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Research article

Clinical characteristics and treatment outcomes of 68 patients with spontaneous iliac vein rupture: A case report and systematic review

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ABSTRACT

Objective: Spontaneous iliac vein rupture (SIVR) is a rare but life-threatening condition with limited understanding regarding its clinical presentation, pathogenesis, diagnosis, management, and risk factors for mortality. This study aims to address this gap by providing comprehensive insights into SIVR through personal case reports and a systematic review of previous cases.

Methods: We detail a case of right SIVR caused by inappropriate positioning of the stent in the inferior vena cava and systematically reviewed previous cases. Logistic regression analysis was used to identify risk factors for mortality.

Results: Our SIVR case was successfully managed with percutaneous mechanical thrombectomy and covered stent placement. In the systematic review, 68 patients were included in the analysis with an average age of 62.01 ± 13.25 years; 86.76% were female, 91.17% had left iliac vein rupture, 55.88% presented hemodynamic instability, 76.47% had lower abdomen or iliac fossa pain, 67.64% had deep venous thrombosis (DVT), and 32.35% had May–Thurner syndrome (MTS). The mortality rates of conservative treatment and open surgery were 2.94% and 17.65%, respectively. All 12 patients receiving endovascular treatment survived. The factors associated with a worse outcome were younger age (52.86 ± 12.96 years, OR: 1.085, 95% CI: 1.002–1.174) and SIVR patients without DVT (OR:10.111, 95% CI: 1.637–62.443).

Conclusion: This first systematic review on SIVR shows that SIVR should be highly suspected in elderly females who develop lower extremity DVT and concurrent lower abdominal pain, particularly those with a retroperitoneal mass and unstable hemodynamics. Thrombosis secondary to MTS may be the main cause of SIVR. Angiography and endovascular therapy should be prioritized for DVT patients with unexplained retroperitoneal hematoma. This study classifies SIVR into two types: iliac vein rupture alone and iliac vein rupture with DVT. These findings provide critical insights for clinicians to accurately diagnose and manage SIVR, thereby improving patient outcomes.

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1. Introduction

Spontaneous iliac vein rupture (SIVR) is a rare but lethal condition that mostly affects women and occurs in the left iliac vein, and it is often related to May–Thurner syndrome (MTS). In fact, only three case reports have been described in the right iliac vein [1–3]. Although the concomitant conditions of SIVR includes deep vein thrombosis (DVT) and thrombophlebitis, whether DVT is the cause or a complication of iliac vein rupture is unclear. SIVR is challenging to diagnose, as it presents with hypovolemic shock or syncope, making it difficult to provide an accurate medical history. Additionally, physical examination results may be normal, although patients may exhibit lower extremity swelling, tenderness, or sudden-onset lower abdominal pain. Abdominal ultrasound can identify retroperitoneal hematoma, but identifying the source of the bleeding is difficult, and bleeding may be misjudged as abdominal aortic aneurysm rupture. Although enhanced abdominal computed tomography (CT) may help considerably in diagnosis, exploratory laparotomy is needed to correctly diagnose most cases. Exploratory laparotomy for iliac vein ligation or repair and hematoma removal followed by anticoagulation has been the most common treatment in the past. The reported operative mortality and morbidity rates are as high as 16.7% and 50%, respectively [4]. The development of endovascular technology has led to the gradual application of percutaneous mechanical thrombectomy, vascular embolization and covered stent placement in the treatment of SIVR. However, whether these techniques reduce the mortality rate remains unclear.

Clinicians' limited understanding of this complex disease is due to its rarity, nonspecific symptoms and signs, unclear pathogenesis, and lack of standardized treatment protocols. These characteristics result in misdiagnosis and contribute to the high mortality and morbidity rates associated with the disease. In this study, we report one case of spontaneous rupture of the right external iliac vein caused by the inappropriate positioning of a venous stent. Additionally, we provide a retrospective analysis of 68 published cases of SIVR from 17 countries around the world to improve the understanding of this condition and promote better outcomes for SIVR patients.

1.1. Case presentation

A 71-year-old female visited the emergency department due to progressive swelling and pain in the left leg over 4 h. On arrival, her left leg showed skin cyanosis, mottling and marked swelling, and the popliteal and dorsalis pedis artery pulses were not palpable (Fig. 2A). Ultrasonography indicated thrombosis in the left iliac vein, femoropopliteal vein, anterior tibial vein and posterior tibial vein as well as obviously reduced blood flow in the left popliteal artery. She had a history of high blood pressure for 10 years that was controlled at 130–150/70-90 mmHg and no history of diabetes mellitus or coronary heart disease but had developed a cough in the last 3 months. Computed tomography pulmonary angiography indicated multiple emboli in branches of the bilateral pulmonary artery and multiple nodules in the lower lobe of the left lung, possibly suggesting lung cancer. Abdominal CT showed a low-density opacity in S5-6 of the liver, possibly suggesting liver cancer. Blood test results were as follows: D-dimer, 25.2 mg/L; hemoglobin (Hb), 89 g/L; and myoglobin, 1750 μg/L. The patient was diagnosed with phlegmasia cerulea dolens (PCD) of the left lower limb. The patient underwent local anesthesia, and the iliac and femoropopliteal venous thrombi were removed using a 10-F catheter (OPTEASE, Cordis, Fig. 2B-E) via popliteal vein access under the protection of a retrievable inferior vena cava (IVC) filter (IVCF, OPTEASE, Cordis). Complete occlusion was observed in the left common iliac vein, and three balloons (8 mm, 12 mm and 14 mm, Mustang, Boston Scientific) were then used to dilate the iliac vein in a stepwise manner (Fig. 2F). Two bare stents (14 mm × 90 mm and 12 mm × 90 mm, Wallstent, Boston Scientific) with an overlap of 20 mm were placed with the proximal end anchoring to the IVC and the distal end anchoring to the proximal inguinal ligament (Fig. 2G). The stent reached the contralateral wall of the IVC, obstructing the flow of the right iliac vein into the IVC and resulting in collateral development (Fig. 2H and I). Angiography showed iliofemoral blood flow recovery without residual thrombi (Fig. 2J). The arterial pulses of the lower extremities recovered, and the skin cyanosis and mottling disappeared immediately (Fig. 2K). After surgery, rivaroxaban (15 mg) was orally administered twice daily for 3 weeks of anticoagulation, followed by 20 mg once daily. The patient was eventually diagnosed with liver cancer with lung metastasis but refused further treatment. The IVCF was retrieved after 14 days.

