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Original research article

Evolution of splenomegaly in liver cirrhosis: Simulation using an electronic circuit

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ABSTRACT

Purpose: The evolution of splenomegaly in patients with liver cirrhosis remains largely unknown. In this study, we followed the changes in splenic volume and established the natural course of splenomegaly. We developed an electronic circuit that simulated splenoportal circulation and identified the underlying hemodynamic mechanisms.

Materials and methods: This retrospective observational study included 93 patients with cirrhosis. Splenic volumes were measured in imaging studies at 6-month intervals and normalized by the ratio of each patient's maximum volume during follow-up (%Vmax). An electronic simulation model was constructed using software and realized on a breadboard.

Results: Overall, the %Vmax increased from 0.77 ± 0.21 to a maximum of 1.00 ± 0.00 ($p < 0.001$) during a median follow-up of 23 (3–162) months and then decreased to 0.84 ± 0.18 ($p < 0.001$) during the next 9 (3–132) months. No interventional radiology procedure was performed to improve hepatic fibrosis and portal hypertension. The evolution of %Vmax showed single-peaked symmetry. An electronic simulation model showed that the upslope of the evolution curve was dependent on the increased intrahepatic vascular resistance and portal hypertension, whereas the downslope was dependent on the decreased portosystemic shunt (PSS) resistance.

Conclusions: Splenomegaly in cirrhotic patients aggravated over a period of 23 months and then regressed spontaneously to its initial volume. Electronic simulation of splenoportal circulation showed that splenic enlargement was due to the advancement of liver cirrhosis and portal hypertension, whereas its regression was due to the development of a PSS.

1. Introduction

Splenomegaly and hypersplenism are clinically important because of their roles in inducing pancytopenia, particularly the platelets [1]. In liver cirrhosis, splenomegaly is not only an indicator of advanced disease and portal hypertension but also a serious complication to be considered in the treatment planning [2]. Although it has been suggested that liver cirrhosis causes splenomegaly through portal hypertension, the precise hemodynamic and pathophysiological mechanisms are yet to be elucidated [3]. It is relatively well-established that portal hypertension is due to periportal fibrosis and increased intrahepatic vascular resistance [4]. On the other hand, contradictory theories coexist as to the causal relationship between splenomegaly and portal hypertension, so-called forward and backward theories [5]. Also, no consistent correlation was found between the splenic volume and hepatic fibrosis [6]. Most studies performed so far have been cross-sectional which is weak in defining the cause and effect. Longitudinal studies are very limited, probably because the progression of liver cirrhosis is slow and long-term clinical observation is required [7]. Animal experiments are technically challenging [8,9]. A novel deductive study is mandatory to further investigate this issue.

The basal topology of splanchnic circulation is so complex that intuitive grasping is difficult. Essentially, the gastrointestinal tract and spleen are arranged in parallel in the pre-portal circulation. These, in turn, are connected in series to two post-portal pathways that are parallel to each other: the liver and the portosystemic shunt (PSS) [10,11]. In liver cirrhosis, splenomegaly can easily be seen as having the same hemodynamic mechanism as a PSS because they are thought to share the draining channel [5,12]. However, the spleen drains into the portal vein, whereas the PSS diverts blood from the portal vein to the inferior vena cava, bypassing the liver [11,13].

Both blood flow and electric current are flow systems and are expected to obey Ohm's law [4,14]. In a previous study, we simulated

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splanchnic circulation using an electronic circuit and investigated the pathophysiology of PSS [11]. Electronic simulations have the advantage of simplifying the topological complexity using circuit theory and shortening the observation time. In the first part of this study, we examined the changes in splenic volume in patients with liver cirrhosis through a longitudinal study. We adopted a ratio rather than absolute volumetry for intrapersonal and interpersonal comparisons. This normalization process enabled us to compensate for individual variations in splenic volume and in the follow-up period. In the second part, we developed an electronic model of the intraabdominal circulation, mainly focused on the splenoportal axis. The model was constructed on a software platform and realized on a breadboard. We simulated the splenoportal circulation and investigated hemodynamic mechanisms underlying the evolution of splenomegaly observed in the clinical study. The causal relationships between liver cirrhosis, portal hypertension, splenomegaly, and PSS were deduced.

2. Materials and methods

2.1. Patients and data collection

From January 2017 to December 2017, 117 consecutive patients diagnosed with liver cirrhosis were admitted to Inha University Hospital, Incheon, Republic of Korea. Among them, 24 (20.5 %) patients were excluded: no prior or follow-up imaging studies (n = 13, 11.1 %); harbouring hepatocellular carcinoma beyond the Milan criteria (n = 6, 5.1 %); concomitant abdominal malignancy (n = 3, 2.6 %); secondary biliary cirrhosis (n = 1, 0.9 %); or history of endoscopic variceal ligation (n = 1, 0.9 %). No included patient had portal vein thrombosis. The medical records of the remaining 93 patients were reviewed retrospectively and relevant data were collected. Splenic volumes were measured using imaging studies (abdominal computed tomography or magnetic resonance imaging) at 6-month intervals from the first examination until the last follow-up or December 2019. When imaging data were not available on the exact date, those taken within 3 months were used instead. PSS was defined as the presence of engorged collateral vessels [15]. No patient underwent interventional shunt procedures or operations. Non-selective beta-adrenergic blockers were given at the attending physician's discretion, according to the Korean Association for the Study of the Liver (KASL) clinical practice guidelines [16].

