

Factors associated with indications for surgery and the presence of intestinal necrosis in patients with hepatic portal venous gas: A multicenter retrospective cohort study

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Abstract

Background The presence of hepatic portal venous gas (HPVG) has been associated with intestinal necrosis and is an indication for surgical intervention. But some cases can be treated conservatively. This study aimed to examine the factors associated with the need for surgical intervention and the development of intestinal necrosis in patients with HPVG.

Methods This was a retrospective, multicenter and observational cohort study consisting of 166 patients who were diagnosed as having HPVG based on CT findings between April 2013 and March 2019. The patients were divided into two groups: surgery Required Group and Non-surgery Required Group. We reviewed medical records for clinical backgrounds, vital signs, laboratory data, CT findings, and compared the two groups using the Chi-square test and Student's t-test with p-values < 0.05 indicating statistical significance.

Results There were 72 patients in the Surgery Required Group and 94 in the Non-surgery Required Group. There were no statistically significant differences in age and sex between the two groups. Pulse rate (PR) (p = 0.004), C-reactive protein (CRP) (p = 0.012), lactate dehydrogenase (LDH) (p = 0.006) and abnormality of the white blood cell count (WBC) (p = 0.012) in the Surgery Required Group were significantly higher than those in the Non-surgery Required Group. The diameter of the superior mesenteric artery (SMA) and vein (SMV), and ratio of SMV/SMA were measured but no statistically significant difference was observed. Band-like pneumatosis (p < 0.001) and ring like pneumatosis(p < 0.001) were observed with a significantly higher frequency in the Surgery Required Group, but no significant difference was observed in bubble-like pneumatosis. Intrahepatic HPVG was significantly more frequent in the Non-surgery Required Group than surgery Required Group (p < 0.001), and extrahepatic HPVG (p < 0.001) was the opposite result. There was no significant difference of HPVG distribution in lobes.

Conclusions PR, CRP, LDH, abnormality of WBC, band-like pneumatosis, ring-like pneumatosis, and extrahepatic HPVG are the factors associated with an indication for surgery indication and intestinal necrosis in patients with HPVG.

Background

Hepatic portal venous gas (HPVG) was first described in 1955 in infants with necrotizing enterocolitis [1], and subsequently described in adults [2] in 1960.

The presence of HPVG has been associated with intestinal necrosis, a potentially fatal condition that requires surgical intervention [3].

Recently, however, the number of patients diagnosed with HPVG has been increasing with the widespread use of computed tomography (CT), and some reports have shown that the presence of HPVG does not always require surgery and suggested that benign HPVG also exists [4,5].

Proposed mechanisms for the development of HPVG include mucosal damage, increased intestinal pressure, and gas-forming bacteria. There are various underlying diseases and it is sometimes idiopathic [6].

One possible reason that some HPVG cases can be treated conservatively is that the cause is not necessarily irreversible intestinal necrosis. If intestinal ischemia is reversible or the cause of HPVG is not intestinal necrosis, it is highly likely that surgery will not be required, nevertheless it is often difficult to make the decision.

Since the most serious cause of HPVG is intestinal necrosis, it is important that the factors indicating surgery should reflect its presence.

This study aimed to examine the factors associated with the need for surgical intervention and the presence of intestinal necrosis in patients with HPVG.

Methods

This is a retrospective, multicenter and observational cohort study conducted in seven Japanese hospitals, Nagoya Tokushukai General Hospital, Aichi, Uji Tokushukai Medical Center, Kyoto, and in Osaka: Nozaki Tokushukai Hospital, Matsubara Tokushukai Hospital, Kishiwada Tokushukai Hospital, Yao Tokushukai General Hospital, and Suita Tokushukai Hospital.

The study consisted of 166 consecutive patients who were diagnosed as having HPVG based on CT findings at these hospitals between April 2013 and March 2019.