Unfortunately, after 65 days, the patient was admitted to the emergency department again with a complaint of a 2-h history of swelling and pain in the right lower limb. Her blood pressure was 86/45 mmHg, and her heart rate was 118 beats/min. On examination, the patient presented with no urine, pale palpebral conjunctivae, obvious swelling with tension in the right leg, skin cyanosis and mottling from the right calf to the middle thigh, obvious skin temperature reduction and hypoesthesia of the right foot, weakening of the right popliteal artery pulses and a nonpalpable right dorsalis pedis artery and posterior tibial artery (Fig. 3A). Ultrasonography revealed thrombosis in the right iliofemoral veins, a hypoechoic area with a size of 15 cm × 18 cm was detected in front of the right iliopsoas muscle, and no blood flow was observed in the right anterior tibial and posterior tibial arteries. Blood test results were as follows: D-dimer, 17.2 mg/L; Hb, 65 g/L; and myoglobin, 1750 μg/L. The patient had no history of trauma but had an intractable cough. The examination results were consistent with PCD of the right lower limb. An emergency percutaneous mechanical thrombectomy was performed. When an IVCF was placed through the left femoral vein access, a large thrombus was found in the lower segment of the IVC (Fig. 3B). Thrombosis in the right iliofemoral veins and active venous extravasation in the right external iliac vein were found by venography, which consisted of iliac vein rupture signs (Fig. 3C, Supplemental video 1). A covered stent (10 mm × 60 mm, Fluency, Bard) was immediately placed into the external iliac vein (Fig. 3D), and then a 10-F catheter (OPTEASE, Cordis) was then used to quickly remove thrombi from the iliofemoral veins (Fig. 3E and F). Next, a bare stent (14 mm × 80 mm, Smart, Cordis) was placed at the proximal end of the covered stent. No venous extravasation was observed after stent placement (Supplemental video 2). The arterial pulses of the lower extremities recovered, and the skin cyanosis and mottling disappeared immediately. The patient was

transfused with 400 mL of red blood cell suspension and 2000 mL of crystalloid solution during surgery and received anticoagulation therapy with rivaroxaban thereafter. After 36 h, the affected limb returned to normal (Fig. 3G). The IVCF was retrieved 18 days after surgery. At 37 days after treatment, abdominal contrast-enhanced CT indicated absorption of a hematoma around the right iliac vein and patency of the bilateral iliac vein stents (Fig. 3H and I). The patient was free of postthrombotic syndrome, thrombotic recurrence and hemorrhagic events at the 3-month follow-up. The patient died 5 months after discharge due to cancer with concurrent multiple organ failure.

Informed consent was obtained from the patient for the publication of this case report and any accompanying images.

2. Methods

2.1. Search strategy

The purpose of the literature review was to retrospectively analyze the clinical characteristics, diagnosis, and treatment of SIVR and the impact of these factors on the prognosis of patients. A literature search in MEDLINE, EMBASE, China National Knowledge Infrastructure (CNKI), National Library Reference Alliance (NLRA), and Google Scholar was performed using "spontaneous/idiopathic iliac vein rupture" and "spontaneous/idiopathic retroperitoneal hematoma" as keywords. Additional references were used to expand the search, which was not limited to English articles but also included original peer-reviewed published articles in Chinese, Spanish, Danish, German, Portuguese, French and Japanese due to the small number of cases. We contacted authors for additional data or clarification when needed.

2.2. Eligibility criteria

Articles were included if they met the following criteria: (1) case report or case series of one or more patients presenting with SIVR in any language and (2) letters to the editor related to SIVR. The following exclusion criteria were applied: (1) articles without full text, (2) autopsy reports without detailed clinical information, (3) reports on retroperitoneal hematoma not caused by iliac vein rupture, (4) reports regarding ovarian vein or iliac vein collateral rupture, and (5) articles regarding the rupture of spontaneous iliac arteriovenous fistula.

2.3. Selection of the reports

Two investigators (L.Z. and R.W.) independently identified potential articles by using the defined inclusion and exclusion criteria. Disagreements between the reviewers were resolved by consensus or through discussion with a third reviewer (Z.Y.). The kappa statistic was used to assess the agreement between the investigators. A kappa value between 0.6 and 0.7 indicates good agreement, and a value of $\geq$0.75 indicates excellent agreement [5].

