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Primitive retroperitoneal tumors. Vascular involvement - a major prognostic factor

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Rezumat

Tumorile retroperitoneale primitive. Implicarea vasculară - factor major de prognostic

Tumorile retroperitoneale primitive, deși foarte rare, suscită un interes ridicat datorită prognosticului prost, rezultatelor chirurgicale cât și ale terapiilor complementare nemulțumitoare. Numărul foarte redus de cazuri a împiedicat obținerea până acum a unei viziuni unitare privind aceste tumori, neexistând un algoritm unanim acceptat de diagnostic și tratament. Nu au putut fi efectuate trialuri randomizate privind efectele diverselor terapii. Principalul factor care poate crește fundamental supraviețuirea acestor pacienți este rezecția radicală, unii autori chiar recomandând chirurgia compartimentală. Nu am descoperit nicio diferență statistică semnificativă între ratele de supraviețuire ale pacienților cu diverse tipuri de intervenții neradicale, care ar trebui deci, pe cât posibil, evitate. Studiul efectuat de noi evidențiază că implicarea vasculară este principal factor limitator în obținerea radicalității. Implicarea vaselor mari retroperitoneale face adesea imposibilă o rezecție radicală, în general datorită absenței unei dotări materiale și umane adecvate practicării unor rezecții vasculare ample urmate de reconstrucții laborioase. De aceea, în studiul nostru, implicarea vasculară a fost asociată cu reducerea ratei de supraviețuire la pacienții operați. Subliniem în acest context necesitatea atât a furnizării unei baze materiale consistente cât și realizării unor echipe chirurgicale multidisciplinare pentru a face posibile intervenții vasculare adecvate în chirurgia generală oncologică.

Cuvinte cheie: tumora retroperitoneală, implicare vasculară, rata de supraviețuire, radicalitate, predictor, recurență, sarcom retroperitoneal

Abstract

Primitive retroperitoneal tumors, although very rare, arouse an increased interest, because of the poor prognosis, unsatisfactory surgical and complementary therapy results. Up to now, the very low number of cases has impeded the acquisition of a unitary view of these tumors, a unanimously accepted algorithm of diagnostic and treatment being absent. Randomized trials regarding the effects of different therapies have not been possible. The main factor that can fundamentally increase the survival of these patients is radical resection, some authors even recommending compartmental surgery. We found no significant statistical difference between the survival rates of the patients with different types of non-radical interventions, that shoud be therefore, as much as possible, avoided. Our study evidences that vascular involvement is the main limiting factor in achieving radicality. The involvement of large retroperitoneal vessels makes often impossible a radical intervention, usually because of the lack of an adequate material and human endowment for ample vascular resections followed by laborious reconstructions. That is why, in our study, vascular involvement was associated with a decreased survival rate for operated patients. Therefore, we underline the necessity both of a solid material base and of establishing multidisciplinary

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surgical teams for adequate vascular interventions in oncologic general surgery.

Key words: retroperitoneal tumor, vascular involvement, survival rate, radicality, predictor, recurrence, retroperitoneal sarcoma