Patients with cardiopulmonary arrest just before CT, under 16 years old, or missing complete records about vital signs, laboratory data, CT findings, or outcomes were excluded.

The patients were divided into two groups, the Surgery Required Group and Non-surgery Required Group. The Surgery Required Group included patients that needed surgical intervention and had bowel resection performed, or patients who received conservative treatment but may have died due to intestinal necrosis within 28 days of diagnosis. The Non-surgery Required Group included patients who improved with conservative treatment only, or who underwent surgery but did not need bowel resection because there was no evidence of intestinal necrosis (Fig. 1).

We reviewed medical records for the following parameters to compare the two groups: clinical backgrounds, vital signs, laboratory data, and CT findings.

The CT findings included the diameter of the superior mesenteric artery (SMA) and vein (SMV), the patterns of pneumatosis intestinalis, and the HPVG distributions.

Using axial images, we measured the diameters of the SMA immediately inferior to the inferior pancreaticoduodenal artery bifurcation. At the same slice levels, we measured the diameters of the SMV.

Pneumatosis intestinalis (PI) (Fig. 2) was classified into two main patterns: bubble-like pneumatosis if it consisted only or mainly of isolated bubbles of air in the bowel wall, or band-like pneumatosis if it consisted of continuous bands of air in the affected bowel wall. Cases with both findings were classified as a more prominent pattern. Additionally, within the band-like pneumatosis, the presence of ring-like pneumatosis which consisted of continuous bands of air around the entire bowel wall, was evaluated (Fig. 2).

HPVG distribution was classified as intrahepatic portal vein, extrahepatic portal vein, or SMV. Additionally, the intrahepatic portal vein was classified into hepatic right lobe, left lobe, or bilateral.

The CT findings were diagnosed by a surgeon or a radiologist.

The study was approved by institutional review board (approval number TGE01241-016)

All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a modified version of R commander (The R Foundation for Statistical Computing, Vienna, Austria) with a graphical user interface, designed to add statistical functions frequently used in biostatistics [7].

We compared the differences between the Surgery Required and the Non-surgery Required Group using the Chi-square test for categorical variables and Student's t-test for continuous variables with p-values < 0.05 indicating statistical significance.

Results

Out of a total of 166 patients with HPVG, 72 were classified into the Surgery Required Group and 94 were classified into the non-surgery Required Group. Clinical characteristics are shown in Table 1.

The mean age was 80.3 ± 11.5 years (range 33–108), and 76 patients were male (45.7%). There were no statistically significant differences of age or sex between the two groups.

Among the vital signs, the pulse rate (PR) of the patients in the Surgery Required Group was significantly higher than in the non-surgery Required Group ($p = 0.004$).

We measured the white blood cell count (WBC), hemoglobin (Hb), hematocrit (Ht), platelet (Plt), C-reactive protein (CRP), blood urea nitrogen (BUN), creatinine (Cr) and lactate dehydrogenase (LDH) and compared the groups. The CRP and LDH levels of the patients in the Surgery Required Group were significantly higher than those in the Non-surgery Required Group (CRP; $p = 0.012$, LDH; $p = 0.006$). No significant differences were observed between the two groups in the other measured values.

Furthermore, we compared the CT findings of the two groups (Table 2). The diameter of the SMA and SMV were measured and the SMV/SMA ratio was calculated but no statistically significant differences were observed.

The characteristics of PI were also compared between the two groups. Band and ring-like pneumatosis were observed with significantly higher frequency in the Surgery Required Group (band-like pneumatosis; $p < 0.001$, ring-like pneumatosis; $p < 0.001$), but no significant difference was observed in bubble-like pneumatosis. The distribution of HPVG was significantly different between the two groups. Intrahepatic HPVG was significantly more frequent in the Non-surgery Required Group ($p < 0.001$). Conversely, extrahepatic HPVG was significantly more frequent in the Surgery Required Group ($p < 0.001$). On the other hand, there was no significant difference between right and left lobes, or bilateral.

