# A 10-Year Experience of Leiomyosarcoma of the Inferior Vena Cava

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**Research**

**Keywords:** leiomyosarcoma, inferior vena cava, primary repair

**Posted Date:** August 17th, 2021

**DOI:** https://doi.org/10.21203/rs.3.rs-797182/v1

# Abstract

**Background:** Leiomyosarcoma of the inferior vena cava (IVC) is rare. The study reviewed patients with IVC leiomyosarcoma in our hospital in the past ten years.

**Methods:** 20 patients diagnosed with IVC leiomyosarcoma between October 2010 and October 2020 were enrolled. Their clinical manifestations, treatments and follow-up results were analyzed.

**Results:** The sarcoma was located in the lower IVC segment in six patients, with 13 in the middle IVC segment and one in the upper IVC segment. The median tumor size was 8.5 cm (range 2.5-27.0). Except for two patients who underwent partial resection, other patients underwent R0 resection. After resection, 16 patients (80%) had primary repair of the IVC, while four patients underwent ligation. Three patients with tumors invading the renal vein but not the kidney underwent renal vein revascularization. There was no perioperative death. During a mean follow-up of 37.7 months, seven patients died due to tumor metastasis, four patients were alive with the tumor recurrence and other nine patients were alive without recurrence.

**Conclusion:** The perioperative mortality was low. The management of the IVC after tumor resection depended on the tumor location and size. R0 resection provided a chance for long term survival.


# Background

Leiomyosarcoma of the inferior vena cava (IVC) is an extremely rare malignant tumor originating from smooth muscle of the vein, accounting for 0.5% of soft tissue sarcoma.[1] Since Pearl described this disease in 1871,[2] only case reports and small case series are available. Up to now, the largest review consists of 377 cases.[3]

Patients are usually asymptomatic in the early stage, which delays the diagnosis and treatment and results in the poor prognosis.[3] It is reported that the 5-year survival rate ranges between 31% and 66.7% for patients receiving complete resection.[3, 4] Since chemotherapy and radiotherapy have limited effect on the tumor, it is generally agreed that surgical resection is the only chance for long-term survival. [4–6] To improve our understanding of this disease, the present study retrospectively investigated 20 patients diagnosed with IVC leiomyosarcoma at the study hospital, First Affiliated Hospital, School of Medicine, Zhejiang University in the past 10 years and aimed to provide new data on the topic.

# Methods

# Study population

Patients diagnosed with leiomyosarcoma of the IVC between October 2010 and October 2020 were reviewed at the study hospital, First Affiliated Hospital, School of Medicine, Zhejiang University. The diagnosis of leiomyosarcoma of the inferior vena cava was made based on both the computed

tomography angiography (CTA) and the post-operation pathology. This study was approved by the Institutional Review Board of the Ethics Committee of our hospital. Informed consent of the patients was obtained for the study.

# Definition

The location of the tumor was classified according to the IVC segment: lower IVC segment (below the renal veins), middle (from the renal veins to hepatic veins), or upper (from the hepatic veins to right atrium).[7] The growth pattern was classified as intraluminal, extraluminal, or both (referred as the dumbbell type).[3] Tumor resection was defined via the AJCC/UICC criteria.[6, 8] R0 resection was considered to be complete and the margin was negative, both microscopically and macroscopically. Microscopically, tumor specimens with positive margins were classified as R1 resection and those with macroscopic residual tumor after surgery as R2.[8] Disease recurrence included local recurrence and metastasis.

# Surgical and medical treatment

A multidisciplinary team comprising of vascular surgeons, radiologists, and oncologists would discuss the optimal treatment plan for each patient. For the operation, it was performed under general anesthesia. Usually we used a long midline laparotomy incision to expose the IVC. After exposure, we dissected it circumferentially and clamped it above and below the tumor. Then we removed the tumor via en bloc resection and resected adjacent organs concurrently if there was invasion. If the tumor was too large to be removed completely or severe complications took place during the operation, partial resection of the tumor would be performed instead. If the tumor expanded to the heart, we performed a thoraco-abdominal incision with cardiac surgeons and extracorporeal circulation was used during its removal. In terms of IVC management, we performed the primary repair when there were more than half of the IVC left after tumor resection. If there was not enough IVC left, we would ligate the residual IVC (lower segment for all patients, middle segment if there was enough collateral circulation before the operation) or reconstruct the IVC (middle segment if there was not enough collateral circulation, upper segment for all patients.). In cases whose tumor invaded the renal vein but the kidney was intact, we resected the renal vein and performed venous-venous bypass to preserve the renal function. After surgery, all patients would receive anticoagulation therapy with warfarin for at least six months post operation and the target International Normalized Ratio was 2.0–3.0. Adjuvant radiotherapy and chemotherapy were used in selected patients according to suggestions from the multidisciplinary team.