2.4. Data extraction

Two investigators (L.Z. and R.W.) independently extracted data by using a standardized data extraction form. Disagreements were resolved by consensus or through discussion with a third reviewer (Z.Y.). The following data were extracted: year and country of publication, study type and language, sex of the patient, hemoglobin, hematocrit, blood pressure, predisposing factors, rupture site, concomitant vascular disease (MTS and DVT), main clinical manifestations (hemodynamic state, abdominal or iliac fossa mass and pain and lower extremity swelling), confirmed methods, treatment, and clinical outcomes. A list of the included studies can be found in Supplemental Table 1.

2.5. Data synthesis

Continuous variables are reported as the mean $\pm$ SD. Categorical data are reported as counts and proportions. To identify the relationship between clinical factors and patient prognosis, univariate comparisons between groups were based on an unpaired Student's *t*-test for continuous variables and chi-square or Fisher's exact tests for categorical variables. In the multivariate analysis, factors with statistical significance in univariate analysis were included for logistic regression analysis. After ensuring no collinearity among the independent variables, odds ratios (ORs) with 95% confidence intervals (CIs) were used to analyze the strength of the associations between independent variables and dependent variables. A two-sided P value < 0.05 was considered statistically significant. Analyses were performed using SPSS Statistics for Mac V.25.0 (IBM SPSS Statistics; Chicago, IL, USA).

3. Results

Our search strategy yielded 91 articles, of which 87 were subjected to title and abstract screening after the removal of duplicates. After a full-text review, 82 articles were considered for inclusion. Of these, 20 articles were excluded, resulting in the inclusion of 63 case reports comprising 68 patients, including the current case, from 1961 to 2022 [1–3,6–64]. The case reports were published in various languages, including English (n = 46), Spanish (n = 6), Japanese (n = 4), Chinese (n = 3), Portuguese (n = 1), Danish (n = 1), French (n = 1), and German (n = 1) (Table 1). Fig. 1 shows the flow diagram of the study. The reviewers demonstrated good agreement, with a kappa value of 0.7.

Table 1
Distribution characteristics of the previous literature included in this study.

Countries	No. of articles	No. of patients	Languages
Belgium	1	1	English
Brazil	1	1	Portuguese
Canada	1	1	English
China	8	10	Three articles in Chinese, five articles in English
Denmark	1	1	Danish
France	5	5	Four articles in English, one article in French
Germany	1	1	German
India	1	1	English
Italy	1	2	English
Japan	10	10	Four articles in Japanese, six articles in English
Korea	5	5	English
Poland	1	1	English
Spain	6	6	Spanish
Sweden	2	3	English
Turkey	1	1	English
UK	6	6	English
USA	11	12	English
Total	62	67	

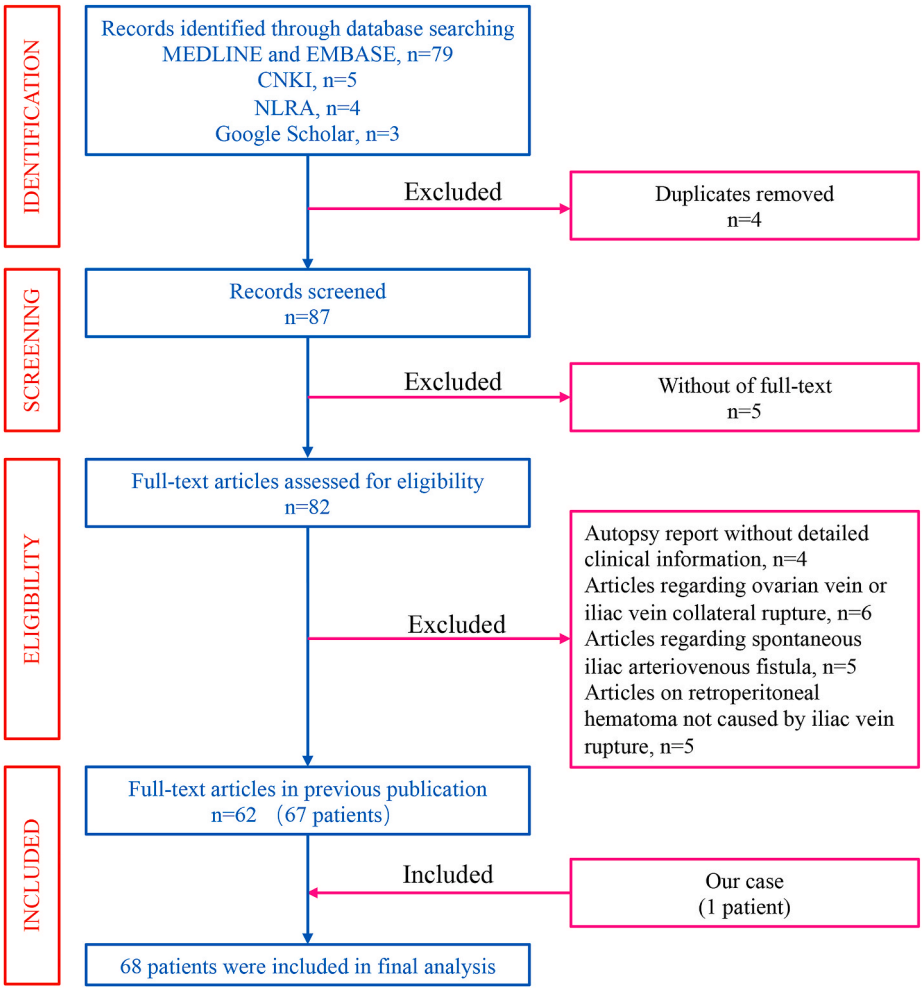

Fig. 1. Identification and selection of articles for review. Abbreviations: CNKI, China National Knowledge Infrastructure; NLRA, National Library Reference Alliance.