2.2. Measurement of splenic volume

The width and thickness of the spleen were measured in the axial view and the length was measured in the coronal view. Images with the largest dimensions were selected. Assuming that the spleen is a half-ellipsoid, the splenic volume can be approximated using this formula (1):

$$\text{Splenic volume} = \frac{4}{3}\pi\left(\frac{\text{width}}{2}\times\text{thickness}\times\frac{\text{length}}{2}\right)\times\frac{1}{2}\left(\text{cm}^3\right)$$

To compensate for individual variations and measurement errors, the splenic volume of each patient was normalized by a ratio to the maximum splenic volume (%Vmax) during follow-up using this formula (2):

$$\%\text{Vmax} = \frac{\text{Splenic volume measured at a given time}}{\text{Maximum splenic volume during the follow}-\text{up}}$$

2.3. Study design

A cross-sectional study was performed to analyse the clinical factors associated with splenic volume. A longitudinal study was performed to analyse the evolution of splenomegaly. The serial values of %Vmax of every patient were matched to a single time point when the splenic volume was at its maximum (%Vmax = 1.00). The mean %Vmax values to and from the maximum date were plotted against time to obtain a splenomegaly evolution curve. Detailed data processing for 5 imaginary patients is exemplified in the Supplementary Tables S1–3 and Supplementary Fig. S1.

2.4. Development of an electronic simulation model of the splenoportal circulation

The splanchnic circulation can be schematically represented by an electronic circuit, as shown in Fig. 1A. According to circuit theory, any number of resistors can be replaced with a single equivalent resistor irrespective of the connection modes (in series or parallel). Thus, the circuit shown in Fig. 1A can be further simplified as shown in Fig. 1B, showing only the components of interest. Liver cirrhosis was represented by a variable resistor (VR) to simulate an increase in the intrahepatic vascular resistance. The splenic volume was simulated by the splenic sinusoidal pressure under the assumption that the splenic volume would be determined at the equilibrium between the internal pressure and tissue elasticity.

The parameters of Ohm's law in hydraulic and electronic systems are flow rate, pressure, and resistance (flow = pressure/resistance). Each parameter was converted using the following conversion factors and the dimensions were determined arbitrarily, considering practicality when realized on a breadboard.

- Flow rate: 1 L/min = 0.001 ampere (A) = 1 miliampere (mA)
- Pressure: 1 mmHg = 0.1 volt (V)
- Resistance = pressure / flow rate: 1 (mmHg) / 1 (L/min) = 0.1 (V) / 1 (mA) = 100 ohm (Ω) = 0.1 kiloohm (kΩ)

2.5. Construction of an electronic circuit using software

The electronic simulation circuit was constructed using Simulink® (MATLAB® Release 2020a. Natick, MA, USA: The MathWorks Inc.) (Fig. 2). The naming rule for an element is as follows: voltage drop across an element, V_element; current through, I_element; and resistance, R_element. The resistance can be calculated once the voltage drop and current are known, which can be obtained from reference values reported in the literature. The resistances were determined individually and the final values are shown in Fig. 2. A semiconductor (bipolar junction transistor, BJT) was required to simulate the conditional adaptation of the PSS. The detailed calculation of the resistors and choice of semiconductors are presented in the Supplementary Material (Section 2. Determination of resistor values and semiconductors). When executed, R_liver_cirrhosis was designed to increase from 0 Ω to 20 kΩ in 1 s to simulate the progression of liver cirrhosis (Fig. 3A), and the splenic sinusoidal pressure (V_sinusoid), portal pressure (V_PV), and PSS flow (I_PSS_cirrhosis) were recorded on the monitor.

2.6. Construction of real component circuit on a breadboard

The electronic circuit shown in Fig. 2 was constructed on a breadboard to see if it actually works (Fig. 4A). Components with approximate values readily available on our workbench were selected. To visualize the pressure and current changes, the voltage (V_sinusoid) and current (I_PSS_cirrhosis) sensors were replaced with red and blue light-emitting diodes (LEDs), respectively. In addition, resistors were adjusted or omitted to accentuate the LED brightness. The final values of each component are shown in Fig. 4A. The brightness of both LEDs was observed while the resistance of R_liver_cirrhosis increased from 0 to 50 kΩ to simulate the progression of liver cirrhosis.

