <1000g increased the risk of death. SV and gestational age <37 weeks increased the risk of IF or dying.

Conclusions: SV and MGV are different entities. Low BW and need for inotropic drugs are risk factors for death. Surgical examination should be performed to rule out volvulus in neonates presenting with such risk factors. Prematurity and SV are risk factors for IF.

Background:

Volvulus is the torsion of an organ over its ligaments, which compromises vascularization and produces ischemia. Intestinal volvulus, then, consists in the twisting of the intestine around the mesentery that supports it, which often results in an obstructive pathophysiology and may evolve to ischemia [1-5]. There are two main types of volvulus: a midgut volvulus (MGV) occurs when all the small bowel and part of the large intestine twists around the superior mesenteric artery and a narrow mesentery, and a segmental volvulus (SV) occurs when an intestinal loop volvulates around itself. However, this classification is not always clear in the literature and patients with different types of volvulus are often included in the same case series.

MGV is mainly related to anomalies of gut development, such as malrotation, which can cause an unstable position of the gut due to a narrowed small bowel mesenteric root. According to the Centers for Disease Control, the prevalence of malrotation is 3.9 per 10,000 live births [6]. Complete MGV is a life-threatening emergency that requires prompt surgical management as it can lead to irreversible intestinal necrosis, and extensive resection may be necessary [1-8]. MGV is the third leading cause of short bowel syndrome or intestinal failure (IF) in the pediatric population, accounting for 14% of cases, after necrotizing enterocolitis and intestinal atresia. An early surgical intervention may mean the difference between intestinal catastrophe and a successful outcome [3,5,7-9]. However, it is also possible to have a subacute MGV without intestinal compromise.

On the other hand, SV refers to the torsion of an extremely dilated intestinal segment over itself. It is an entirely different entity from MGV, and mostly observed during the perinatal period. It is often associated with intestinal atresia, meconium ileus or, occasionally, other conditions such as postoperative bands, a duplication cyst, internal herniation, etc. [1]. In the neonatal period, the clinical presentation of midgut and SV may be quite similar [1].

We believe that the confusion between these entities may affect the perception of how severe "intestinal volvulus" is. Consequently, the main objective of this study was to create a predictive model of death and IF in neonatal intestinal volvulus. As a secondary objective, we studied the main differences between the two types of volvulus.

Methods:

This was a retrospective cohort study of the cases of neonatal “intestinal volvulus” diagnosed at Hospital Sant Joan de Déu, a tertiary hospital in Barcelona, Spain, over a 20-year- period (1999 to 2019). All data were codified in order to preserve the privacy of the patients. Our hospital Ethics Committee (Hospital Sant Joan de Déu) accepted and approved this study (reference code: PIC-135-20). Patients were selected through the review of the hospital’s neonatal and surgical databases for the diagnosis of neonatal “intestinal volvulus”. These databases have been available since mid-1998, therefore we chose to identify all patients who met study inclusion criteria from 1999 to 2019. We limited our review from birth up to two months of age because we wanted to achieve complete distribution of neonatal volvuli. Inclusion criteria: the diagnosis or presence of MGV (acute and subacute), SV, infants younger than 60 days old or admitted to our hospital with a confirmed intestinal volvulus during surgery. Classification of volvulus was done according to the available surgical operative reports and medical records. Exclusion criteria: gastric volvulus or volvulus of any organs other than the small intestine (such as ovarian torsion or exclusive colonic volvulus); patients with a diagnosis of “volvulus” which was not confirmed during surgery; patients with a diagnosis of “volvulus” who did not undergo any surgical procedure or necropsy; and patients with intestinal volvulus presenting after 2 months of age.

