ONCOLOGICAL PRINCIPLES IN THE SURGICAL TREATMENT OF PRIMARY RETROPERITONEAL SOFT TISSUE SARCOMAS

Retroperitoneal tumors are uncommon neoplasms which account approximately 15% of all soft tissue sarcomas. The aim of the study is to define the optimal principles in the surgical treatment of primary retroperitoneal soft tissue sarcomas.

Material and Methods: The present study includes 84 patients with retroperitoneal soft tissue sarcomas hospitalized and operated in Universal Hospital “Queen Joanna” and Specialized Hospital for Active Treatment in Oncology - Sofia between 2001-2012. We assessed several factors – patients’ demographics, tumor characteristics, type of treatment and treatment related outcome, 3- and 5-years survival. All data was analyzed with SPSS 19 (Kaplan-Maier methods, Cox-regression and the long-rank test, univariate analysis and comparison of studied variables). Results: In our study the median age was 55 years and 7 months. Radical surgery was carried out in 60.7% (51 patients) and combined resection of organs and/or blood vessels was needed in 35.7% (30 patients). Explorative laparotomies with biopsy or partial resections were performed in 39.3%. The goal of surgical resection was negative macroscopic margins and the adjacent organs were resected only in cases with certain infiltration. Metastases were detected in ~20% (17 patients) of the cases. Type of the operation is an important prognostic factor of survival. 3-year and 5-year survival rates were 48.2% and 36.6% in patients with retroperitoneal sarcoma. CONCLUSION: Surgical treatment is the only opportunity for cure to the patients with retroperitoneal sarcomas. Radical resection with macroscopically negative margins is an important prognostic factor.

Keywords: Retroperitoneal; soft-tissue sarcomas; retroperitoneal sarcomas; surgical treatment; prognostic factor

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Introduction

Retroperitoneal tumors are uncommon neoplasms which account approximately 15% of all soft tissue sarcomas (Jemal, Siegel, Ward, Murray, Xu, and Thun, 2007; Strauss and Hayes, 2010) Peculiarity in the diagnosis and treatment is result from the specificity of the retroperitoneal space - often close to or involving vital structures, relatively late clinical presentation when tumors are already large and locally advanced. The close relationship to major blood vessels limits the ability to perform a radical wide resection with tumor free margins. Local recurrence occurs in 40 - 80% of the cases (Lewis, Leung, Woodruff et al., 1998; Strauss and Hayes, 2010).

Seventy five percent of retroperitoneal sarcoma-related deaths were shown to be caused by local recurrence and progression of the disease (Lewis et al., 1998). Surgical resection is the main choice for treatment. Radical extirpation of the tumor is the only opportunity for cure. High rate of local recurrence clearly demonstrates the need of new treatment strategies - radio- and chemotherapy.
Material and methods

The present study includes 84 patients with retroperitoneal soft tissue sarcomas hospitalized and operated in Universal Hospital “Queen Joanna” and Specialized Hospital for Active Treatment in Oncology - Sofia between 2001- 2012. We assessed several factors - patients’ demographics, tumor characteristics, type of treatment and treatment related outcome, 5- and 5-years survival. Patients’ sex, age and duration of clinical symptoms were analyzed too. Tumors were characterized by their histological type, size, grade and presence of metastases. We used American Joint Comity of Cancer staging system for soft tissue sarcomas. The exact type of surgical technique and the need of combined organs or blood vessel resection were assessed. All data was analyzed with SPSS 19 (Kaplan-Maier methods, Cox- regression and the long-rank test, univariate analysis and comparison of studied variables).

Results

The study included 84 patients - 42 men and 42 women which determined ratio of 1:1. Retroperitoneal soft tissue sarcomas can occur in any age and in our study the median age was 55 years and 7 months. Those tumors are heterogeneous group with large histopathological diversity. Liposarcomas, followed by leiomyosarcomas and fibrosarcomas were the most common tumors. Other subtypes were extremely rare (Figure 1).

At the time of diagnosis retroperitoneal tumors were already large and only few of them were smaller than 5 cm due to the long asymptomatic period. In our study 56% of the cases were with tumor size between 11 and 20 cm. In only one patient tumor was less than 5 cm. Table 1 shows the distribution of patients according to the tumor size.

Tumor size affects the overall survival. Formation larger than 20 cm was a poor prognostic factor in the study (Figure 2).