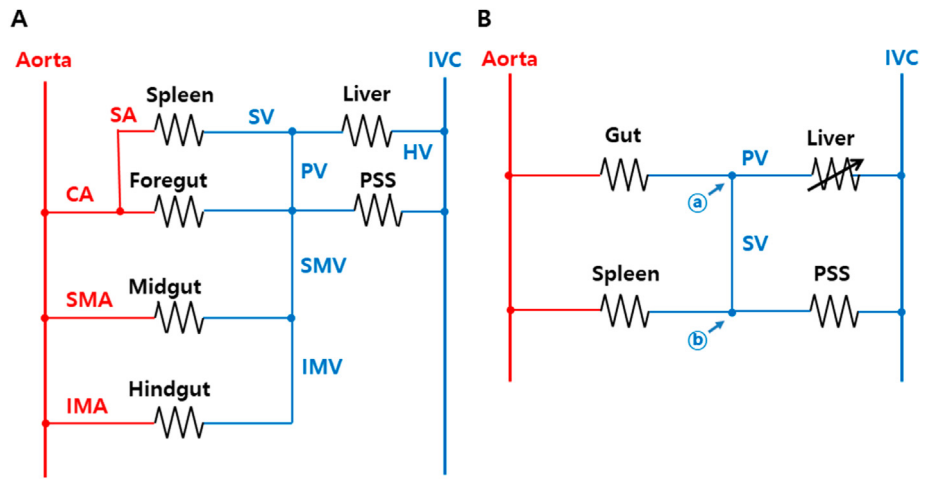

Fig. 1. Schematic diagram of splanchnic vascular connections using electronic circuit symbols. (A) The spatial relations and resistance values are ignored. (B) Simplified basic configuration. The liver is replaced by a variable resistor to simulate the increasing intrahepatic vascular resistance in liver cirrhosis. Splenic venous resistance (R_SV) that provides a potential difference between points ⓐ and ⓑ is not shown (Wheatstone bridge).

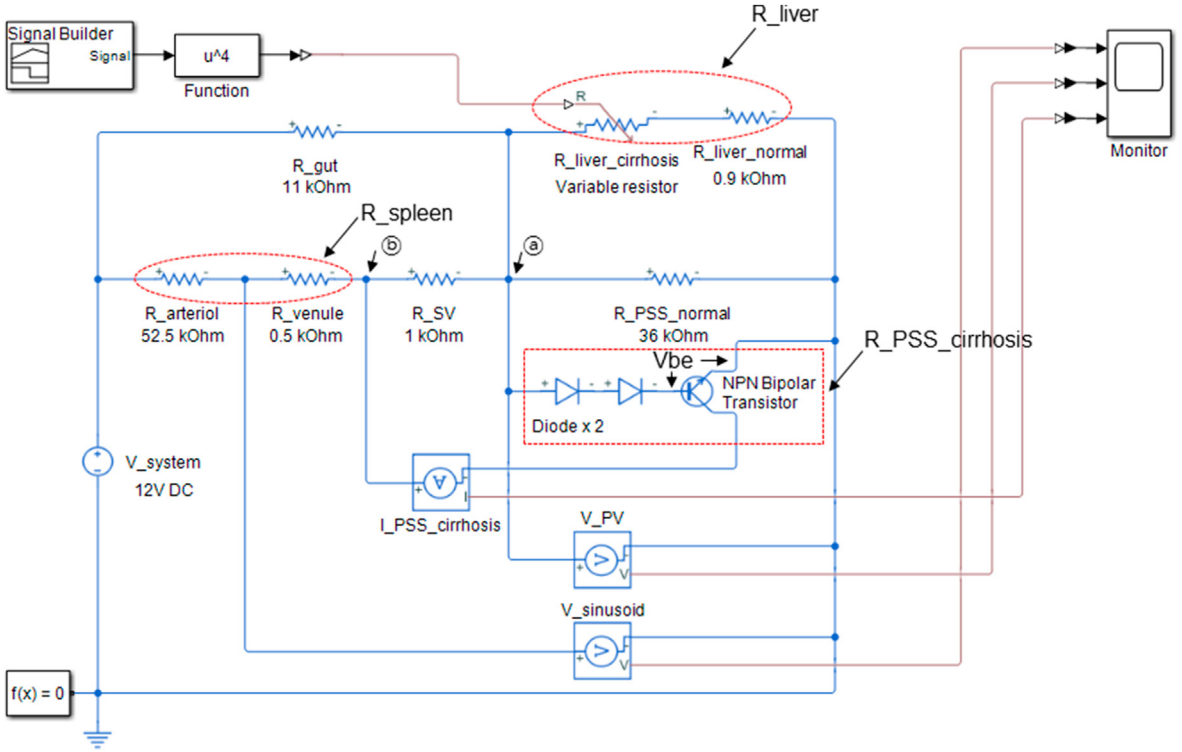

Fig. 2. The electronic circuit diagram of splenoportal circulation shown in Fig. 1B constructed using Simulink®. Points ⓐ and ⓑ correspond to those shown in Fig. 1B.

2.7. Statistical analysis

Categorical variables were presented as number (%) and numerical variables were presented as mean ± standard deviation (SD) or median (range), where appropriate. Data normality was tested using the Kolmogorov-Smirnov test. In the cross-sectional study, categorical variables were analysed using the Mann-Whitney *U* test or Kruskal-Wallis test, and numerical variables were analysed using Spearman's correlation analysis. In the longitudinal study, paired samples were tested using the Wilcoxon signed-rank test. The agreement between the two datasets was tested using intraclass correlation coefficient (ICC) estimates [17]. Missing data were handled by listwise deletion. All analyses were performed using IBM SPSS Statistics for Windows, Version 19.0 (IBM Corp., Armonk, NY, USA), and p-values <0.05 were considered statistically significant.

2.8. Ethical approval

The study protocol was approved by the Inha University Hospital Institutional Review Board, Incheon, Republic of Korea (approval no. 2022-03-015). This study was conducted according to the ethical principles of the 1964 Declaration of Helsinki with its later amendments, and written informed consent was obtained from all participants.