Data on demographic, clinical, surgical and outcome variables were collected. Table 1 lists the variables that were registered in every case. Many variables are self-explanatory (gender, birth weight…). We defined volvulus as “acute” when signs of ischemia were present at the time of surgery. Those signs included the presence of a volvulus with intestinal necrosis or the evidence of intense intestinal pallor which resolved after devolvulation. Normally perfused intestines, simple congestion of intestinal loops, or chylous ascites without intestinal compromise were considered “subacute volvulus”. We defined “emergent surgery” as surgery performed on the same day, usually within a few hours of when the decision was made for surgical intervention. Any planned or deferred surgery (such as that for malrotation) was considered not emergent. The need for inotropic drugs is an objective variable to evaluate the presence of shock or hemodynamic instability (which was more difficult to measure).IF was defined as the need for prolonged parenteral nutrition for weeks or months, which corresponds to type II IF according to Pironi. This prolonged acute condition, often in metabolically unstable patients, requires complex multi-

disciplinary care and intravenous supplementation over periods of weeks or months [10,11]. From a practical point of view, all the patients with IF were dependent on total parenteral nutrition (TPN) for at least three months. The main goal of this study was to characterize the risk factors for the outcome variables: death and IF. Outcome variables were the dependent variables, and all the other variables were the independent variables.

Table 1: Summary of study variables

	Study variable (how it was measured)	
	Main variable	**Other related variables**
Demographic	Gender (%* of males)	
	Gestational age (wk days)	Term (>37 wk)/preterm (<37 wk)
	Birth weight (grams)	≥2500g/1500-2499g/1000-1499g/<1000g
Clinical	Prenatal diagnosis (%)	Intestinal atresia (%), cystic fibrosis (%), other diagnoses (CDH, gastroschisis) (%)
	Abdominal distension (%)	
	Bilious vomiting (%)	
	Need for inotropic drugs (%)	
Surgical	Age at surgery (days); emergent surgery (%)	
	Type of volvulus (segmental/midgut) (%); acute/subacute (%); intestinal malrotation (%)	
	Need for intestinal resection (%); length of resected bowel (cm)	
Outcome	Death (%)	
	Intestinal Failure (IF) (%)	

*(%) Proportion of patients with this variable.

wk: weeks

Statistical analyses: Data were described using frequencies for binary and categorical variables. Median and interquartile range (IQR) were used for continuous data. We included all available patients from the study period. For this reason, we calculated the power of the study to predict mortality instead of previously calculating sample size. We assessed binary and categorical data using Fisher's exact test and continuous data with the Mann-Whitney's U test. We calculated predictive models of death and IF with a backward stepwise logistic regression. Independent variables that significantly differed in death or IF

were included as potential predictive variables for the models. In order to evaluate the accuracy of our predictions, we calculated the pseudo-R^2 and the receiver operating characteristic curves (ROC curves). Statistical analyses were performed with Stata 14.2 (StataCorp, Texas, USA). Statistical signification was established for p-values less than 0.05.

Results:

One hundred twenty three patients received the diagnosis of “volvulus” over the 20 year review period. After excluding patients with other kinds of volvulus (gastric, colonic), other diagnoses (such as simple malrotation without MGV, chronic abdominal pain, ovarian torsion or torsion of epiploic appendices) and four patients with MGV older than 2 months of age, we included 39 patients younger than 60 days with “intestinal volvulus” in our study (figure 1). Of these, there were 28 cases of MGV and 11 of SV.

Malrotation was almost exclusive of MGV, whereas intestinal atresia, meconial conditions and cystic fibrosis were significantly associated with SV. Prenatal diagnosis was more frequent in SV, as well as the need for intestinal resection. Table 2 describes the characteristics of our main groups (MGV and SV) as well as a comparison between acute and subacute MGV. Among patients with MGV, only those with an acute presentation had mortality or IF.

Table 2: Characteristics of our study population and groups. Detailed comparison of midgut volvulus patients.