Discussion

Some studies have reported on the disease severity and mortality associated with HPVG [4,8,9], but there are few large studies of the surgical indications for HPVG.

Wayne et al [10] examined 88 patients with HPVG in a single institution and proposed an algorithm to classify the etiology into three groups based on a vascular disease score. To the best of our knowledge this study involves the largest number of patients investigated to determine the indications for surgery in cases of HPVG.

The overall mortality rate of our series was 36.1%, which is similar to the rates that have been reported recently in the literature, which range from 16.5% [9] to 57.5% [11].

In our study, only PR had a statistically significant difference among vital signs. Patients with irreversible intestinal necrosis requiring surgical intervention may be more severely ill than those with reversible intestinal ischemia and may have a higher pulse rate reflecting hypovolemia and infection. However, it is unclear why there was no significant difference in sBP or BT, therefore further study is needed.

Concerning laboratory data, CRP and LDH in the Surgery Required Group were significantly higher. Kanamaru et al [12] analyzed 12 patients with HPVG and reported that CRP is more important than WBC for surgical indication in HPVG. In our study, CRP was useful for surgical indication, but there was no significant difference in the WBC. However, when WBC was classified into abnormal values less than 4000 or more than 9000 and normal values, the Surgery Required Group had significantly more abnormal values ($p = 0.012$).

Since critically ill patients can have either a high or low WBC, that would explain why there was no significant difference in WBC between groups. Additionally, LDH was significantly higher in the Surgery Required Group in our study. Koami [13] et al. analyzed 33 patients with HPVG and reported that LDH is one of the independent risk factors for intestinal necrosis. The higher LDH levels may reflect enzymes deviating from the necrotic intestine.

It has been reported that the diameters of the SMV are significantly narrowed and become smaller than the SMA in intestinal ischemic diseases such as SMA thrombosis or non-occlusive mesenteric ischemia (NOMI) [14,15]. It is called the 'smaller SMV sign'.

However, in our study, there were no significant differences in the diameter of the SMA, SMV, or in the ratio of SMV/SMA. A smaller SMV sign suggests intestinal hypoperfusion and a decrease in blood flow to the SMA. Even if there is a difference compared to the non-ischemic group, it may be that there is no difference between the Surgery Required and the Non-surgery Required Group because the blood flow of the SMA decreases in both groups.

Wiesner [16] et al. examined 23 patients and classified PI as bubble-like pneumatosis and band-like pneumatosis and reported that band like pneumatosis had a worse prognosis. In our study, there was no significant difference for bubble-like pneumatosis but band-like pneumatosis was significantly higher in the Surgery Required Group. Furthermore, in some of the band-like pneumatosis images, air encircles the lumen like a ring, and we classified it as ring-like pneumatosis. This was observed with significantly higher frequency in the Surgery Required Group than the Non-surgery Required Group, and 85.1% of the patients with ring-like pneumatosis were in the Surgery Required Group. Mild ischemia often remains as bubble-like pneumatosis, but as the blood flow obstruction progresses, PI may progress to band like pneumatosis, then ring-like pneumatosis. Ring-like pneumatosis is strongly associated with requiring surgical intervention.

Muratsu [8] et al. reported that the quantity and distribution of HPVG was associated with intestinal necrosis, especially, the presence of gas in the extrahepatic portal vein because it indicates the presence of a large quantity of gas overall. Similarly, intrahepatic HPVG was significantly more frequent in the non-surgery Required Group, and extrahepatic HPVG was significantly more frequent in the Surgery Required Group in our study. On the other hand, there was no statistically significant difference in HPVG distribution in the liver. Of note is the fact that only one case showed HPVG limited to the right lobe; all other cases had gas in the left lobe or bilaterally. Shiotani [17] et al. reported that the distribution of HPVG shifts in the order of left lobe, anterior segment, and posterior segment as the amount of gas increases according to gravity, and our study showed a similar tendency.