Although tumors are often locally advanced and with large sizes at the time of diagnoses, they rarely metastasize. According to the literature only 11-12% of the retroperitoneal soft tissue sarcomas have metastases at the time of diagnosis (Strauss and Hayes, 2010; Pisters, 2009). Sarcomas rarely spread via the lymphatic
system - only 1-2% of the cases. In our study metastases were detected in ~20% (17 patients) of the cases - mainly in the liver (8 patients). In 6 patients we detected peritoneal metastases. Distribution of tumor grading showed that 36 patients were at G1, 24 patients - G2 and 24 cases - G3 stage. The analysis of the data showed that higher grade increased the frequency of metastases.

**TABLE 1**

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>No of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 cm</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>6-10 cm</td>
<td>6</td>
<td>7.1</td>
</tr>
<tr>
<td>11-20 cm</td>
<td>47</td>
<td>56.0</td>
</tr>
<tr>
<td>21-30 cm</td>
<td>23</td>
<td>27.4</td>
</tr>
<tr>
<td>&gt;30 cm</td>
<td>7</td>
<td>8.3</td>
</tr>
</tbody>
</table>

**FIGURE 2**

Cumulative Survival of the patients with retroperitoneal tumors according to the tumor size

**FIGURE 3**

Survival according to grading

**FIGURE 4**

Survival according to presence of lymphnode metastases
Each one of these factors was analyzed as a predictor of survival. Presence of metastases and tumor grading were the major prognostic factors. (Figures 3, 4) Radical surgery was carried out in 60.7% (51 patients) and combined resection of organs and/or blood vessels was needed in 35.7% (30 patients) (Figure 5). Explorative laparotomies with biopsy or partial resections were performed in 39.3%. The goal of surgical resection was negative macroscopic margins and the adjacent organs were resected only in cases with certain infiltration.

**FIGURE 5**

![Combined radical resections of retroperitoneal tumors](image)

**FIGURE 6**

![Postoperative morbidity (N of patients - 16)](image)

Observed mortality rate was 3.57% - 3 patients (equal to the literature data - 2-7%) and morbidity in 16 patients (14.68%). Figure 6 presents the most common postoperative complications.

Type of the operation is an important prognostic factor of survival. Patients with palliative operations or explorative laparotomies had poor prognosis (Figure 7). There was no benefit for overall survival in patients with explorative laparotomy.
or palliative operations. We did not detect any differences between patients with R0 or R1 resection.

**Figure 7**

Recurrence was found in ~ 40% (34 patients) of all cases with retroperitoneal soft tissue sarcomas. In patients with retroperitoneal sarcoma 3-year and 5-year survival rates were 48.2% and 36.6% respectively.

**Discussion**

At the time of diagnosis retroperitoneal sarcomas are locally advanced, with large tumor size in the most cases (McCallum, Burke, Childs, Ferro, and Gallup, 2006). Lewis et al. (1998) reported that over than 94% of these tumors are larger than 5 cm and over than 64% of cases are larger than 10 cm. According to Guiterrez et al. (2007), 1 of 5 tumors is larger than 20 cm (Guiterrez, Perez, Franceschi, Moffat et al., 2007). These malignancies can achieve sizes even over 50 pounds (Strauss and Hayes, 2010).

Radical surgery provides the only opportunity for cure (Dalton, Donohue, Mucha, van Heerden et al., 1989). The goal is the achievement of macroscopically negative resection margins (Lewis et al., 1998; Strauss and Hayes, 2010). This is often challenging because of the displacement of adjacent structures by the tumor, the close relationship to vital blood vessels and the involvement of the surrounding structures and organs. Practically the exact exploration for blood vessel infiltration behind the tumor is impossible because of the large tumor size so the adequate control over the blood vessels is hard to be achieved.

In the recent years several studies reported results from the performance of radical operations called liberal visceral en bloc resections with an envelope of normal tissue around the tumor (Strauss and Hayes, 2010). The treatment goal is the removal of the tumor along with the adjacent organs or parts of them with avoidance of tumor spilling. Another more radical direction is the compartmental resection of the tumor in which there is complete removal of surrounding tissues and organs and blood vessels and nerves in some cases (Gholami, Jacobs, Kapp, Parast, and Norton, 2009). The data of these studies are quite controversial. Pisters (2009) is one of the authors who widely criticizes this approach and pays attention to the methodology (Pisters, 2009). Despite of the lower recurrence rate reported after that surgical resection it is noted that these studies have short
follow-up period and better survival is not really assessed (Strauss and Hayes, 2010).