	Global n = 39	Segmental volvulus n = 11 (28.2%)	Midgut volvulus n = 28 (71.8%)	p	Midgut volvulus		
					Acute n = 16 (57.1%)	Subacute n = 12 (42.9%)	p
Gender (male %)	22 (56.4)	6 (54.5)	16 (57.1)	1[a]	9 (56.3)	8 (61.5)	1[a]
Gestational age (weeks ^{days}) (median, IQR 25-75)	38 $^{0/7}$ (33 $^{0/7}$ - 39 $^{4/7}$)	36 $^{4/7}$ (32 $^{5/7}$ - 39 $^{4/7}$)	38 $^{0/7}$ (33 $^{0/7}$ - 39 $^{3/7}$)	0.587[b]	35 $^{3/7}$ (26 $^{0/7}$ - 39 $^{3/7}$	38 $^{3/7}$ (38 $^{0/7}$ - 39 $^{5/7}$	0.192[b]
Birth weight (g) (median, IQR 25-75)	2935 (1534-3241)	2755 (1880-3090)	3050 (1345 3770)	0.403[b]	1863 (797-3255)	3075 (2835-3830)	0.062[b]
Prematurity[1] (%)	14 (40.0)	6 (54.5)	8 (33.3)	0.283[a]	7 (50)	1 (9.1)	0.079[a]
Prenatal diagnosis[2] (%)	10 (26.3)	7 (70)	3 (10.7)	0.001[a]	1 (6.3)	3 (23.1)	0.56[a]
Malrotation (%)	27 (69.2)	1 (9.1)	26 (92.8)	0.000[a]	-	-	-
Cystic fibrosis (%)	3 (7.7)	3 (27.3)	0 (0)	0.018[a]	-	-	-
Intestinal atresia (%)	5 (12.8)	4 (36.3)	1 (3.6)	0.017[a]	-	-	-
Abdominal distension[3] (%)	28 (75.7)	10 (90.9)	18 (69.2)	0.229[a]	14 (87.5)	5 (45.5)	0.026[a]
Bilious vomiting[3] (%)	36 (97.3)	11 (100)	25 (96.2)	1[a]	15 (100)	10 (90.9)	0.423[a]
Need for inotropic drugs[2] (%)	12 (31.6)	0 (0)	12 (42.9)	0.016[a]	12 (75)	0 (0)	0.000[a]
Age at surgery (days) (median, IQR 25-75)	6 (3-15)	2 (0-3)	8.5 (4-20.7)	0.001[b]	12.5 (5.2-31)	6 (3-10)	0.100[b]
Emergent surgery[3] (%)	27 (73.0)	7 (70)	20 (74.1)	1[a]	14 (93.3)	6 (46.2)	0.024[a]
Intestinal resection (%)	16 (41)	10 (90.9)	6 (21.4)	0.000[a]	6 (37.5)	1 (7.7)	0.024[a]
Intestinal resection (cm) (median, IQR	21 (11.2-	18 (10-39)	51.5 (14.5-65)	0.428[b]	51.5 (14.5-	10 (10-10)[5]	-

25-75)	63.7)				65)		
Death (%)	9 (23.1)	2 (18.2)	7 (25)	1[a]	7 (43.8)	0 (0)	0.01[a]
IF[4] (%)	7 (21.2)	5 (45.4)	2 (9.1)	0.027[a]	2 (20)	0 (0)	0.195[a]

IQR: interquartile range. IF: intestinal failure.

[1]Data missing from 4 cases. [2]Data missing from 1 case. [3]Data missing from 2 cases. [4]Data missing from 6 cases. [5]Data from only 1 case.

[a]Fisher's exact test. [b]Mann-Whitney's U test

Predictive models: The distribution of the variable preterm, gender, shock, type of volvulus and categorized weight showed significant differences with at least one of our dependent variables: death, IF, "bad outcome". Consequently, the former variables were considered for our predictive model. Table 3 summarizes the results of the logistic regression.

Table 3: Logistic regression predictive models for outcome variables.

Predictive model	Risk variable	OR	95% CI	p	R^2	AUC	95% CI
Mortality risk	Shock	19.3	1.64-226.15	0.018	40%	0.912	0.81-1
	Birth weight 1500-2499 g*	20.26	1.07-383.6	0.045			
	Birth weight 1000-1499 g*	7.38	0.14-381.1	0.32			
	Birth weight <1000 g*	2.69	0.17-40.84	0.47			
IF risk	Segmental volvulus	10.27	0.79-133.3	0.075	45%	0.88	0.77-1
	Gestational age <37 weeks	31.13	2.04-474.4	0.013			
"Bad outcome" risk*	Gestational age <37 weeks	10.8	2.09-55.66	0.04	21%	0.766	0.592-0.941

OR: odds ratio; CI: confidence interval; AUC: area under the ROC curve; IF: intestinal failure.

*Compared to the reference group "Birth weight >2500 g".