There were statistically significant differences in the values of PR, LDH, and CRP, but they can be difficult to use in making decisions actually because the differences are small. Therefore, CT findings such as the patterns of PI and HPVG may be more useful for factors associated with indications for surgery.

This study has some limitations. First, this was a retrospective study. Second, the patients who received conservative treatment but may have died due to intestinal necrosis within 28 days of diagnosis were classified in the Surgery Required Group, but they did not actually confirm intestinal necrosis by surgery.

This study is one of the largest conducted and is a multicenter study, therefore it demonstrates new and significant findings related to the factors associated with surgical indication and intestinal necrosis in patients with HPVG.

Conclusions

We examined factors associated with indication for surgery and with the development of intestinal necrosis in patients with HPVG. This study revealed that PR, CRP, LDH, abnormality of WBC, band-like pneumatosis, ring-like pneumatosis, and both intrahepatic and extrahepatic HPVG are factors associated with an indication for surgery and intestinal necrosis in patients with HPVG.

Abbreviations

HPVG, hepatic portal venous gas; PR, Pulse Rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BT, body temperature; sBP, systolic blood pressure; BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; Hb, hemoglobin; Ht, hematocrit; LDH, lactate dehydrogenase; Plt, platelet; T-Bil, total bilirubin; WBC, white blood cell count; PI, pneumatosis intestinalis; SMA, superior mesenteric artery; SMV, superior mesenteric vein

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the Tokushukai Group Joint Ethics Review Committee (approval number TGE01241-016), and the need for informed consent was waived

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Not applicable

Authors' contributions

All authors selected the patients of hepatic portal venous gas at each institute, and RM analyzed the patient data. All authors read and approved the final manuscript.

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Not applicable

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Tables

Table 1. Comparison of clinical characteristics between the surgery Required and the non-surgery Required Group.

		Total HPVG (n=166)	Surgery required group (n=72)	Non surgery required group (n=94)	p-value
Patient characteristics					
age	years	80.3±11.5	80.4±13.3	80.4±10.0	0.961
sex	male	76(45.7)	34(47)	42(44)	0.756
Vital signs					
sBP	mmHg	112.5±27.6	109.3±31.3	115.0±24.3	0.187
PR	/min	92.5±23.7	98.5±24.0	87.9±22.6	0.004*
BT	°C	36.6±0.8	36.6±0.8	36.6±0.8	0.984
Laboratory data					
WBC	/μL	12582±7633	12719±7233	12477±7963	0.84
	4000/μL> or 9000/μL<	111(66.8)	56(77.8)	55(58.5)	0.012*
Hb	/μL	11.9±2.2	12.1±2.4	11.8±2.0	0.375
Ht	%	35.8±6.2	36.5±6.7	35.2±5.8	0.185
Plt	×10 ⁴ /μL	21.8±8.0	21.3±7.8	22.2±8.2	0.485
CRP	mg/dL	7±8.4	8.8±9.8	5.5±6.9	0.012*
LDH	U/L	302±191	347±169	267±200	0.006*
AST	U/L	58±135	73±136	47±135	0.222
ALT	U/L	33±49	38±54	28±44	0.216
T-Bil	mg/dL	0.9±1.40	1.12±1.97	0.73±0.69	0.079
BUN	mg/dL	35.4±22.0	37.8±22.1	33.5±21.9	0.211
Cr	mg/dL	1.7±1.51	1.81±1.58	1.62±1.46	0.429

*p-values significant at p<0.05

Data are shown as n(%) or mean±standard deviation(Student's t-test).

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BT, body temperature;

sBP, systolic blood pressure; BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; Hb, hemoglobin; HPVG, hepatic portal venous gas; Ht, hematocrit; LDH, lactate dehydrogenase; Plt, platelet; PR, pulse rate; T-Bil, total bilirubin; WBC, white blood cell count.