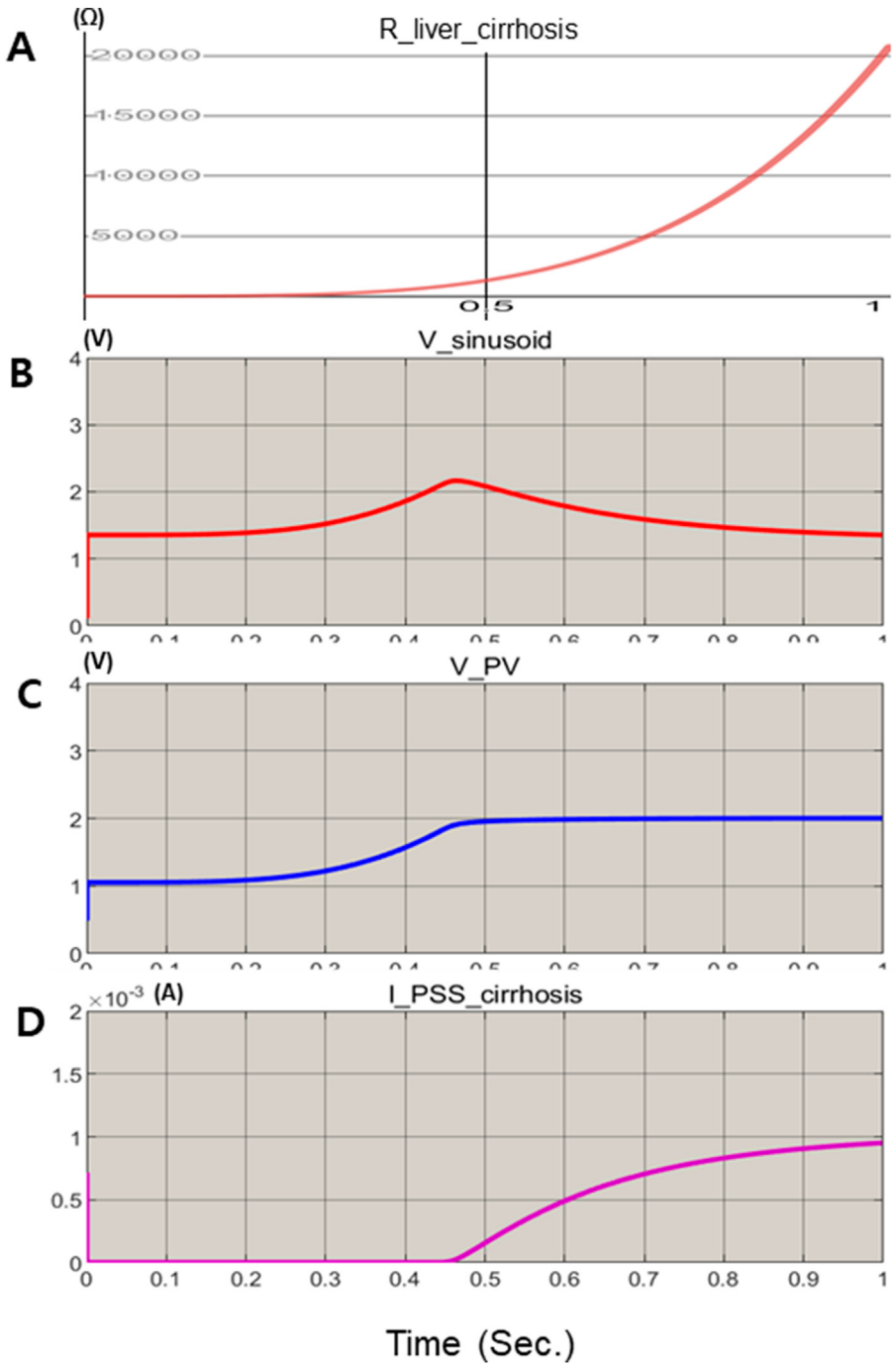

Fig. 3. Tracings of the Signal Builder and Monitors after running the circuit shown in Fig. 2. (A) Signal of R_liver_cirrhosis representing intrahepatic vascular resistance. (B) V_sinusoid representing splenic sinusoidal pressure simulating the splenic volume. (C) V_PV representing portal pressure. (D) I_PSS_cirrhosis representing portosystemic shunt flow.

3. Results

3.1. Demographic data and factor analysis

Of the 93 enrolled patients, 64 (68.8 %) were male and 29 (31.2 %) were female, with a male-to-female ratio of 2.2:1. The median age of all the patients was 61 (25–84) years. Cross-sectional factor analyses at the time of enrolment are summarized in Table 1. The splenic volume did not differ depending on sex, height, body mass index, or cause of liver cirrhosis. Antiviral medications were administered to 96.0 % (24 out of 25) of hepatitis B patients, whereas among hepatitis C patients none received antiviral treatment. Neither medication nor duration of antiviral therapy was related to splenic volume. We observed a weakly negative but statistically significant correlation between patient age and splenic volume ($\rho = -0.381$, $p < 0.001$). Additionally, there were weakly positive yet statistically significant correlations observed between weight, Child-Pugh score, model for end-stage liver disease score, and splenic volume ($\rho = 0.355$, $p < 0.001$; $\rho = 0.294$, $p = 0.004$; $\rho = 0.258$, $p = 0.012$, respectively). Patients with a PSS had significantly larger spleens compared to those without PSS (402.6 ± 202.5 vs. 198.2 ± 103.4, $p < 0.001$). However, we found no correlation between transient elastographic liver stiffness and splenic volume.

