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ORIGINAL ARTICLE

Leiomyosarcoma of inferior vena cava (IVC): do we really need to reconstruct IVC post resection? Single institution experience

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Abstract

Background Inferior vena cava (IVC) leiomyosarcomas (LMS) are a rare group of retroperitoneal tumors. R0 surgical resection is the only curative modality of treatment. IVC resection for retroperitoneal sarcoma is a complex surgery with no definitive guidelines for reconstruction.

Methods Retrospective review of all patients who underwent surgical resection of primary leiomyosarcoma of the IVC requiring resection from 2010 to 2020 at our tertiary care center was performed.

Results Among 24 patients who required IVC resection for LMS, only 7 (29%) required reconstruction of IVC. According to Clavien-Dindo classification, there was one grade 3 or more morbidity and 1 post-operative mortality. Seventeen patients underwent R0 resection whereas 7 patients had R1 resection on final histopathology. At a median follow-up of 25 months (range 8–91 months), the median OS was 40 months with median DFS of 28 months. Two patients presented with local recurrence while 13 patients developed systemic recurrence on follow-up.

Conclusion Careful preoperative multidisciplinary planning can make IVC resection without reconstruction feasible with acceptable perioperative morbidity, mortality, and oncological outcomes for IVC LMS.

Keywords Inferior vena cava sarcoma · Resection · Reconstruction

Introduction

Leiomyosarcomas (LMS) are rare tumors accounting for 5–7% of all sarcomas [1]. LMS arise from the mesenchymal smooth muscle cells. One to two percent of all LMS originate from large vessel wall, with 60% in the inferior vena cava (IVC) [2]. However, there have been few case reports of LMS from other vessels such as portal vein and renal vein. Resection with clear margins remains the mainstay of treatment with expected 5-year survival of 30–50% [3, 4]. Perl first described IVC sarcoma in 1871 with majority of the reports in the form of autopsy findings [5]. Advances in surgical technique and perioperative management resulted in the first IVC leiomyosarcoma resection at Lexington Memorial Hospital in Chicago, in 1951 [6]. Surgery for IVC sarcoma is technically demanding requiring multidisciplinary surgical approach. We present one of the largest single institution experiences of IVC resection for LMS.

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Aim

The primary aim of our study was to study perioperative morbidity and mortality in patients undergoing IVC resection with or without reconstruction. Secondary objective was to analyze the short-term oncological outcomes.

Material and methods

The design was retrospective in nature with a study population of patients with retroperitoneal tumor undergoing IVC resection.

Data of patients who underwent surgery for retroperitoneal tumors from January 2008 to December 2020 was evaluated. The histological and radiological details were obtained from the electronic medical records of the patients. Data collection was in accordance with the Declaration of Helsinki. All patients with who underwent IVC resection with LMS on final histopathology were included for the analysis. Patients who underwent IVC resection for a non-LMS histology were excluded from the study.

Patients were evaluated with a triphasic contrast-enhanced computed tomography (CECT) of thorax, abdomen, and pelvis. The following details were carefully assessed:

a. Level of IVC involved
b. Local extent and organ invasion
c. Presence of collaterals
d. Distant metastasis

Three-dimensional reformatted images were obtained to assess extension of tumor into renal veins, hepatic veins, and iliac veins. A functional renogram was performed in patients likely to require nephrectomy based on imaging. Patients who were judged to be resectable were operated without prior tissue diagnosis.

IVC LMS and resections are classified according to the level of involvement of the IVC (Fig. 1) [7, 8]. A right thoracoabdominal approach was preferred for patients with involvement of retrohepatic IVC or requiring venous bypass and midline abdominal or Makuuchi incision for patients with inter-renal and infrarenal segment involvement of IVC. Surgical team included a retroperitoneal cancer surgeon with or without a vascular surgeon. Perioperative details were recorded. Post-operative complications were graded according to the Clavien-Dindo classification and grade 3 or higher were considered major morbidity [9].

Statistical analysis

Analysis was performed using SPSS version 25 software. Survival analysis was done using Kaplan–Meier curves.