# Follow-up

Patients were evaluated one, three, and six months after operation and annually thereafter. CT scan was performed at each follow-up.

# Statistical analysis

Continuous variables are reported as the mean. Comparisons of continuous data were analyzed using independent Student’s t-test, whereas categorical data were analyzed using the chi-square test. All

statistical analyses were performed using SPSS 26.0 software (SPSS, Chicago, IL, USA). P-values of < 0.05 were considered statistically significant.

## Results

# Patient demographics

Patient characteristics were shown in Table 1. A total of 20 patients receiving operations were enrolled in this retrospective study (Refer to Additional file for individual patient data). Sixteen (80%) patients were female. Their median age was 56 years (range 33–77). The most common symptoms were abdominal pain (35%), back pain (30%) and abdominal mass (15%). According to the classification of location, six (30%) were located in the lower IVC segment, with 13 (65%) in the middle IVC segment and one (5%) in the upper IVC segment. Its growth pattern was classified as extraluminal, intraluminal, or dumbbell shaped based on CT images, with nine patients (45%), one patient (5%), and 10 patients (50%) in each pattern, respectively.

Table 1
Demographics of the cohort and the review

| Item | Total | Wachtel et al. | P |
|---|---|---|---|
| **Sample size** | 20 (100.0) | 377 (100.0) | |
| Time range | 2010–2020 | 1951–2013 | |
| Female | 16 (80.0) | 286 (75.9) | 0.660 |
| Age (median, range) –year | 56 (33–77) | 55 (45–63) | 0.658 |
| **Symptom*** | | | |
| Abdominal pain | 7 (35.0) | 142 (59.9) | 0.034 |
| Back pain | 6 (30.0) | 23 (9.7) | 0.068 |
| Abdominal mass/distension | 3 (15.0) | 22 (9.3) | 0.494 |
| Incidental finding | 4 (20.0) | 20 (8.4) | 0.221 |
| Nausea/vomiting | 2 (10.0) | 10 (4.2) | 0.409 |
| **Location on the IVC ** ** | | | |
| Lower | 6 (30.0) | 78 (22.5) | 0.484 |
| Middle | 13 (65.0) | 176 (50.7) | 0.206 |
| Upper | 1 (5.0) | 19 (5.5) | 0.921 |
| **Growth pattern#** | | | |
| Intraluminal | 1 (5.0) | 56 (24.9) | 0.000 |
| Extraluminal | 9 (45.0) | 133 (59.1) | 0.105 |
| Dumbbell | 10 (50.0) | 36 (16.0) | 0.019 |
| NR = not reported; IVC = inferior vena cava | | | |
| *Patients had more than one clinical symptom. | | | |
| **Lower, below the renal veins; Middle, from the renal to hepatic veins; Upper, from the hepatic veins to the right atrium. Tumors beyond one segment are represented by the maximum extent they occupy. | | | |
| #Tumor growth pattern was classified as intraluminal, extraluminal, and dumbbell shaped. | | | |

# Treatment

Perioperative information was shown in Table 2. The median tumor size was 8.5 cm (range, 2.5–27.0 cm). Except two patients, the remaining patients underwent R0 resection. One patient's tumor extended from the iliac veins to the right atrium, making the radical resection difficult. Then the patient underwent

partial resection, lived with tumor in the past 16 months and is still under follow-up. The tumor in another female patient tightly surrounded the aorta. During the dissection, massive bleeding took place, forcing the surgeon to abort the radical resection. She received partial resection alternatively. In the end, she died of brain metastasis in 9-month post-operation. Among patients receiving R0 resection, one patient received partial sigmoid colon and small intestine resection and another two patients underwent single nephrectomy due to the tumor invasion. Leiomyosarcoma of the IVC were confirmed by histologic examination of the surgical specimens (Fig. 2). After resection, IVC management was the other important issue. 16 patients (80%) received primary repair of the IVC. IVC segment ligation with no reconstruction was performed in 4 patients (20%) (Fig. 1). In 3 patients (15%) who underwent renal vein resection, venous reconstruction of the renal vein (two prosthetic grafts, one auto graft) was performed. Hemorrhage as the only perioperative complication was observed in one patient (5%). Other complications such as thrombosis, graft infection and severe edema were not found in our cohort. After surgery, two patients who underwent partial resection received radiotherapy, and another three patients received chemotherapy.