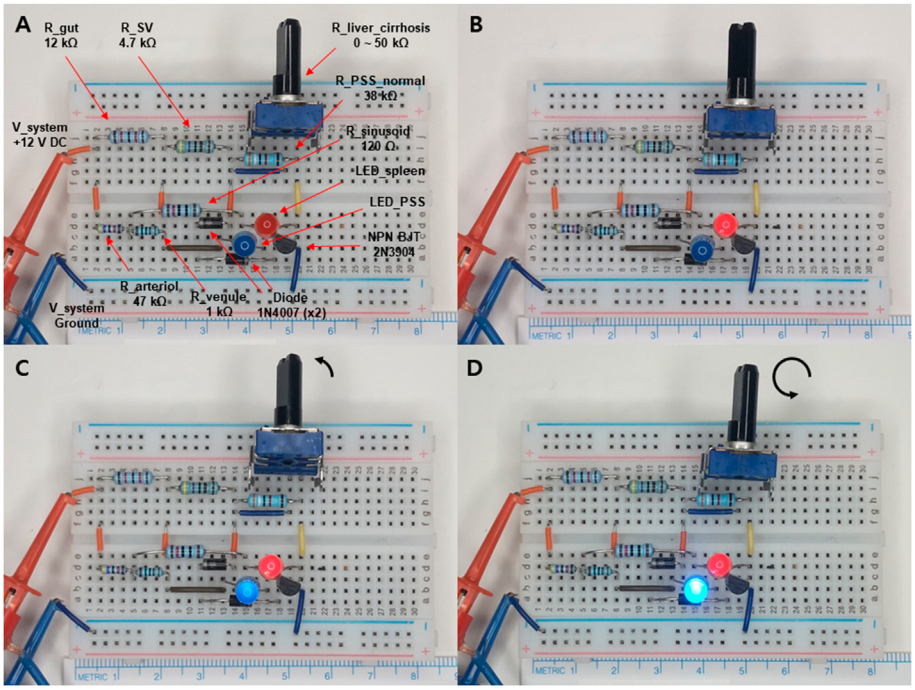

Fig. 4. The construction of a real circuit shown in Fig. 3 on a breadboard. (A) No voltage source is connected. (B) A 12 V DC source is connected with R_liver_cirrhosis set to 0 Ω, representing normal condition. LED_spleen is on and LED_PSS is off, representing the splenic volume with no PSS flow. (C) As R_liver_cirrhosis increases, LED_spleen glows brighter and LED_PSS is turned on, representing an increase in the splenic volume and the PSS starts to flow. (D) As R_liver_cirrhosis increases further, LED_spleen becomes dimmer while LED_PSS is fully on, representing the spontaneous regression of splenomegaly and full-blown PSS. Note that the change in the LED_spleen brightness is somewhat hard to recognize in a photograph.

Table 1
Patient characteristics and factor analyses for splenic volume.

Patients (N = 93)		Splenic volume (cm^3)	p-value
Overall		347.6 ± 202.3	
Age (years)	61 (25–84)		<0.001, ρ = −0.381
Sex			0.400
Male	64 (68.8)	361.9 ± 211.0	
Female	29 (31.2)	316.1 ± 181.3	
Height (cm)	162.7 ± 11.3		0.051, ρ = 0.203
Weight (kg)	66.4 ± 13.3		<0.001, ρ = 0.355
Body mass index	25.3 ± 7.0		0.076, ρ = 0.185
Causes of liver cirrhosis (No. %)			0.270
Alcoholic	45 (48.4)	341.0 ± 195.3	
Viral hepatitis B	25 (26.9)	406.6 ± 245.3	
Viral hepatitis C	13 (14.0)	387.3 ± 224.9	
Others	10 (10.8)	241.1 ± 123.0	
Antiviral therapy			0.650
Yes	24 (63.2)	388.8 ± 233.4	
Hepatitis B	24 (100.0)	388.8 ± 233.4	
Hepatitis C	0 (0.0)		
No	14 (36.8)	419.2 ± 246.9	
Hepatitis B	1 (7.1)	834.1	
Hepatitis C	13 (92.9)	387.3 ± 224.9	
Duration of antiviral therapy (months)	87 (3–202)		0.565, ρ = −0.124
Child-Pugh score	6.7 ± 1.9		0.004, ρ = 0.294
MELD score	12.7 ± 6.7		0.012, ρ = 0.258
Presence of PSS			<0.001
Yes	68 (73.1)	402.6 ± 202.5	
No	25 (26.9)	198.2 ± 103.4	
Transient elastography (n = 20, kPa)	30.8 ± 23.2	448.0 ± 272.8	0.214, ρ = 0.291

Values are presented as number (%), median (range), or mean ± standard deviation.
Abbreviations: PSS: portosystemic shunt; MELD: model for end-stage liver disease.