Table 2. Comparison of CT findings between the surgery Required and the non-surgery Required Group.

		Total HPVG (n=166)	Surgery required group (n=72)	Non surgery required group (n=94)	p-value
Blood vessel diameter					
SMA	mm	8.54 ± 1.82	8.32 ± 1.95	8.70 ± 1.70	0.183
SMV	mm	11.16 ± 2.73	10.90 ± 2.87	11.36 ± 2.62	0.279
SMV/SMA		1.33 ± 0.32	1.34 ± 0.35	1.32 ± 0.29	0.75
PI					
bubble like pneumatosis		30(18.0)	16(22.2)	14(14.9)	0.231
band like pneumatosis		62(37.3)	43(59.7)	19(20.2)	<0.001*
ring like pneumatosis		27(16.2)	23(31.9)	4(4.3)	<0.001*
HPVG					
intrahepatic		60(36.1)	11(15.3)	49(52.1)	<0.001*
extrahepatic		106(63.8)	61(84.7)	45(47.9)	<0.001*
right robe		1(0.6)	0(0)	1(1.1)	1
left robe		82(49.3)	33(45.8)	49(52.1)	0.438
bilateral robe		83(50.0)	39(54.2)	44(46.8)	0.434

*p-values significant at p<0.05

Data are shown as n(%) or mean ± standard deviation(Student's t-test).

Abbreviations : HPVG, hepatic portal venous gas ; PI , pneumatosis intestinalis ; SMA , superior mesenteric aretry ; SMV , superior mesenteric vein