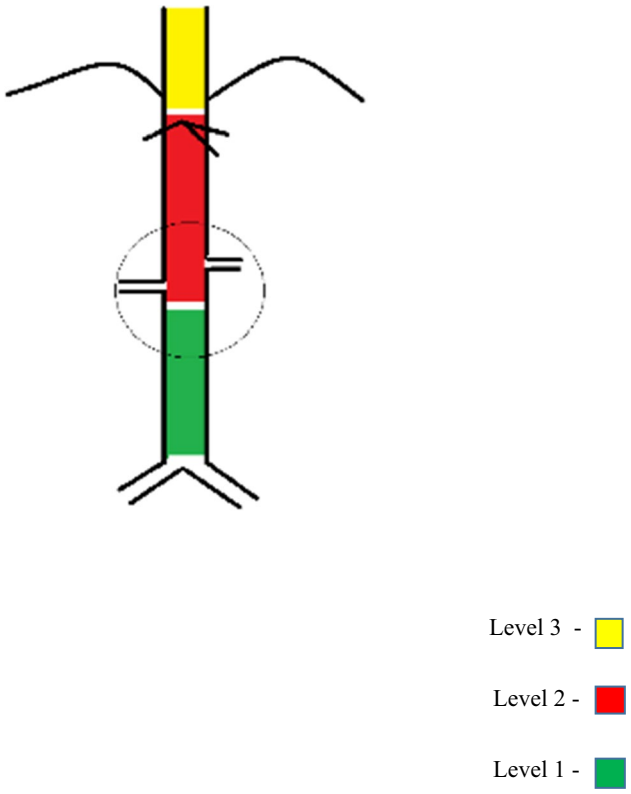

Fig. 1 Classification of IVC LMS according level of involvement. Level I, infrarenal segment; level II, inter- and suprarenal segment up to but not including the main suprahepatic vein; level III, suprahepatic segment with possible intracardiac extension

Patients with non-LMS histology were excluded from the analysis. Overall survival (OS) was calculated from the date of surgery to the date of death or date of last follow-up. Disease-free interval (DFS) was calculated from the date of surgery to the date of first recurrence.

Results

Over the duration of the study period, we operated 28 patients of retroperitoneal tumors requiring resection of IVC. Of these, 24 were reported to have LMS on final histopathology. The median age in our group was 47 years (25–73). Seventeen patients were females and 7 were males (Table 1).

The most common tumor location was around renal ostium in the current study. We performed level 1 + 2 resections in 14 patients, level 1 resections in 7 (including 3 patients requiring resection of iliac veins too), cavoplasty (for less than one third of circumference involvement) in 2 patients, and pure level 2 resection in one patient.

Of the 14 patients of level 1 + 2 resection, nine underwent right nephrectomy with ligation of left renal vein (Fig. 2), 1 patient underwent ligation of both renal veins

Table 1 Overview of patient characteristics and treatment details

Patient characteristics	Number of patients
Age	
< 50	14 (58%)
> 50	10 (42%)
Gender	
Male	7 (29%)
Female	17 (71%)
Resection of IVC	
Cavoplasty	2 (8%)
Level 1	4 (16%)
Level 2	1 (4%)
Level 3	0
Level 1 + 2	14 (59%)
Level 1 + iliac vein	3 (13%)
Multi-visceral resection	
Single organ	14 (59%)
Two organs	4 (16%)
No	6 (25%)
Tumour size (max dimension)	
5–10 cm	10 (42%)
> 10 cm	14 (58%)
IVC reconstruction	
Yes	7 (29%)
No	17 (71%)
Resection	
R0	17 (71%)
R1	7 (29%)
R2	0
Adjuvant treatment	
Neoadjuvant chemoradiotherapy	1 (4%)
Adjuvant radiotherapy	14 (59%)
Adjuvant chemotherapy	1 (4%)
Adjuvant chemoradiotherapy	2 (8%)
No	6 (25%)
Recurrence*	
Local	2 (9%)
Systemic	13 (57%)