3.2. Evolution of splenomegaly

Overall, the splenic volume increased from 343.4 ± 209.5 cm^3 (%Vmax, 0.77 ± 0.21) to a maximum of 446.0 ± 257.6 cm^3 (%Vmax, 1.00 ± 0.00, $p < 0.001$) during a follow-up period of 23 (3–162) months, and then decreased to 375.4 ± 240.0 cm^3 (%Vmax, 0.84 ± 0.18, $p < 0.001$) during the next 9 (3–132) months. The splenomegaly evolution curve showed single-peaked symmetry (Fig. 5A). When the values of %Vmax before the peak (Pre-peak %Vmax) were reversed, a statistically significant good agreement with the values after the peak (Post-peak %Vmax) was observed (ICC (2,1) = 0.805, 95 % confidence interval = 0.538–0.916, $p < 0.001$) (Fig. 5B).

3.3. Electronic simulation of splenoportal circulation in liver cirrhosis using software

V_sinusoid, V_PV, and I_PSS_cirrhosis tracings are shown in Fig. 3B, 3C, and 3D, respectively. At the beginning of the tracing, V_sinusoid was 1.36 V (splenic sinusoidal pressure, 13.6 mmHg), V_PV was 1.05 V (portal pressure, 10.5 mmHg), and I_PSS_cirrhosis was 0.00 mA (no PSS flow). As the Signal Builder signal (R_liver_cirrhosis) increased (representing the progression of cirrhosis), V_sinusoid increased until it reached its maximum of 2.16 V (= 21.6 mmHg), when the PSS started to flow and V_PV approached 1.90 V (= 19.0 mmHg). From this point onward, V_sinusoid started to decrease as I_PSS_cirrhosis increased despite the increasing R_liver_cirrhosis. Meanwhile, V_PV reached a plateau and maintained the pressure for the rest of the cycle. At the end of the running time of 1 s when R_liver_cirrhosis reached its maximum of 20 kΩ, the V_sinusoid was 1.36 V, V_PV was 2.00 V, and the I_PSS_cirrhosis was 0.94 mA.

3.4. Simulation using real components

Changes in the brightness of the LEDs are shown in Fig. 4. In Fig. 4A, no voltage source was applied, and both the LEDs were turned off. When the electronic circuit was connected to a 12 V direct current (DC) voltage source and R_liver_cirrhosis was set to 0 Ω, we observed that the red LED