Table 2
Treatment and perioperative results

| Item | Total | Wachtel et al. | P |
|---|---|---|---|
| **IVC management‡** | | | |
| Ligation | 4 (20.0) | 64 (16.9) | 0.271 |
| Primary repair | 16 (80.0) | 69 (18.3) | 0.000 |
| Graft | 0 (0) | 155 (41.2) | 0.005 |
| **Size of tumor (median, range) –cm** | 8.5 (2.5–27.0) | 8.3 (6.0-12.4) | 0.840 |
| **Resection** | | | |
| R0 resection | 18 (90.0) | 162 (76.1) | 0.112 |
| R1 resection | 0 | 38 (17.8) | 0.191 |
| R2 resection | 2 (10.0) | 13 (6.1) | 0.375 |
| **Renal vein involvement** | 5 (25.0) | NR | |
| Concurrent kidney involvement: nephrectomy | 2 (10.0) | NR | |
| No kidney invasion: renal vein reconstruction | 3 (15.0) | NR | |
| Prosthetic graft | 2 (10.0) | NR | |
| Auto graft | 1 (5.0) | NR | |
| **Perioperative Complications** | | | |
| Hemorrhage | 1 | NR | |
| Acute kidney injury | 0 | NR | |
| Thrombosis | 0 | NR | |
| NR = not reported; IVC = inferior vena cava | | | |
| ‡IVC management includes ligation of the IVC, primary repair, and reconstruction of the IVC by grafts. | | | |

# Follow-up

There was no perioperative mortality in our cohort. Follow-up results were shown in Table 3. None of the patients had leg edema or skin pigmentation. During a mean follow-up of 37.7 months, seven patients (35%) died due to tumor metastasis. In the remaining patients who were still alive and under follow-up, three patients (15%) had local recurrence and secondary surgery and one patient (5%) had distant metastasis. The other nine patients (45%) were disease-free. There was one long-term survivor (187 months). The female patient underwent surgery 15 years ago. Eight years ago, a local recurrence was

found through a routine annual computed tomography scan and the patient received a second surgery. Since then, there was no recurrence and the patient is still under follow-up.

Table 3
Follow-up

| Item | Total | Wachtel et al. | P |
|---|---|---|---|
| **Postoperative hospital day (median, range) –day** | 9 (4–56) | NR | |
| **30-day operative mortality** | 0 (0) | 7(1.9) | - |
| **Postoperative therapy** | | | |
| Chemotherapy | 3 | NR | |
| Radiation | 2 | NR | |
| **Follow-up (mean, range) –month** | 37.7 (3-187) | NR | |
| **Leg symptom** | | | |
| **edema** | 0 | NR | |
| **pigmentation** | 0 | NR | |
| **Outcome** | | | |
| Death | 7 (35) | NR | |
| Alive | 13 (65) | NR | |
| No recurrence | 9 (45) | NR | |
| Recurrence† | 4 (20) | NR | |
| Second surgery↕ | 3 (15) | NR | |
| Observation | 1 (5) | NR | |
| NR = not reported | | | |
| †Disease recurrence includes local recurrence and metastasis. | | | |
| Seven patients died due to tumor metastasis. | | | |
| ↕ Three patients received second surgery because of local recurrence. | | | |

# Discussion

IVC leiomyosarcoma was an extremely rare form of retroperitoneal sarcoma. The leiomyosarcoma predominated in females, with the female/male ratio 3:1 reported.[3, 9] 5-year disease free survival after resection of IVC leiomyosarcoma was approximately 6%.[3] And the overall 5-year survival ranged 33–

67%.[3] It was confirmed that complete surgical resection with R0 margin provided a chance of long-term survival.[5, 8, 10] The operation involving the IVC was sophisticated and challenging, raising concerns on its mortality and operative techniques. For a long period of time, surgeons were baffled for IVC sarcoma because of its easy invasion into critical organs.[9] With the developments of cardiopulmonary bypass and the commencement of multidisciplinary collaboration, surgical treatment became feasible.[8, 9, 11, 12] The first resection of the IVC tumor was recorded at Lexington Memorial Hospital in 1951.[10] In 1974, Mandelbaum et al reported the first successful resection of IVC leiomyoma involving right atrium.[13]