Figures

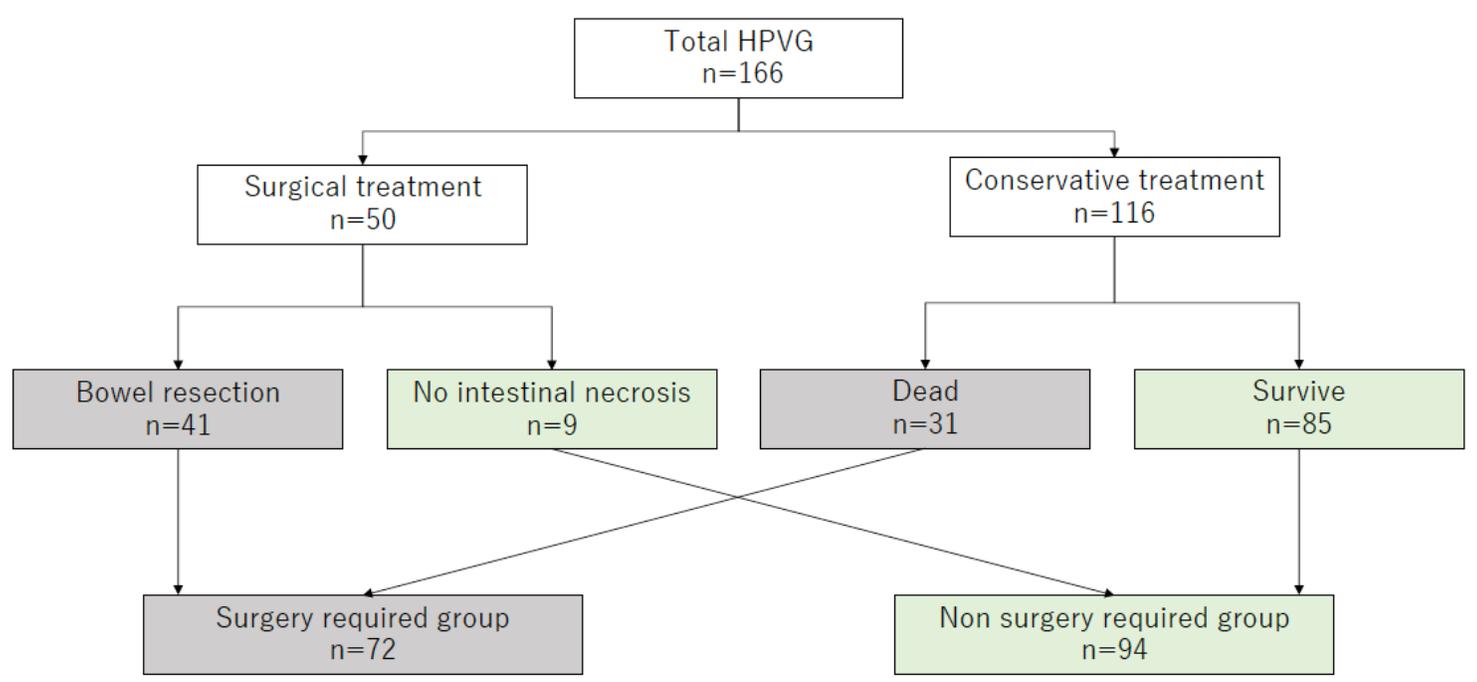


Figure 1

Classification of 166 patients with hepatic portal venous gas (HPVG). The patients who had no intestinal necrosis at surgery were included in the Non-surgery Required Group and the patients who had conservative treatment but died were included in the surgery Required Group.

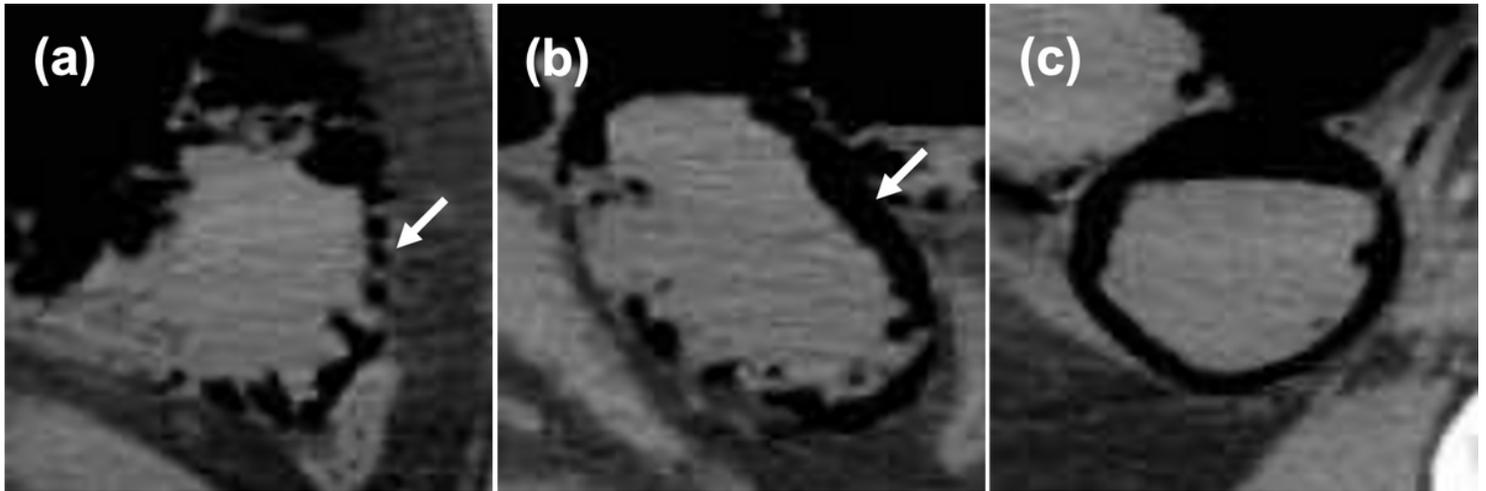


Figure 2

Classification of Pneumatosis Intestinalis. (a) bubble-like pneumatosis, (b) band-like pneumatosis, (c) ring-like pneumatosis