*Excludes 1 patient who died of post-operative complication

with both kidneys left in situ without any reconstruction, and the remaining 4 patients underwent IVC reconstruction with polytetrafluorethylene (PTFE) or Dacron graft with re-implantation of renal vein. In all the patients with ligation of left renal vein, renal venous outflow was confirmed by intraoperative Doppler of renal vessels and absence of renal congestion. The only patient who underwent level 2 resection did not require any reconstruction. Of the 7 patients who underwent level 1 resection, 1 required reconstruction in view of hypotension following IVC clamping and other two required reconstruction of external iliac vein. Decision for reconstruction of external iliac vein was taken based on lack of demonstrable collaterals on preoperative imaging. Reconstruction was performed using a Dacron Y graft of a size that matched the lumen of the iliac vein. The anastomosis was completed using continuous 6–0 Prolene sutures.

Thus, among 24 patients, only 7 (29%) patients underwent venous reconstruction with graft, with most of them being performed in earlier part of our series (Supplementary Table 1). No reconstruction of the IVC was performed in the remaining 17 patients.

Median operative time was 345 min (180–1200 min) with a median blood loss of 2.4 L (0.7–8.0 L). In the post-operative period, one patient developed lower limb edema that was managed conservatively. Two patients developed deep venous thrombosis that were managed with anticoagulation and one patient had a biliary leak requiring re-exploration with hepaticojejunostomy, whereas other perioperative complications of chyle leak and retroperitoneal hematoma each in a patient were managed conservatively. According to Clavien-Dindo classification, only 1 patient (4%) had grade 3 or more complication. There was one (4%) perioperative 30-day mortality because of multi-organ dysfunction secondary to intraoperative pulmonary embolism. The median hospital stay was 10 days (4–24 days).

Seventeen patients underwent R0 resection whereas 7 patients had R1 resection on final histopathology. The median tumor size was 11.5 cm (5–18 cm). Fourteen patients received adjuvant radiotherapy to the tumor bed, one patient was given adjuvant chemotherapy, and 2 patients received adjuvant chemoradiotherapy. Only one patient received neoadjuvant chemoradiotherapy (Supplementary Table 2).

At a median follow-up of 25 months (range 8–91 months), the median OS was 40 months with median DFS of 28 months (Figs. 3 and 4). Two patients presented with local recurrence while 13 patients developed systemic recurrence on follow-up.

Discussion

Approximately 400 IVC sarcoma cases have been reported in literature, most in the form of case reports or case series with a female preponderance, commonly affecting individuals in the fifth decade of life [9]. In our series also, 71% ($n = 17$) patients were female. En bloc resection of the IVC sarcoma is the only effective treatment option available at present. Excision of the IVC with ligation, cavoplasty, and graft replacement represents major therapeutic options.

IVC LMS are classified according to the level of involvement of the IVC (Fig. 1) [7, 8]. Type 1 accounts for 36% of cases, type 2 for 44% of cases, and type 3 for suprahepatic vena cava 20% of cases [10, 11].