Since IVC leiomyosarcoma had an asymptomatic insidious onset, the early diagnosis was difficult.[14] The non-specific complaints included abdominal pain, nausea, vomiting, abdominal distension and edema of lower extremities.[9] In the present study, the majority of patients (35%) presented with abdominal pain. In comparison to a review with 377 cases,[3] patient with intraluminal tumor were less in our center (5% vs. 24.9%; P = 0.000), while those with dumbbell shaped sarcoma were predominant in our cohort (50% vs. 16%; P = 0.019). The perioperative mortality was 1.2% in the review and 0% in our cohort.[3] Possible explanations included: a) Advances in surgical equipment and perioperative care. b) Partial resection. Complete resection might be difficult in some cases and could cause fatal complications. Partial resection was an alternative. The patient receiving partial resection had a better chance of surviving the operation. The tumor in one patient in our cohort tightly surrounded the aorta. During the dissecting, massive bleeding took place, we aborted the radical resection and performed partial resection. The patient survived for 9 months post-operation. c) If the preoperative evaluation suggested that the patient could not survive the surgery, the surgery was aborted. Therefore, both the review and our data suggested that the risk of death was low in selected cases.

One important issue following radical resection was the management of the IVC. There were several options for IVC repair, including ligation, primary repair and IVC reconstruction.[6, 15–17] According to Yoshidome et al, it was necessary to reconstruct vena cava only in patients with poor collateral circulation or unstable hemodynamics.[17] On the contrary, Illuminati et al suggested vascular reconstruction if applicable.[18] In additional, Elodie Gaignard et al suggested that the reconstruction of IVC should be based on tumor location and its extension. ligation was preferred if the tumor was located in the lower segment of the IVC and in the middle segment of IVC when there was well-established collateral drainage.[15] When vascular reconstruction was required, they preferred prosthetic PTFE graft.[15] In our center, we were in favor of reconstruction via graft when there was bad collateral circulation in the upper and/or middle segments of IVC.[4, 15] For the lower segment of IVC and middle segment of IVC with enough collateral circulation, we preferred primary repair. Compared to ligation, the IVC after primary repair was patent at least to some extent, providing an outflow for venous drainage. Besides, there was no IVC thrombosis nor leg edema and/or pigmentation recorded after surgery, indicating the safety and effectiveness of the technique. In terms of IVC leiomyosarcoma involving the renal vein, preserving venous outflow could avoid nephrectomy in patients whose kidney was not affected.[16] We also advocated this approach. In our cohort, we found renal vein invasion in five patients. Two patients' kidneys were invaded in the same time while the other three were not. Therefore, we performed two

nephrectomy and three renal vein reconstruction. All three patients remained asymptomatic and did well throughout follow-up without renal dysfunction.

The limitation of this study lies in its sample size. Considering the rarity of this sarcoma, it is impossible to conduct randomized clinical trials. Multicenter retrospective cohorts with large sample size are needed for further analysis.

# Conclusion

In conclusion, leiomyosarcoma of the IVC is a rare and challenging disease. Complete resection is the only option providing the chance of the long-term survival. The perioperative mortality was low. Intraoperative management of IVC after tumor resection was depended on the tumor location and size.

# Abbreviations

IVC
inferior vena cava

# Declarations


### Acknowledgements

Not applicable.


### Authors' contributions

HZ, FC, JP and CQ conceived and designed the study. JP, CQ, YH, XX, ZW, DL, LT, FC, HZ were responsible for the collection, analysis and interpretation of the data. JP and CQ drafted the manuscript. YH, XX, ZW, DL, LT, FC and HZ revised the manuscript critically for important intellectual content. All authors read and approved the fnal manuscript.


### Funding

Not applicable.


### Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Ethics approval and consent to participate

The study was approved by the Institutional Review Board of the Ethics Committee of the First Affiliated Hospital, School of Medicine, Zhejiang University. Informed consent of the patients was obtained for the

study.

### Consent for publication

Written informed consent was obtained from all patients.

### Competing interests

The authors declare that they have no competing interests.