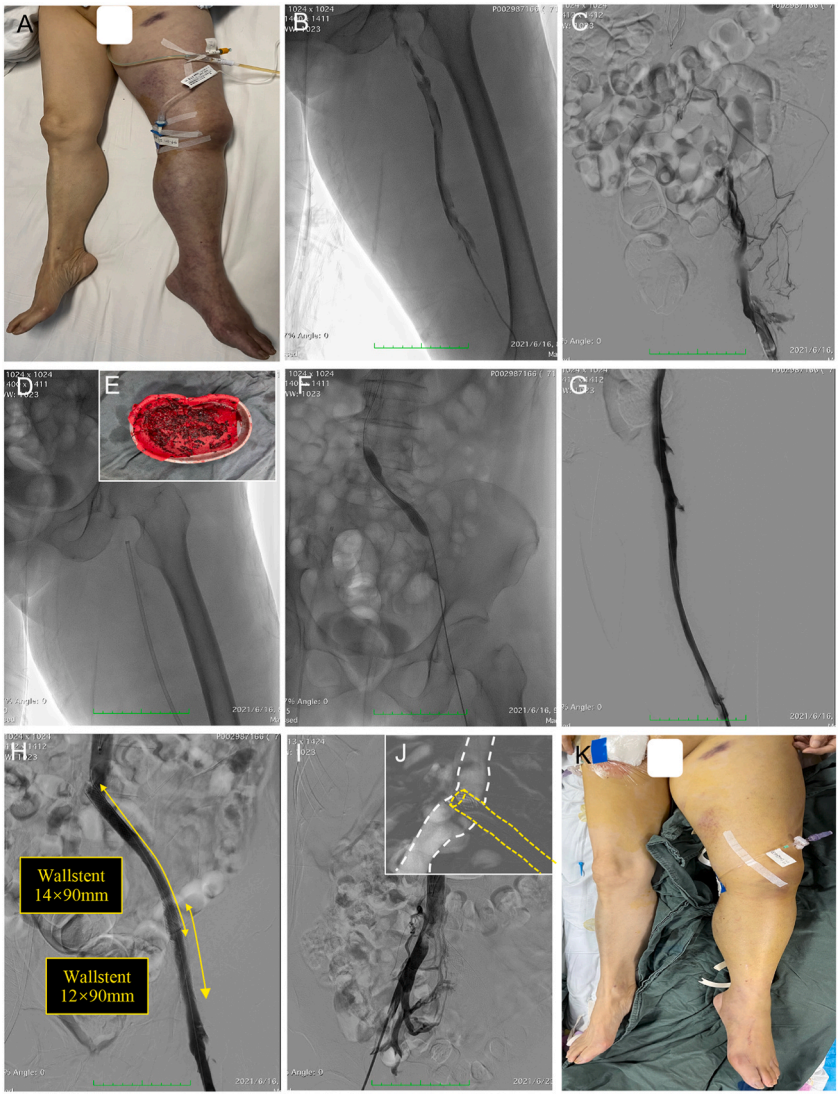

Fig. 2. PCD in the left lower extremity and the endovascular treatment procedure. (**A**) Clinical manifestation of PCD in the left lower extremity. (**B** and **C**) Venous angiography shows femoropopliteal and iliac venous thrombosis. (**D** and **E**) The thrombi in the iliofemoral vein were removed using a 10-F catheter, and the thrombi are shown in Figure E. (**F**) Endovenous angioplasty in the common iliac vein. (G) Femoropopliteal vein blood flow was restored. (**H**) A 12 mm × 90 mm and a 14 mm × 90 mm nitinol self-expanding stent were deployed to relieve compression in the iliac vein. (**I**) Collateral branches of the right iliac vein were visible after stent placement. (**J**) The stent (yellow dotted line) reached the contralateral wall of the inferior vena cava (white dotted line). (**K**) Skin cyanosis and mottling disappeared immediately after treatment. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.1. Clinical characteristics of SIVR patients

A total of 68 patients with a mean age of 62.01 ± 13.25 years (ranging from 31 to 83 years) in 63 studies from 17 countries, including 59 females and nine males, met the enrollment criteria and were reviewed. Among these patients, left external iliac vein rupture accounted for 57.35% (39/68) of the cases, and left internal iliac vein rupture accounted for 33.82% (23/68). Approximately 76.47% (52/68) of the patients presented with lower abdomen or iliac fossa pain, and 52.94% (36/68) of the patients had palpable nonpulsatile masses in the above areas and ipsilateral lower limb swelling. Thirty-eight patients (38/68, 55.88%) had hemodynamic instability when they arrived at the hospital. A total of 67.64% (46/68) and 32.35% (22/68) of patients had lower extremity DVT (four patients had PCD) and MTS, respectively. In some documented cases, the mean hemoglobin was 7.75 ± 2.48 g/dL (36 patients), the mean hematocrit was 26.8 ± 0.07% (23 patients), and the mean arterial systolic blood pressure was 78.61 ± 22.88 mmHg (38 patients). The clinical characteristics of the SIVR patients are summarized in Table 2.