**This model is built upon the only common variable associated to mortality and IF risk. Prematurity and Birth weight had a strong lineal correlation, which prevented us from including both in the same model. We chose between prematurity and birth weight according to the best predictive model result.

a) Mortality risk: The variable with the strongest correlation with mortality on a univariate analysis was the need for inotropic drugs. Volvulated neonates who needed inotropic drugs had a higher risk of mortality (OR 16.8, 95% CI 2.65-106.1; p = 0.003). For the main outcome, the power of this study to predict mortality was 84%, calculated with the two-sided normal corrected test. In the logistic regression model, birth weight and gestational age showed a strong correlation with each other, which made it impossible to use both variables at the same time for the model. The best predicting model for mortality included the variables “need for inotropic drugs” and the categorized birth weight. This model could explain 40% of the mortality variability. In this model, the need for inotropic drugs was associated with and OR of 19.3 (95% CI 1.64-226.15; p=0.018) for mortality. Compared to neonates with a birth weight >2500g, birth weight 1500-2499g had an OR of 20.26 (95% CI 1.07-383.6; p=0.045) for mortality, whereas birth weight 1000-1499g had an OR of 7.38 (95% CI 0.14-381.1; p=0.32) and birth weight <1000g also increased the risk of death with an OR of 2.69 (95% CI 0.17-40.84; p=0.47). The area under the ROC curve for this model was 0.912 (95% CI 0.81-1).

b) IF risk: The best model for predicting IF contained the following variables: “type of volvulus” and categorized gestational age. SV carried an OR 10.27 for IF (95% CI 0.79-133.3; p=0.075) compared to MGV. Gestational age <37 weeks had an OR 31.13 for IF (95% CI 2.04-474.4; p=0.013) in relation to full-term infants. Pseudo-R^2 for this model was 0.45. The area under the ROC curve for the model was 0.88 (95% CI 0.77-1).

Discussion:

This study was based on a comprehensive review of cases of neonatal intestinal volvuli over a 20-year-period diagnosed at a tertiary hospital in Barcelona, Spain. We classified patients into two groups, midgut and segmental volvuli, and analyzed whether they had different characteristics. The study also identified the two main features responsible for mortality in our population: the need for inotropic drugs and low birth weight. Furthermore, the likelihood of IF increased with SV and prematurity.

By definition, subacute MGV does not compromise the intestine. It can be a casual diagnosis during a Ladd’s procedure for intestinal malrotation, or suspected by image studies. All the patients in whom a subacute volvulus was found during their intervention recovered without any major complications. We did not record other possible complications such as bowel adhesions. On the other hand, acute MGV can be considered as a sudden intestinal event, and may be extremely severe.

The incidence of MGV in the general population ranges between 1.7 and 60 per 100,000 [12]. We have not found any studies exclusively focused on neonatal volvulus and it is difficult to find the mortality rate for acute volvulus in the medical literature, and because such references often date from decades ago [13-

17]. Reviews offer a mortality rate for intestinal malrotation around 14%, which mostly refers to acute MGV [18,19]. Rescorla et al, in a classic review of 447 cases, found a mortality rate of 28% in infants with MGV [14]. They also noted that acute MGV presented early in life. If we only selected for the acute MGV patients, we observed that mortality was almost 44%, and acknowledge that this mortality rate seems very high. When combined with the subacute MGV group (whose mortality was 0%), mortality dropped to 25%. If patients with SV were also considered, we obtained a mortality rate of 23%, which compares more favorably to the numbers previously mentioned, however this also included older children.

Up to 75% of volvulus occurs within the first month of life and another 15% during the first year. In our review, we identified 32 patients with MGV, of whom only 4 were older than two months and were excluded for the study. At our hospital 87.5% of midgut volvuli occurred within the first two months of life, which is similar to what others have previously reported [7,12]. The majority of volvulus occurred during the neonatal period, but a few, especially in preterm babies, still appeared during the second month of life, while still at the hospital. Premature patients with an acute MGV had a higher mortality rate according to our research. MGV among preterm neonates appeared later than segmental volvuli: 25% during the second week of life and 44% of cases were diagnosed at the third week of life or later. At that time in those patients, it was easy to misdiagnose MGV for necrotizing enterocolitis [5]. Based on our report, we advise that acute MGV be considered in the differential diagnosis of a newborn, especially if born premature and who suddenly presents with abdominal distention, metabolic acidosis, may occasionally have bloody feces, and no signs of intestinal pneumatosis in the abdominal x ray. While our study was based at a tertiary hospital which acts as a referral center for surgical newborns from a large region, our incidence of acute MGV is less than one case per year on average. Although it is difficult to measure, we feel that delay in diagnosis of acute MGV may be related to not considering this entity in the differential diagnosis.