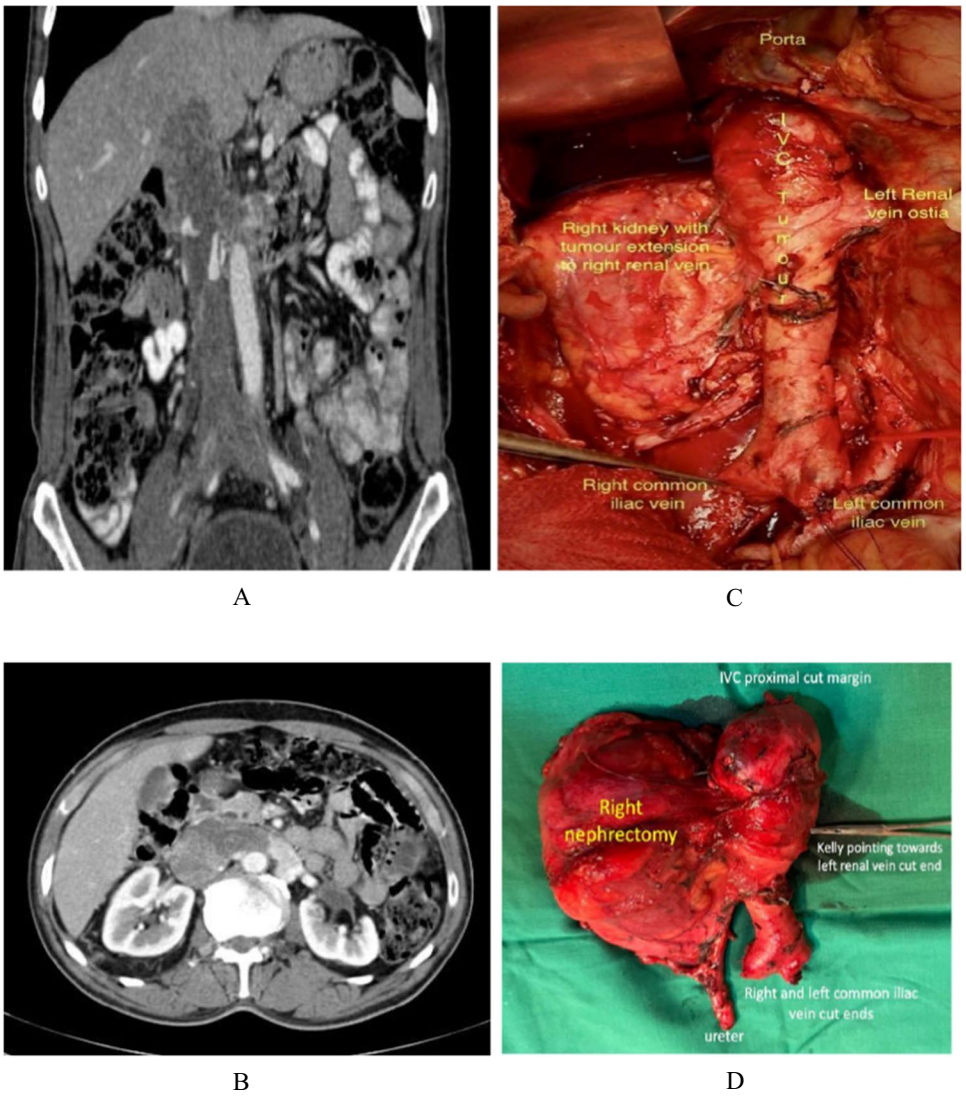

Fig. 2 Preoperative CT scan and intraoperative image of resection of IVC LMS without reconstruction. **A** Sagittal section showing the extent of IVC involvement; **B** coronal section showing tumor involvement up to left renal vein ostium; **C** intraoperative image; **D** excised specimen

The clinical presentation may vary according to its location and extent—for type I IVC sarcomas, patients can present with lower limb edema, which can be transitory because of collateral venous development. Type II can cause abdominal pain and renal failure in late cases, else are usually asymptomatic. Type III can present with Budd-Chiari syndrome [12].

Partial wall excision of IVC for management of primary sarcoma is usually considered oncologically unsafe. However, it can be considered for purely exophytic tumors requiring less than one third of IVC wall excision. For level 1 IVC involvement, ligation of IVC is usually well-tolerated by the patients [13]. It has been hypothesized that if the internal and external iliac bifurcation is not involved, the venous return from the lower limbs is ensured by the internal iliac vein and pelvic venous anastomosis, and if involved, then there arises the need to reconstruct in view of inadequacy of collaterals [12]. In the latter scenario, to facilitate reconstruction, an end-to-side anastomosis between the external iliac vein and the internal iliac vein or graft can be placed from IVC to external iliac vein with ligation of internal iliac vein. For level 2 tumors, proximity to the renal vessels poses a technical challenge for resection. Right renal vein has a short extrarenal course and absence of collateral drainage makes it vulnerable even after reconstruction. Compared to right renal vein, left renal vein has longer extrarenal course and abundant collaterals in the form of lumbar, adrenal, and gonadal veins, thus making simple ligation a feasible option if ligated proximal to collateral drainage.