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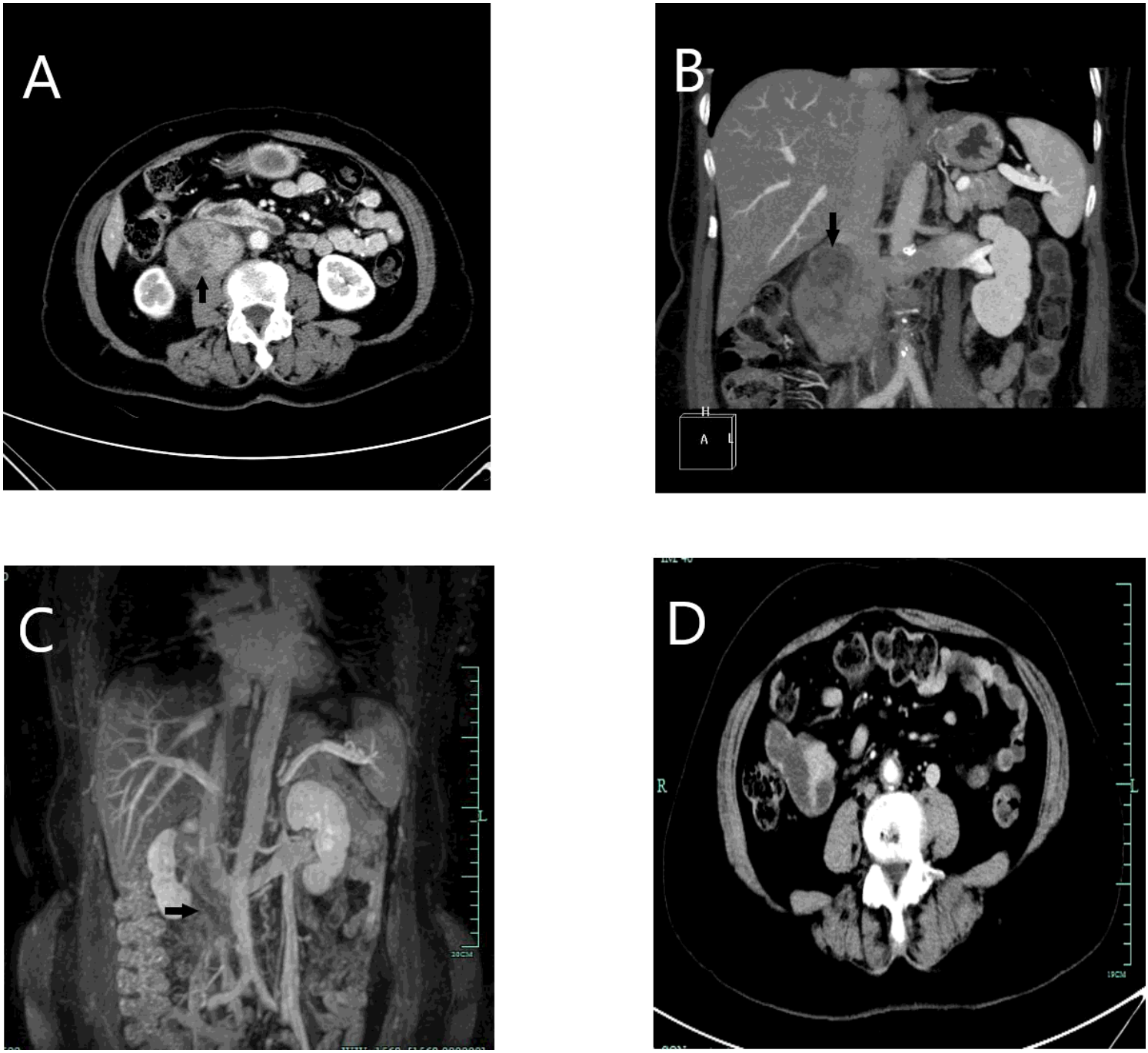
# Figures




## Figure 1

Pre- and post-operation images of IVC leiomyosarcoma (Patient 7 in the Additional file). A&B, Abdominal contrast-enhanced computed tomography (the arrow indicates the inferior vena cava tumor). The tumor located at the middle segment of the IVC was close to the right renal vein. C, Abdominal magnetic resonance imaging after tumor resection (the arrow indicates the ligation of IVC). D, Postoperative computed tomography venography image showed the resection of the IVC with no recurrence of the tumor. (1 year at follow-up)