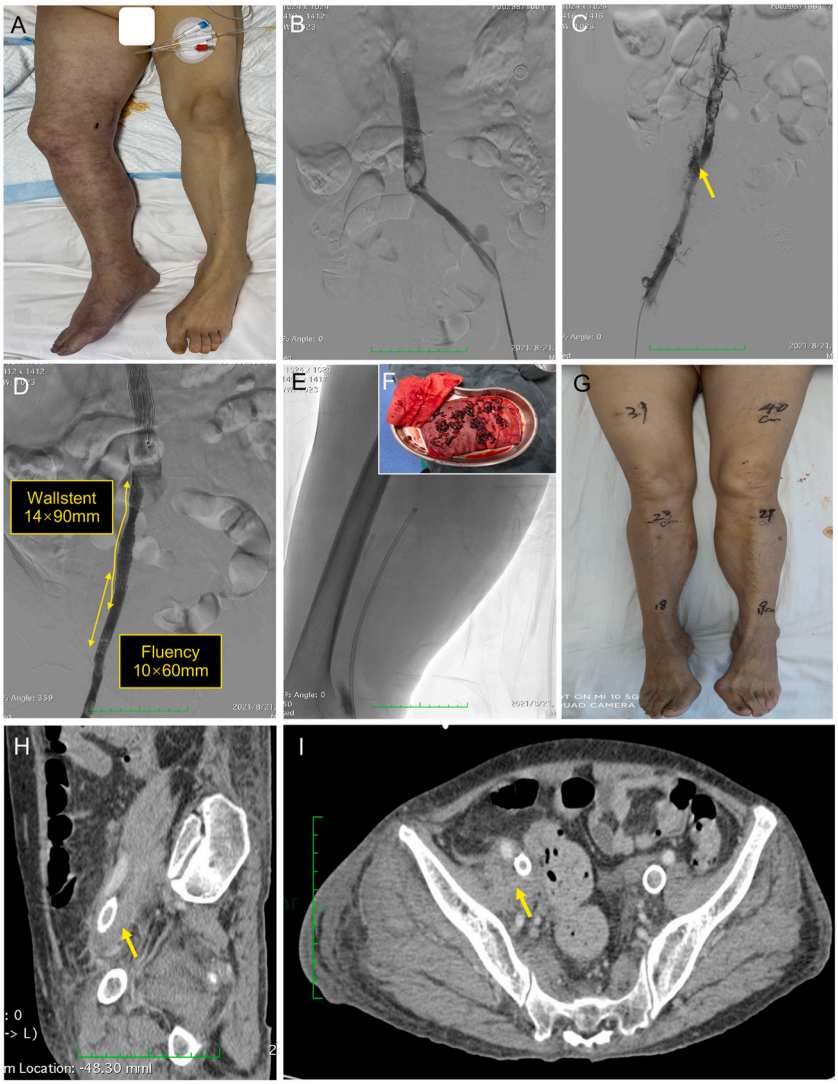

Fig. 3. PCD in the right lower extremity and the endovascular treatment procedure. (**A**) Clinical manifestation of PCD in the right lower extremity. (**B**) The outflow tract of the right iliac vein was obstructed by a thrombus. (**C**) Angiography revealed active venous extravasation (yellow arrow). (**D**) A 10 mm × 60 mm covered stent was deployed for hemostasis in the external iliac vein, and then a 14 mm × 90 mm nitinol self-expanding stent was deployed in the common iliac vein. (**E** and **F**) The thrombus was removed using a 10-F catheter, and the thrombi are shown in Figure F. (**G**) The swelling of the right lower extremity disappeared at 36 h after treatment. (**H** and **I**) Abdominal contrast-enhanced CT indicated absorption of a hematoma around the right iliac vein (yellow arrows) and patency of the bilateral iliac vein stents at 37 days after treatment. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.2. Clinical outcomes of SIVR patients

Approximately 69.12% (47/68) of the cases were diagnosed by exploratory laparotomy, some of which were followed by DSA and CT scanning, accounting for 14.70% (10/68) and 10.29% of cases (7/68), respectively. However, no cases were diagnosed with iliac vein rupture by abdominal ultrasound. Open iliac vein repair was the main treatment for this disease, accounting for approximately 61.76% (42/68) of cases, followed by endovascular repair (embolization or stent implantation), accounting for approximately 17.64% (12/68). A total of 14 of 68 patients died, and the overall mortality rate was 20.59% (14/68). The mortality rates of conservative treatment and open surgery were 2.94% (2/68) and 17.65% (12/68), respectively. Twelve patients receiving endovascular treatment survived (Table 2).

3.3. High-risk factors for mortality in SIVR patients

To reveal the high-risk factors for mortality in SIVR patients, demographic characteristics, iliac vein rupture site, concomitant

Table 2
Demographic and clinical characteristics of patients with spontaneous iliac vein rupture.