Neonatal SV is a completely different entity and tends to have a longer evolution until the clinical need for surgery. The problem usually starts prenatally as an intestinal dilation secondary to an intestinal atresia or a meconium-related condition. Volvulus occurs as a consequence of the massive bowel dilation, often before birth [8]. For this is the reason we did not consider differentiating acute from subacute SV. A palpable mass and notable abdominal distention are common signs at birth. Interestingly, and in line with other authors, we found that segmental volvuli had a higher risk of IF than acute midgut volvuli despite the relatively shorter intestinal resection of segmental volvuli [1,8]. The reason was that acute midgut volvuli had much more impact on mortality: those newborns were hemodynamically unstable and had an OR of dying of 19.3. Thus, there were fewer patients capable of developing IF. Ultimately, all the patients with volvulus in our series who developed IF and survived were weaned off TPN and achieved full enteral feeding, which was expectable given the length of resected intestine (median = 21 cm). According to the logistic analysis, prematurity and low birth weight were two major risk factors for all our outcome variables (death and IF). Because these parameters were strongly correlated in a multivariate analysis, we could not differentiate and provide the risk for each one separately. Considering that most patients with SV had a previous intestinal condition (atresia, meconium ileus) which evolved during pregnancy until the volvulus occurred, prematurity and low birth weight may have been, indeed, a consequence of that

intestinal problem. From a practical point of view, avoidance of a premature delivery is strongly recommended in a pregnancy where a progressive digestive problem is observed, as long as fetal well-being is not affected [2,8].

In the cases with massive intestinal length of obvious necrosis (during the first or second-look surgery) and severe compromise of the newborn (persistent pH <7, coagulopathy or need for aggressive hemodynamic support) the critical situation was clearly explained to the parents including the poor prognosis and quality of life. Among all possible options, withdrawing of life-sustaining medical treatment was also discussed with the parents. This fact could also justify the relatively high mortality and low rate of IF, as well as the fact that no newborn with volvulus has been referred for intestinal transplantation.

The main limitation of this study is its retrospective design and the long study period required to achieve a significant number of cases. However, medical care and clinical practice were comparable during the 20 years of the study period, and the many neonatologists and surgeons caring for the patients had more than a decade of expertise at the same institution. It is also interesting to note that the incidence and complication rate of volvulus were constant over the duration of the study period. We observed that the mortality rate between patients attended during the first decade was homogeneous compared to those of the second decade (results not shown).

Another limitation of the study is the lack of objective and comparable measures among patients. It was difficult to determine the time from the onset of symptoms until surgery. Additionally, we could not obtain all the patients' vital signs (heart and breathing rates, blood pressure, etc.). Also the medication, blood tests or other diagnostic tools that the patients received were difficult to compare. For all these reasons, we limited the study to broad binary categories such as the need for inotropic drugs, presence of abdominal distention or bilious vomiting. Intestinal resection was expressed in absolute numbers (centimeters of resection), without considering the remaining intestinal length (which quite often was not reported) or the gestational age.

The age at recruitment was arbitrarily limited to the first two months of life and not to the neonatal period. We did not perform any corrections regarding the gestational age. Only two patients who were operated at 60 days of life had a postmenstrual age beyond the neonatal period. Both had an acute MGV, and only one survived.

Our study has several strong points. First, it offers a very large, recent series of neonatal volvulus and classifies two types of volvulus, their nature, and complications. Additionally, we identified the risk factors for a poor outcome.

Conclusions:

Segmental and midgut volvuli are two different entities. Low birth weight and need for inotropic durgs are the major risk factors for death among neonates with an intestinal volvulus; on the other hand,

prematurity and SV are risk factors for IF.

Abbreviations:

MGV: midgut volvulus; SV: segmental volvulus; IF: intestinal failure; TPN: total parenteral nutrition; IQR: interquartile range; ROC: receiver operating characteristic; OR: odds ratio; CI: confidence interval.