Jiang et al. have proposed guidelines for simple IVC ligation: (1) the duration of the disease is longer than 1 year, so that collateral venous circulation could be sufficient. (2) At least 75% of the IVC is obstructed. (3) A preoperative intravenous injection of 20 mg furosemide leading to more than 100 mL urine within 30 min after the IVC is temporarily blocked [14]. Level 3 is the most

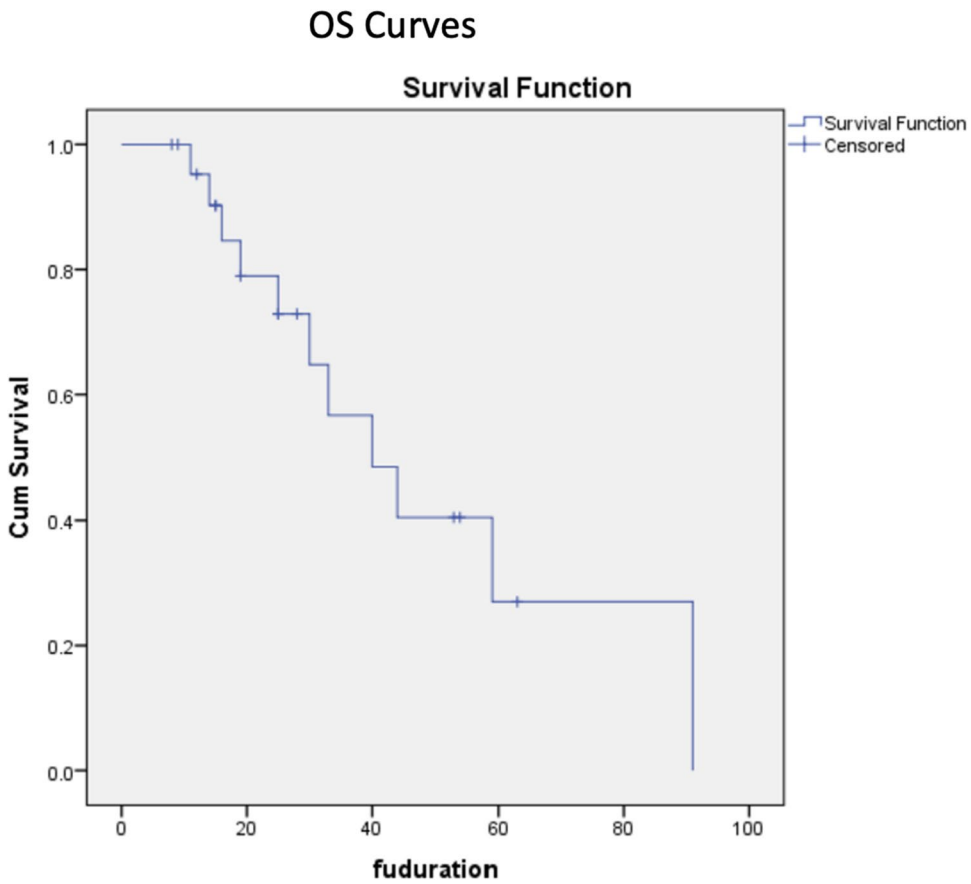

Fig. 3 Overall survival

challenging of all types. These need to be tackled on a case-to-case basis, often requiring the help of vascular, hepatic, and oncological surgeon. These cases can be approached via a thoracoabdominal incision or midline laparotomy with sternotomy. Intraoperatively, they may need cardiac bypass and major hepatectomies for complete resection.

Kalchev et al. in their paper on congenital absence of IVC have described alternate pathway of venous return in case of absence of IVC [15]. They have divided IVC into 4 parts as hepatic, suprarenal, renal, and infrarenal. Collateral pathways described by them are as follows:

a) Deep pathway—formed by communication between ascending lumbar veins and azygous venous system.
b) Intermediate pathway—formed by deep venous plexus in the pelvis in patients with obstruction/absence of infrarenal IVC. The blood flow is from the external and internal iliac veins to the uterine/prostatic plexuses and then through the ovarian/pampiniform plexus to the left gonadal vein which flows into the left renal vein.
c) Superficial pathway—blood returns from the external iliac veins to epigastric veins which drain into internal mammary and to the brachiocephalic veins.
d) Portal pathway—formed by internal iliac vein which drains into rectal veins and via the portal system which reaches into the systemic circulation.