Number of patients (N)	68
Mortality rate	14/68 (20.59%)
Mean age (years)	62.01 ± 13.25 (range, 31–83 years)
Mean hemoglobin (g/dL)	7.75 ± 2.48 (36 patients)
Mean hematocrit (%)	26.8 ± 0.07 (23 patients)
MSBP (mm Hg)	78.61 ± 22.88 (38 patients)
MDBP (mm Hg)	47.86 ± 18.01 (35 patients)
Sex	
Female	59/68 (86.76%)
Male	9/68 (13.24%)
Rupture site	
LCIV	23/68 (33.82%)
LEIV	39/68 (57.35%)
LIIV	2/68 (2.94%)
REIV	4/68 (5.88%)
Concomitant vascular disease	
DVT	46/68 (67.64%)
PCD	4/68 (5.88%)
MTS	22/68 (32.35%)
None	18/68 (26.47%)
Main clinical manifestations	
Hemodynamic instability	38/68 (55.88%)
Lower abdominal or iliac fossa pain	52/68 (76.47%)
Abdominal or iliac fossa mass	36/68 (52.94%)
Lower extremity swelling	36/68 (52.94%)
Confirmed methods	
Ultrasound	0/68 (0)
Computerized tomography	7/68 (10.29%)
Magnetic resonance imaging	2/68 (2.94%)
Digital subtraction angiography	10/68 (14.70%)
Laparotomy	47/68 (69.12%)
Autopsy	2/68 (2.94%)
Treatment	
Conservative	6/68 (8.82%)
Open repair	42/68 (61.76%)
Ligation/Palma-Dale bypass	8/68 (11.76%)
Endovascular repair	12/68 (17.64%)

Hemodynamic instability is defined as SIVR patients with systolic blood pressure <90 mmHg or "hemodynamic instability" directly documented in previous case reports.
Open repair refers to suturing and repair of the iliac vein under an open surgical procedure.
MSBP, mean systolic blood pressure; MDBP, mean diastolic blood pressure; LCIV, left common iliac vein; LEIV, left external iliac vein, LIIV, left internal iliac vein; REIV, right external iliac vein; DVT, deep vein thrombosis; PCD, phlegmasia cerulea dolens; MTS, May–Thurner syndrome.

vascular disease, main clinical manifestations including hemodynamic state, lower abdominal mass and pain, and treatment were included in the statistical analysis. Upon univariate analysis, age, DVT and/or MTS, hemodynamic state and treatment were associated with death. However, sex, rupture site and the presence or absence of an abdominal mass and lower limb swelling were not significantly correlated with mortality (Table 3). The four significant variables from the univariate analysis were included in the logistic regression analysis. As shown in Table 4, younger age (52.86 ± 12.96 vs. 64.39 ± 12.37, P value 0.044) and patients without DVT (11/14 vs. 11/54, P value 0.013) were independent risk factors for mortality among SIVR patients. However, the hemodynamic state and open surgery did not influence patient survival.

4. Discussion

SIVR is extremely rare in the clinic. To the best of our knowledge, this study describes the first case of SIVR due to inappropriate positioning of the venous stent. Since the report by Hossne in 1961, approximately 67 patients with SIVR have been documented in detail worldwide as of 2022. Our literature review revealed that 86.76% (59/68, including the present case) of the reported patients were female with a mean age of 62.01 ± 13.25 years (ranging from 31 to 83 years), and 94.12% (64/68) of the patients developed left iliac vein rupture, whereas only four had right iliac vein rupture. The overall mortality rate was 20.59% (14/68).

The pathogenesis of SIVR is multifactorial. We found that lower extremity DVT occurred in 67.64% (46/68) of SIVR patients, and 32.35% (22/68) of cases were associated with MTS. Most iliac vein ruptures occur at the left common or external iliac vein distal to the compression site. The incidence rate of left external iliac vein rupture was 57.35% (39/68), whereas that of left common iliac vein rupture was 33.82% (23/68). MTS was considered a major cause of SIVR in previous publications; however, in most cases, iliac vein compression alone is likely not sufficient to produce venous wall rupture because iliac vein compression is a chronic course

Table 3
Univariate analysis of risk factors for mortality in SIVR patients.

Factor	Died (n = 14)	Survived (n = 54)	p value
Age (years)	52.86 ± 12.96	64.39 ± 12.37	0.003
Sex			0.567
Female	11/14 (78.57%)	48/54 (88.89%)	
Male	3/14 (21.43%)	6/54 (11.11%)	
Rupture site			0.528
LCIV	7/14 (50.00%)	16/54 (29.63%)	
LEIV	7/14 (50.00%)	32/54 (59.26%)	
LIIV	0/14 (0)	2/54 (3.70%)	
REIV	0/14 (0)	4/54 (7.41%)	
Concomitant vascular disease			0.000
DVT/MTS	4/14 (28.57%)	46/54 (85.19%)	
None	10/14 (71.43%)	8/54 (14.81%)	
Main clinical manifestations			
Hemodynamic state			0.055
Stability	3/14 (21.43%)	27/54 (50%)	
Instability	11/14 (78.57%)	27/54 (50%)	
Abdominal or iliac fossa pain			0.954
Yes	12/14 (85.71%)	49/54 (90.74%)	
No	2/14 (14.29%)	5/54 (9.26%)	
Abdominal or iliac fossa mass			0.147
Yes	5/14 (35.71%)	31/54 (57.41%)	
No	9/14 (64.29%)	23/54 (42.59%)	
Lower extremity swelling			0.742
Yes	8/14 (57.14%)	28/54 (51.85%)	
No	6/14 (42.86%)	26/54 (48.15%)	
Treatment			0.000
Conservative	2/14 (14.29%)	4/54 (7.41%)	
Open repair	6/14 (42.86%)	36/54 (66.67%)	
Ligation/P-D bypass	6/14 (42.86%)	2/54 (3.70%)	
Endovascular repair	0/14 (0)	12/54 (22.22%)	

LCIV, left common iliac vein; LEIV, left external iliac vein, LIIV, left internal iliac vein; REIV, right external iliac vein; DVT, deep vein thrombosis; MTS, May–Thurner syndrome; P-D, Palma-Dale.