Declarations:

Ethics approval and consent to participate: This article does not contain any studies with human participants or animals performed by any of the authors. Our hospital Ethics Committee approved this study (reference code: PIC-135-20).Consent to participate: not applicable.

Consent for publication: not aplicable.

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Figures

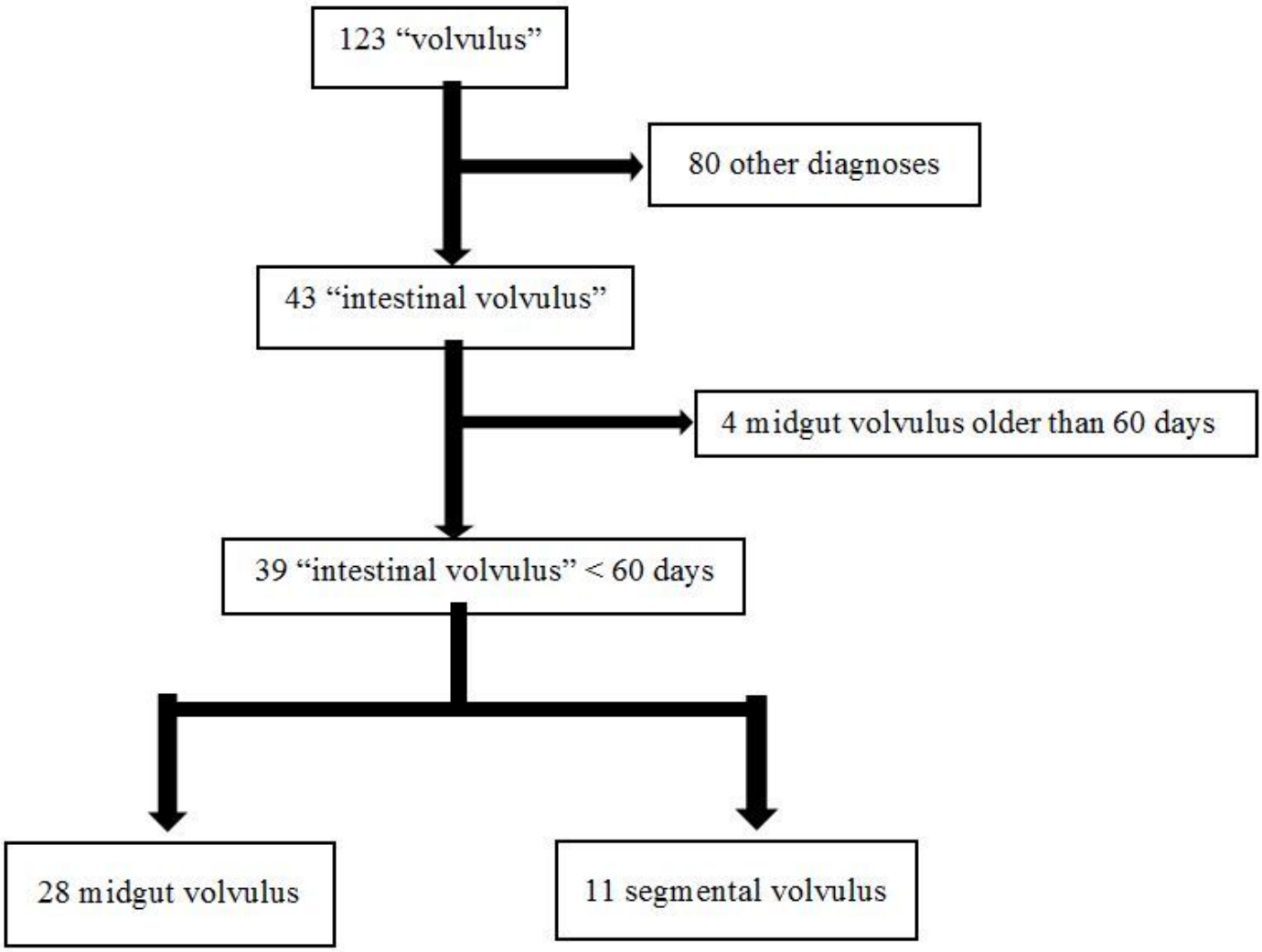

Figure 1

Flow diagram of patients.