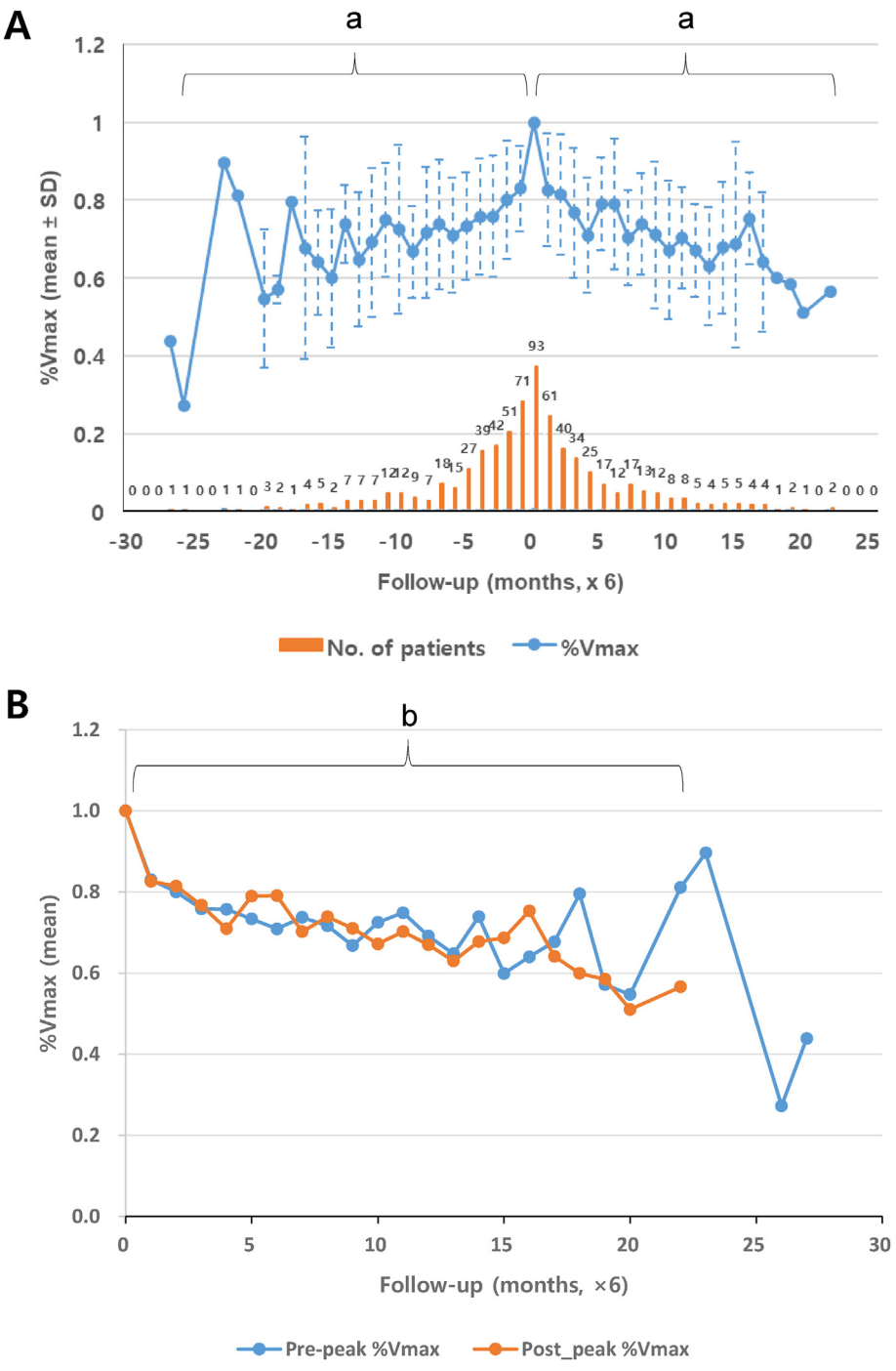

Fig. 5. Splenomegaly evolution curve obtained from the normalization of splenic volume to its maximum value (%Vmax). (A) All patients' evolution curves were matched centred on the day of the maximum splenic volume. The splenic volume increased and then decreased spontaneously. Note that %Vmax fluctuated further as the available data became fewer (bar chart). (B) When rearranged from the maximum day, the ascending (Pre-peak %Vmax) and the descending (Post-peak %Vmax) limbs of the evolution curve showed a good match. [a] $p < 0.001$, Wilcoxon signed-rank test; [b] $p < 0.001$, intraclass correlation coefficient (2,1) = 0.805, 95 % confidence interval = 0.538–0.916.

was lit and the blue LED remained turned off (Fig. 4B). The brightness of the red LED represented splenic volume in the normal condition. As the resistance of R_liver_cirrhosis increased, the brightness of the red LED increased, suggesting an increase in the splenic volume. At one point along with the increasing R_liver_cirrhosis, the blue LED started to glow and the red LED reached its maximum intensity (Fig. 4C). From that point onward, the intensity of the blue LED increased whereas that of the red LED decreased as R_liver_cirrhosis continued to increase, representing clinically the full-blown PSS and decreasing splenic volume despite the progression of liver cirrhosis (Fig. 4D).

4. Discussion

The current cross-sectional study showed that the degree of functional impairment of the liver and the presence of PSS were related to splenic volume, whereas the degree of liver stiffness was not. These inconsistencies between liver cirrhosis and splenomegaly were similar to other studies [5,6]. To further investigate this issue, we examined the evolution of splenic volume with the progression of liver cirrhosis. Considering that liver cirrhosis is a progressive disease, splenic volume is expected to increase over time and the evolution curve to be somewhat

hyperbolic or sigmoidal [18]. Interestingly, however, the current longitudinal study showed that the splenic volume increased to a maximum and then decreased to its original volume at almost the same rate. It was puzzling how the spleen enlarged and then regressed spontaneously in the face of ever-progressing liver cirrhosis.

The splenoportal axis consists of two pre-portal resistances connected in parallel, which in turn are connected in series to two post-portal resistances connected in parallel (Fig. 1B) [10,11,13]. From this configuration which is a pressure divider between the pre- and post-portal resistances, it is clear that there are two ways for portal pressure to increase: by decreasing the pre-portal resistance or by increasing the post-portal resistance. Because the pre-portal resistances are composed of the spleen and gut connected in parallel, a decrease in any of these resistances could increase the portal pressure. A clinical example of decreased pre-portal vascular resistance is an arteriovenous malformation of the gut or spleen that leads to portal hypertension and its complications [19,20]. None of the patients in the present study had any of these conditions. An increase in the post-portal resistance can come from increased intrahepatic hepatic vascular resistance or PSS resistance which are connected in parallel. As the PSS resistance is high in normal conditions, an increase in the hepatic vascular resistance could explain portal hypertension accompanying liver cirrhosis [4,14]. This is represented in the current study by the ascending limb of the splenomegaly evolution curve. As for the descending limb of the evolution curve, splenic volume can be decreased by an increase in the pre-portal resistance or a decrease in the post-portal resistance. A clinical example of increased pre-portal resistance is splenectomy which none of our patients underwent [21]. A decrease in the post-portal resistance could be due to a decrease in intrahepatic vascular or PSS resistance. Decreased intrahepatic vascular resistance can occur after liver transplantation or intrahepatic shunt procedures, none of which were applied to our patients [22,23]. Non-selective beta-blockers may decrease portal pressure [24]. We could not find a study directly analysing the effect of beta-blockers on splenomegaly, but it is improbable that these medications influenced the descending limb of the curve which was constructed using a ratio. Intrahepatic vascular resistance can also be decreased by the reversal of hepatic fibrosis [25]. Historically, liver cirrhosis has been considered an incessantly progressive and irreversible process [18]. However, recent reviews have suggested that hepatic fibrosis in patients with cirrhosis is potentially reversible after antiviral therapy [25,26]. The current cross-sectional analysis showed that antiviral therapy is unrelated to splenic volume. While abstinence from alcohol may improve overall survival in cases of alcohol-associated cirrhosis, there is currently no evidence to suggest that it can lead to the reversal of hepatic fibrosis [27]. Accordingly, we accepted the decrease in PSS resistance as a plausible explanation for the descending limb of the evolution curve and, hence, the spontaneous regression of splenomegaly.