We hypothesize that in case of IVC sarcoma due to chronic venous obstruction, one of these collateral pathways is developed allowing safe ligation of IVC after resection.

Reconstruction of IVC has been described in literature in the form of isolated case reports. There are no clear guidelines which are on the type of prosthesis to be used and the need for post-operative anticoagulation. Various options include (a) autologous tissue which includes superficial femoral vein, internal jugular vein, saphenous vein, pericardial graft, and cryopreserved vein graft and (b) prosthesis which includes PTFE and Dacron grafts. Study by Quinones et al. demonstrated 92% patency rate of graft at 5 years with no mortality and 2% graft-related complication rate [16]. At our center, patients undergoing graft reconstruction are started on anticoagulant in immediate post-operative period followed by oral anticoagulants. Oral anticoagulants are usually stopped between 3 and 6 months. Surgical techniques used to prevent thrombosis of graft include use of ringed graft, use of 14–16 size of graft, and arteriovenous fistula. Thus,

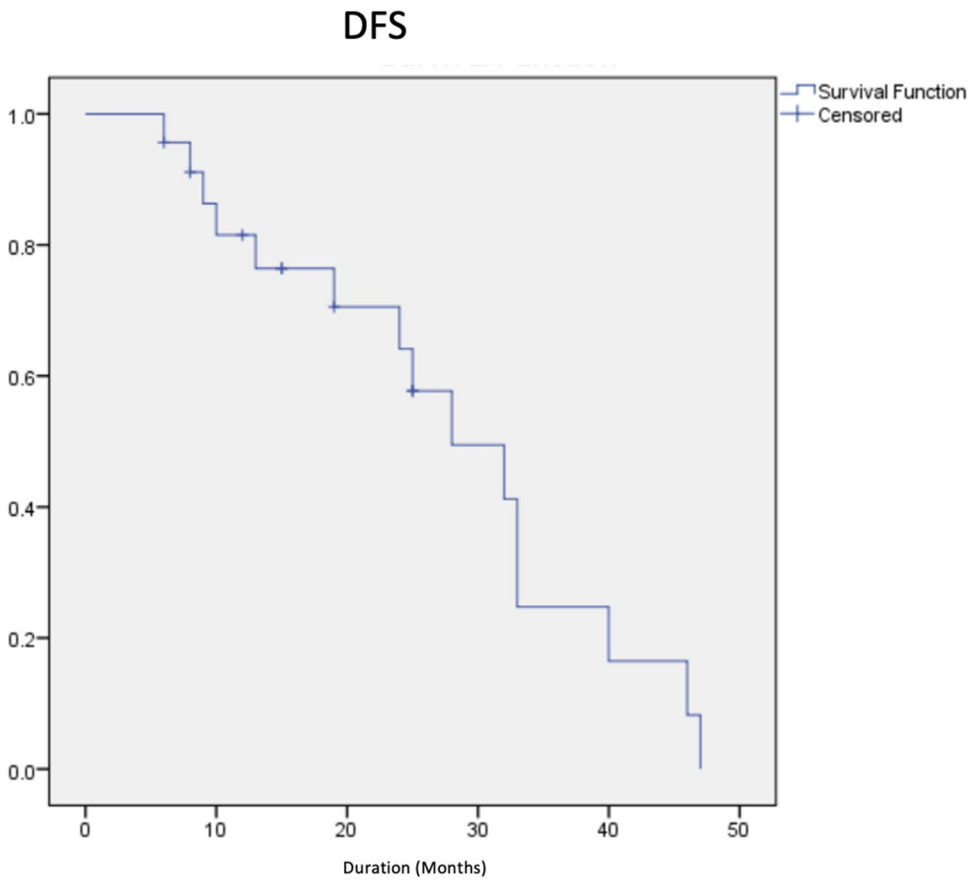

Fig. 4 Disease-free survival

prosthesis reconstruction is a feasible option if deemed necessary.