Table 4
Logistic regression analysis of risk factors for mortality in SIVR patients.

Factor	Died (n = 14)	Survived (n = 54)	OR (95% CI)	P value
Age (years)	52.86 ± 12.96	64.39 ± 12.37	1.085 (1.002–1.174)	0.044
Concomitant DVT			10.111 (1.637–62.443)	0.013
Yes	3/14 (21.43%)	43/54 (79.63%)		
No	11/14 (78.57%)	11/54 (20.37%)		
Hemodynamic state			0.674 (0.106–4.269)	0.068
Stability	3/14 (21.43%)	27/54 (50%)		
Instability	11/14 (78.57%)	27/54 (50%)		
Treatment				0.137
Conservative (ref.)	2/14 (14.29%)	4/54 (7.41%)		
Open repair	6/14 (42.86%)	36/54 (66.67%)	3.799 (0.348–41.428)	0.274
Ligation/P-D bypass	6/14 (42.86%)	2/54 (3.70%)	0.203 (0.010–4.157)	0.301
Endovascular repair	0/14 (0)	12/54 (22.22%)		

characterized by collateral circulation, which can relieve iliac vein pressure. Based on chronic stenosis or occlusion, thrombosis leads to collateral circulation occlusion. When the blood pressure increases suddenly, particularly when the patient experiences vomiting, coughing, bending over, defecation, or performing a Valsalva maneuver, the pressure cannot be relieved, which leads to venous wall rupture. In an autopsy report by Rhome et al., fibrous bands formed at the junction of the left common iliac vein and IVC. Within the left common iliac vein distal to the fibrous bands, a large thrombus was adherent to the venous wall, creating an intraluminal obstruction [62]. A pathological report of a Japanese case found an obsolescent thrombus in the vascular lumen [56]. In addition, symptoms of lower extremity DVT prior to the symptoms of iliac vein rupture such as hypovolemic shock, syncope, and lower abdominal pain have been described in several case reports [40,50]. In our case, proximal to the iliac vein rupture site (downstream), a massive thrombus was found in the right iliac vein outflow tract that completely blocked it (Fig. 3B). Therefore, DVT is more likely to be the cause of iliac vein rupture rather than the result of compression of the iliac vein by a retroperitoneal hematoma. In addition, malignancies, venous inflammation, and reduced estrogen levels in postmenopausal women resulting in decreased elasticity of the blood vessel walls are also potential factors for iliac vein rupture.

In our case, no collateral circulation was noted in the right iliac vein before stent placement, whereas the collateral branches of the

right iliac vein were displayed after stent placement in the IVC, revealing outflow tract obstruction and high blood flow pressure. On the second admission, massive, accumulated thrombi were identified at the junction of the right common iliac vein and IVC, which completely blocked the blood flow to the IVC. The blood pressure was raised drastically when the patient experienced coughing, resulting in iliac vein rupture. As recommended by the European Society of Cardiovascular and Interventional Radiology, when stenting a lesion adjacent to the confluence of the common iliac veins, the depth of the stent into the IVC should be < 10 mm [65]. This technique does not limit the venous flow from the contralateral limb. Vascular surgeons should be aware that the placement of iliac vein stents should avoid blocking the outflow tract of the contralateral iliac vein, which may lead to thrombosis in the contralateral iliofemoral vein and even SIVR.

An accurate diagnosis during the initial evaluation remains challenging in SIVR patients, and although the retroperitoneal hematoma in most patients is clear preoperatively, the source of bleeding remains indeterminate and requires emergency laparotomy due to failed resuscitation. Nearly 62% of patients were diagnosed by exploratory laparotomy in previous reports. In terms of clinical manifestations, 76.47% (52/68) of patients presented with lower abdominal or left iliac fossa pain, 52.94% (36/68) of patients had concurrent lower extremity swelling, and most patients developed moderate anemia (7.75 ± 2.48 g/dL in 36 patients). However, these symptoms or signs are nonspecific, and the clinical manifestation mimics a ruptured abdominal aortic aneurysm or abdominal catastrophe due to a gynecological problem. Similarly, diagnosis of SIVR is more difficult in patients with PCD because some of the specific symptoms of SIVR such as hypovolemic shock, syncope and iliac fossa pain are also present in PCD patients. Clinicians may be more concerned with lower limb ischemia than with the presence of SIVR. Ultrasonography is the preferred method to diagnose DVT, but it cannot accurately detect sources of bleeding in SIVR patients. For patients with a retroperitoneal mass, abdominal contrast-enhanced CT or digital subtraction angiography (DSA) is needed. Yuji Nishimoto, a Japanese scholar, suggested that dynamic enhanced CT examination including the venous phase should be performed for DVT patients with unexplained retroperitoneal hematoma [50]. However, the CT angiogram does not always show active extravasation in the venous phase. Only seven SIVR patients (10.29%) had the source of retroperitoneal hematoma confirmed by contrast-enhanced CT. In a study reported by Jiang et al., two out of nine patients were misdiagnosed, one of whom was misjudged as having a retroperitoneal tumor by CT images [4]. Of the 12 patients receiving endovascular therapy, 10 were confirmed by venography. Thus, venography through femoral vein access may provide more accurate diagnostic information for unexplained retroperitoneal hematoma, such as dynamic contrast extravasation. Direct venography has higher venous pressure, and contrast extravasation is more likely to be observed. Some cases with stable hemodynamics were also diagnosed by magnetic resonance imaging [47,59].