To investigate the factors that determine splenic volume in patients with liver cirrhosis and portal hypertension, we developed an electronic simulation model that can be easily and safely manipulated within a short running time. In Fig. 2, V_system, R_gut, R_liver_normal, R_spleen, and R_PSS_normal are of fixed values. R_liver_cirrhosis is the independent variable that simulated increased intrahepatic vascular resistance in cirrhosis. The splenic venous resistance (R_SV) and R_PSS_cirrhosis are the contributing factors to the V_sinusoid, which is the dependent variable that represents splenic volume. The upslope of the V_sinusoid in Fig. 3B is dependent on R_liver_cirrhosis, indicating that the degree and rate of progression of liver cirrhosis and accompanying portal hypertension determine the ascending limb of the splenomegaly evolution curve. In contrast, the downslope is dependent on R_SV, which represents the vascular resistance of the channel connecting the portal vein to the spleen and PSS (Fig. 1B). The resistance of R_SV plays a pivotal role in providing a potential difference between the gut-liver axis and spleen-PSS axis (between points ⓐ and ⓑ in Fig. 1B), together of which constitute the configuration of a Wheatstone Bridge. Without it, the liver and PSS would function as single resistance. Of note, a PSS should be located on the splenic side of R_SV and the portal pressure (point ⓐ) should be higher than the splenic venous pressure (point ⓑ) for the direction of splenic venous flow to be reversed and the spleen decompressed through the PSS [28,29]. This hemodynamics defies the 'forward' theory of portal hypertension in liver cirrhosis. If R_spleen decreased first, the pressure at the point ⓑ would be higher than the point ⓐ and the splenic venous flow cannot be reversed. Finally, the inflexion point of the V_sinusoid is dependent on Vbe, which is an intrinsic characteristic of the BJT. The clinical implication is that the maximum size and regression of splenomegaly are dependent on the location and extent of the PSS [29]. The V_sinusoid tracings according to the experimental changes in R_SV or Vbe are presented in Supplementary Fig. S2. Meanwhile, V_PV reached a plateau and remained there, explaining why no correlation between splenic volume and portal pressure has been found [5,6]. Through the real circuit simulation, we hoped to show that the electronic simulation can be easily and safely performed on a workbench, dispensing the need for delicate and complicated clinical or animal experiments. To summarize in clinical terms, the portal pressure and splenic volume increase as liver cirrhosis progresses until the PSS channel is open, and subsequently regresses depending on the location and characteristics of the PSS.

4.1. *Limitations of the study*

This study has some limitations. Firstly, as a retrospective study, we could not obtain portal pressure data. We referred to previous studies in the literature and V_PV in the simulation circuit may be different from the real portal pressure measurements. However, it is unlikely that the portal pressure measurements would have altered our conclusions. Secondly, we interpreted the causal relationship between liver cirrhosis, portal hypertension, and splenomegaly solely by the electronic analogy of hemodynamics. Many cellular and humoral factors may be involved in these clinical manifestations [1,3]. Further investigations are warranted to fully understand the pathophysiological mechanisms underlying these vascular changes. Thirdly, we assumed that the splenic sinusoidal pressure represented the splenic volume. Although, logically, the splenic volume would be determined by the balance between splenic sinusoidal pressure and tissue elasticity, studies based on direct measurements would make it clearer [5]. Fourthly and finally, engorged collateral vessels do not necessarily indicate the reversed splenic venous flow, which is required for the spleen to be decompressed. Future studies on the characteristics of a PSS and its natural course is needed to confirm our hypothesis. Despite all these limitations, we believe that the electronic simulation is a valid and novel methodology and hope it is widely adopted in hemodynamic research.

5. Conclusions

The evolution of splenomegaly in patients with liver cirrhosis has a peak at one time during the natural course of the disease. Electronic simulation of the splenoportal axis showed that the increase in splenic volume is dependent on the progression of liver cirrhosis and portal hypertension, whereas the decrease is dependent on PSS development. Our simulation strategy offers a novel approach to modelling the evolution of splenomegaly in cirrhotic patients. While it provides a rapid and efficient means of analysis, it is important to acknowledge its limitations, including potential oversimplification of biological systems and reliance on input parameters. Recognizing these strengths and weaknesses can guide future research in refining electronic simulation techniques for biomedical applications, ultimately improving our understanding of disease progression and clinical interventions.

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The author contributions

Study Design: Shin-Young Park, Kyeong Deok Kim, Keon-Young Lee
Data Collection: Jae Cheol Jung, Keon-Young Lee
Statistical Analysis: Woo Young Shin
Data Interpretation: Woo Young Shin, Keon-Young Lee
Manuscript Preparation: Keon-Young Lee
Literature Search: Jae Cheol Jung, Woo Young Shin
Fund Collection: Keon-Young Lee

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data statement/Availability of data and material

The data that support the results of this study are available on request from the corresponding author.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors did not use any AI-assisted technology.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.advms.2024.08.001.

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