Major morbidity associated with IVC resection without reconstruction includes (a) lower limb DVT, (b) lower limb edema, and (c) renal failure. In our series, 2 patients developed DVT of lower limb in the immediate post-operative period and were managed conservatively with anticoagulation therapy. Both these patients had undergone resection without reconstruction of IVC. Also, one patient had symptomatic lower limb edema in post-operative period which was managed conservatively. None of these patients had functional impairment on follow-up at 3 months. In a series by Fiore et al., IVC resection with ligation was performed in 25% of the patients and it was observed that lower extremity edema was transitory phenomena and well-tolerated [17]. In our series, none of the patients developed acute kidney injury post-operatively requiring dialysis. We assume that normal preoperative renal function, presence of collaterals on imaging, and confirmation of outflow on intraoperative Doppler are sufficient to consider renal vein ligation without reconstruction especially for left renal vein.

In our series, one patient (4%) died in the perioperative period and 1 (4%) patients had Clavien-Dindo grade 3 or more morbidity. Pooled analysis of 377 patients reported by Wachet et al. showed a 30-day mortality of 1.9% (7 of 377 patients) and 30-day morbidity of 27.5% with most common being lower limb edema 10% followed by renal failure in 3.5% [9]. In our study, only 7 patients required IVC/iliac reconstruction. The most common reason for reconstruction was persistent hypotension after IVC clamping and extensive resection requiring resection of collaterals or damage during surgery. Hence, we propose IVC resection without reconstruction as a feasible option in order to avoid short- and long-term complications associated with graft in suitable cases.

Surgical resection aims at R0 resection; however, in literature, R1 resections are reported to be as high as 58% in case series published by Ito et al. [18]. In our study, R1 resection rates were 29% that is comparable to literature worldwide. R1 resection after gross total excision of tumor represents either aggressive biology of tumor or location of tumor adjacent to vital organs. All of our patients who had R1 resection on final histopathology report underwent adjuvant radiotherapy. Despite R1 resection in 7 patients, only 2 patients recurred locally on long-term follow-up. Interestingly, in literature, R1 resections have not always shown to affect the oncological outcome of the patient [19].

Compared to liposarcoma that tends to occur locally, LMS have the tendency to recur at distant sites. Wachet et al. have reported a median DFS of 12 months in a pooled

analysis of 377 patients while Joung et al. have reported a DFS of 23 months in a study of 8 patients, while in our series, median DFS was 28 months [9, 20]. In our series, 57% of the patients developed systemic recurrence while 9% of the patients developed local recurrence, which is comparable to study, published by Ito et al. [18].

Adjuvant and neoadjuvant treatment of IVC LMS is controversial with conflicting data in literature. Poor survival and rarity of the disease make developing level 1 evidence near to impossible. Since most of the patients fail systemically post R0 resection, there is an emerging role of chemotherapy in adjuvant or neoadjuvant setting. Also, STRASS 2 multicenter randomized controlled trial is looking at role of neoadjuvant chemotherapy followed by surgery versus surgery alone for high-risk retroperitoneal tumors.

Role of neoadjuvant radiotherapy has been already addressed by the STRASS trial, which failed to demonstrate its benefit for RPS [21]. Few studies in literature support the use of adjuvant radiotherapy in R1 resection; however, some benefit may also be achieved for R0 resection [22, 23]. However, the optimal timing of radiotherapy still remains a contentious issue. There is an unmet need to generate more evidence for adjuvant therapy, as most of the patients with LMS tend to fail at distant sites.

Conclusion

IVC sarcoma is a rare group of retroperitoneal tumors requiring multidisciplinary management. Surgical resection is often challenging, requiring multispecialty surgeons and a team approach. Careful preoperative multidisciplinary planning can make IVC resection without reconstruction feasible with acceptable perioperative morbidity, mortality, and oncological outcomes.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00423-021-02408-1.

Declarations

Conflict of interest The authors declare no competing interests.

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