The concept of compartmentalization that is typical to limb sarcomas is difficult to be achieved in cases with retroperitoneal sarcomas. Although it is clear that certain structures were liberally resected in these cases, other structures intimately associated with the tumor (aorta, inferior vena cava) were not resected. So it is not possible to perform a radical resection that could provide a wide margin in all directions because of the close relationship to vital blood vessels (aorta, IVC, superior mesenteric artery, portal vein), important organs that are difficult for resection (duodenum, pancreas, liver), bones (spine, pelvis), muscles and nerves. Commonly a limiting factor is the reduced vital capacity of the patient. The assessment of the achieved microscopically margins is extremely difficult because of the fact that tumors have large sizes and wide surfaces. Several studies reported that there was no difference between survival rates after R0 and R1 resections and in other studies related to prognostic survival factors these types of resection were been united (Anaya, Lev, and Pollock, 2008; Brennan, 2007; Stojadinovic, Leung, Hoos, Jaques et al., 2002).

We support the state that the treatment goal is the achievement of macroscopically negative margins and the resection of adjacent organs has to be performed only in cases with their certain infiltration and dysfunction. Radical tumor resection significantly improves the long-term results - 5-year survival was achieved in 54-70% (van Dalen, Plooij, van Coevorden, van Geel, Hoekstra et al., 2007; Catton et al., 1994; Storm, Eilber, Mirra, and Morton, 1981; Stoeckle, Coindre, Bonvalot, Kantor et al., 2001; Zornig, Weh, Krull, Schwarz et al., 1992; Heslin, Lewis, Nadler, Newman et al., 1997). 41-50% of these patients will recur for a period of 5 years and about 40% of them - until 10 years after the operation (McGrath et al., 1984; Jemal et al., 2007; Pierie, Betensky, Choudry, Willet, Souba, and Ott, 2006; Lewis and Brennan, 1999). Despite of the low metastatic potential the overall 5-year survival was 33-39% (Jemal et al., 2007). This can be explained with the high percentage of local recurrences which are the reason for death in 75% of these cases (Pierie et al., 2006; McGrath et al., 1984; Karakousis, Velez, and Emrich, 1985; Jemal et al., 2007; Jaques, Coit, Hajdu, and Brennan, 1990; van Dalen et al., 2007).

A multivariable study of prognostic factors showed that grading, metastases and achieved radical resection were very important to survival. Blood vessel involvement significantly reduced survival. Because of this several authors suggest that vessel resection is obligatory in cases with their involvement even the tumor cannot be separated from them (Schwarzbach et al., 2006).

High incidence of local recurrence and poor prognosis show the necessity of additional treatment methods supporting the surgery. The efficacy of radiotherapy is clear in patients with extremity sarcomas. In cases with retroperitoneal sarcomas there are some problems (Strauss and Hayes, 2010; Feng, Murphy, Griffith, Sondak et al., 2007; Yang, Chang, Baker et al., 1998; Cheifetz, Catton, Kandel, O'Sullivan et al., 2001; Goffman, Tochner, and Glatstein, 1991).

Tumors are often large and close to organs and structures with high sensitivity to radiation. One of the major limiting factors is difficulty in delivering sufficient radiation dose because of toxicity to adjacent organs including bowel, kidneys, liver and spinal cord. In the recent years there have been studies that reported results from the performance of preoperative radiotherapy separately or combined with intra- or postoperative radiotherapy which lead to graduate increase of overall dose (Alektiar, Hu, Anderson, Brennan, and Harrison, 2000; Bossi, De Wever, Van Limbergen, and Vanstraalen, 2007; Catton et al., 1994). The preoperative radiotherapy or combined with intraoperative one has been increasingly recommended so the adjuvant radiotherapy has been left behind. There are no
previous large randomized studies about this problem. The role of radiotherapy is considered to be proven in local recurrence control but overall survival has not been improved (Hassan et al., 2004; Tepper, Suit, and Wood, 1984; Fein, Corn, Lanciano et al., 1995; Strauss, Hayes, Thway, Moskovic et al., 2010; Yang, Chang, Baker et al., 1998; Zlotecki, Katz, Morris, Lind, and Hochwald, 2005).

The therapeutic possibilities of chemotherapy are now investigated and results for different chemosensitivity of the subtypes of retroperitoneal sarcomas are already published. Chemotherapy is not routinely used except in cases with unresectable tumors or in patients included in clinical trials (Grimer, Judson, Peake, and Seddon, 2010).

**Conclusion**

Surgical treatment is the only opportunity for cure to the patients with retroperitoneal sarcomas. Radical resection with macroscopically negative margins is an important prognostic factor. Radical compartmental resections and liberal en bloc resections do not improve the survival and lead frequently lead to complications. Despite of the different surgical methods the incidence of local recurrence and poor prognosis remain high which show the need of complex and multimodal approach to these tumors.

**References**


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