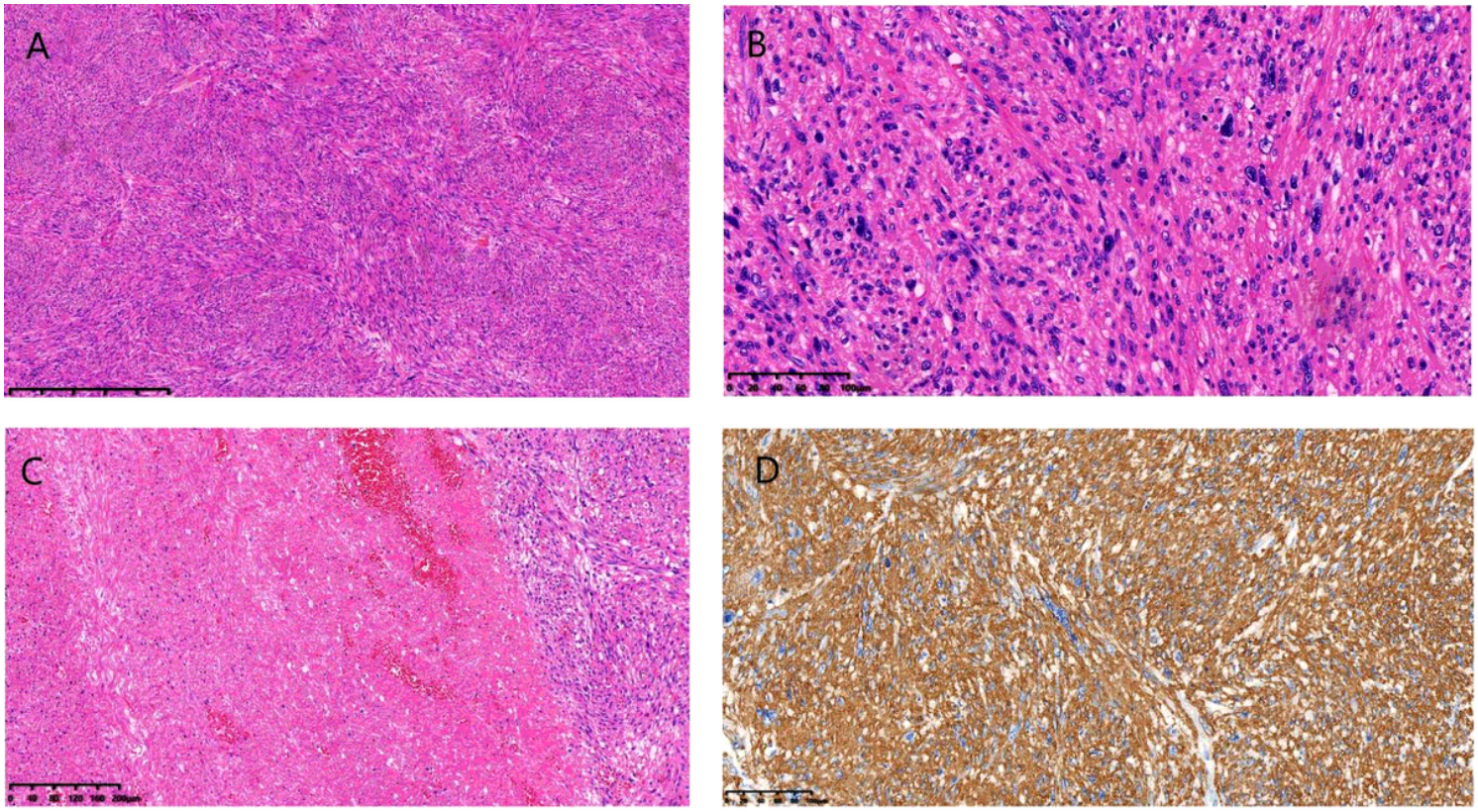



**Figure 2**

Pathology of the IVC leiomyosarcoma. A&B, Cytological and architectural features of smooth muscle neoplasms with elongated, blunt-ended, vesicular nuclei and brightly eosinophilic fibrillary cytoplasm arranged into compact intersecting fascicles. (HE staining, 100×&200×) C, Areas of coagulation necrosis. HE staining, 100×D, Representative images of immunohistochemical staining of smooth muscle actin. (200×) (The same patient in Fig 1.)

## Supplementary Files

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