No consensus has been reached on the treatment of SIVR. Hosn et al. held that hemodynamically stable patients after fluid resuscitation and blood transfusion can be managed conservatively and given anticoagulation 24 h after onset, which is safe [45]. However, anticoagulation alone may increase postthrombotic syndrome risk in severe iliofemoral DVT; thus, thrombi should be actively removed in these patients [66]. In previous reports, for resuscitation-failed patients, hematoma sources were identified via open surgery to implement vascular repair or ligation and hematoma removal to achieve abdominal decompression. Most patients undergo open surgery without an accurate diagnosis of SIVR, leading to high operative mortality and morbidity. Eight patients underwent iliac vein ligation with or without the Palma-Dale bypass grafting procedure but showed a mortality rate of 75.0% (6/8), whereas 61.76% (42/68) of patients received open iliac vein repair with or without anticoagulation therapy, which had a mortality rate of 14.29% (6/42). The overall mortality rate in open surgery was 17.65% (12/68). However, univariate and multivariate analyses showed that open surgery did not increase the risk of death in SIVR patients. In 2004, Zeiber reported the first patient undergoing endovascular covered stent repair [38]. In the last 20 years, an increasing number of patients have received endovascular therapy, and all 12 patients who underwent endovascular repair survived. For hemodynamically stable patients, endovascular therapy can remove thrombi while repairing blood vessels and relieving compression, thus decreasing the risk of chronic venous insufficiency in the chronic period. For patients with hemodynamic instability, angiography helps rapidly diagnose blood vessel lacerations for repair using a covered stent, quickly corrects hemodynamic instabilities and gains time for open removal of the hematoma and for abdominal decompression in patients with abdominal compartment syndrome. Several previous reports have shown that endovascular therapy, including the placement of covered stents, is safe and effective not only to stop bleeding and relieve occlusions in the acute phase but also to prevent the development of postthrombotic syndrome in the chronic phase [29,38,39,45]. The clinical course of our case supported these previous reports. For DVT patients with unexplained retroperitoneal hematoma, angiography followed by endovascular therapy should be considered regardless of hemodynamic stability.

In our study, the mortality rate for SIVR was approximately 20.59% (14/68), but it was still lower than the real-world mortality rate because several autopsy reports without detailed clinical information were excluded from the study. Although the disease demonstrated a female predominance and the left side was the most frequent site of rupture, our univariate analysis did not reveal any significant association between mortality and sex, rupture site, the presence of a retroperitoneal mass, or lower limb swelling. However, we observed that SIVR patients who died were younger than patients who survived. Furthermore, the logistic regression analysis identified younger age as a risk factor for mortality. The hemodynamic state and open surgery did not affect the prognosis of patients. In addition, although SIVR was more common in patients with DVT, DVT was a protective factor for death in SIVR, as both univariate and logistic regression analyses found a significantly increased risk of death in patients without venous thrombosis. This finding may be explained by the reduced rate and volume of bleeding with thrombosis and the increased risk of thrombosis with increasing age, making older age a protective factor [67]. Because the presence or absence of lower extremity DVT predicts a different prognosis, we suggest that SIVR may be divided into two types: iliac vein rupture alone (Type I) and iliac vein rupture with DVT (Type II).

The present study had several limitations. First, the small sample size used in this study may have led to statistical bias in identifying younger age as a significant risk factor for mortality in SIVR patients. Future studies with larger sample sizes and more rigorous

methodologies are needed to confirm or refute this finding. Second, the study did not include some factors that could potentially impact patient prognosis. Previous reports have either not recorded or only infrequently recorded variables such as race, medical history of cardiovascular and cerebrovascular diseases, presence of cancer, degree of shock, amount of bleeding, and occurrence of pulmonary embolism. Third, left lower extremity DVT is often secondary to the MTS; however, in some of the previously reported cases, only lower extremity DVT was diagnosed by ultrasound, and the potential MTS in these patients was not detected, which resulted in a statistical bias in MTS.

4. Conclusion

SIVR is a rare clinical event that has a high mortality rate and complex etiology. Improper positioning of stents in the IVC resulting in obstruction of the outflow tract of the contralateral iliac vein may also lead to SIVR. SIVR is more difficult to diagnose in PCD patients, and vascular surgeons should be aware of PCD patients with iliac vein rupture. Thrombosis secondary to MTS may be the main cause of SIVR. For elderly females who develop lower extremity DVT and concurrent lower abdominal pain, particularly those with a retroperitoneal mass and unstable hemodynamics, SIVR should be highly suspected. SIVR patients without lower extremity DVT may have a poorer prognosis. Angiography and endovenous therapy may be an optimal diagnosis and treatment for SIVR regardless of hemodynamic stability.

Ethics statement

This study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University.

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Author contribution statement

Li Zhui: Conceived and designed the experiments; Performed the experiments; Wrote the paper.
Feng Yangyang: Performed the experiments.
Wei Miao & Cui Hong: Analyzed and interpreted the data.
Zeng Qiu & Huang Wen: Contributed reagents, materials, analysis tools or data.
Ren Wei & Zhao Yu: Conceived and designed the experiments.

Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of competing interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e16382.

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