Introduction

Retroperitoneal space constitutes an enigmatic land, "lacking a precise, accepted map" (1), being able to hide a large variety of pathologies, from inflammatory processes to diverse tumor forms (2). Primitive retroperitoneal tumors are extremely rare, representing approximately 0.2-0.6% of all neoplasias (3,4,5). The majority are malignant (80% malignant, 20% benign), retroperitoneal sarcomas and lymphomas being predominant, but carcinomas and tumors derived from embryonic tissues, especially urogenital, can also be found (6,7,8). There are several classification systems of these tumors, their accurate identification and classification holding a special importance for an optimal treatment (3). Retroperitoneal tumors represent a heterogenous group, but frequently they present significant histopathologic similarities, that impede a specific correct therapeutic approach of different forms of neoplasias. Due to their development into such an easy distensible space, lacking clear limits, retroperitoneal tumors are characterised by an insidious growth, reaching large, even gigantic dimensions, until they generate unspecific symptoms and are diagnosed (9,10). The symptomatology is caused by tumor extension, with direct involvement by invasion or indirectly by compression of nearby retroperitoneal or peritoneal structures (11-13). Delayed diagnosis of these tumors, with neighbouring structures involvement, increases the complexity of the surgical intervention, but also is associated with unsatisfactory distant results (14,15). Sometimes, these cases arrive in already surgically and medically outrun stages. Tumor localization into the retroperitoneal space brings a major ill-fated prognostic element due to the big associated visceral and vascular risks and to the difficulty of achieveing a radical negative-margin resection at this anatomic level. Currently, the only treatment considered to significantly increase the prognosis of patients with malignant retroperitoneal tumors is radical resection, with negative margins (9,16-18). There are still controversies regarding the type of radical resection, some centres being the promoters of an extremely aggressive surgery, reaching a compartment surgery, where uninvolved visceral and vascular structures situated in the vicinity of the tumor are resected along with the tumor (19-23). For benign tumors, a complete tumor excision is considered to be sufficient (6). The utility of radio- and chemotherapy is subjected to an intense debate (24-27), excepting malignant lymphomas known to be sensitive to these therapies. Retroperitoneal tumors, even benign forms, associate a high recurrence rate after a radical excision, especially in the first two years following the operation, metastatic rate being of approximately 20% (15). Global survival rate of these patients is low, being of 50-75% at 5 years, mortality in operated patients being caused by multiple, more and more aggressive recurrences, that become, in the end, unoperative (12,25). The extreme rarity of these tumors has impeded, up to now, the acquisition of satisfactory knowledge on their biological behaviour, the achievement of randomized trials in relation to the different forms of surgical and complementary types of treatment, and the concordance upon a unanimously accepted staging, diagnostic and treatment algorithm between centres (16,25,27-31). This explains the large diversity of results reported by different centres, having various degrees of experience with the management of these tumors. Additionally, due to the low prevalence of these tumors, there are insufficient information regarding a differentiated surgical approach for tumors with vascular involvement. In our study, we tried to identify the predictors of a higher global and free-disease survival in operated patients, to evaluate the impact of vascular involvement and to interpret the results of complementary therapies of the patients having retroperitoneal tumors.

Patients and methods

We have carried out both a retrospective (1999-2008) and a prospective study (2009- September 2011), on a group of 41 patients having the diagnosis of primitive retroperitoneal tumor, treated in the First Surgical Clinic, Bucharest Oncology Institute. These patients have been selected from a larger group of 144 patients with extra-digestive primitive and secondary retroperitoneal tumors, treated in the same period. A series of variables has been subjected to statistical analysis: describing patient characteristics, the tumor (primary/ recurrence, dimension, histopathologic type), the impact of visceral and vascular involvement, the impact of precocious or late diagnosis (after a long period of subjective complaints), regarding medical imaging tools and their diagnostic value, the complexity of the surgical intervention (type of operation, surgical approach, resected visceral and vascular structures, the duration of the intervention, intraoperative complications and their management), postoperative complications and their treatment, hospitalization period and period of stay in the intensive care unit, complementary treatments, patient follow-up, records of recurrence and metastases.

Statistical analysis has been performed with the use of Microsoft Excel 2003 and EpiInfo 3.5.1. software, with a descriptive analysis of the data and their type of distribution. Kaplan-Meier estimations of survival rate from the operation date with a 95% Rothman confidence interval have been made. Log-rank test has been useful in comparing survival time distributions between several groups of patients. Factors that have proved to have a significant influence on survival have been included into a multivariate analysis of survival predictors. In all cases a p value less than 0.05 has been considered to be significant.

Results

Primitive retroperitoneal tumors represented only 28% of the total number of extra-digestive primitive and secondary retroperitoneal neoplasias. The medium follow-up period of operated patients was of 36.65 months with a median of 29.5 months, with extreme values of 1.34 and 143 months. An approximately equal involvement of the two sexes by retroperitoneal tumors was registered, with a women/men ratio of 1.05/1 (49% men, 51% women). The most affected age category was of 51-60 years, followed by 61-70 years, the least involved being that of 71-80 years. Patient medium age was of 51.6 years, with a minimum of 22 years and a maximum of 79 years, and a median of 54 years.

In the primitive retroperitoneal tumors group, at the initial presentation to our clinic, only 34 patients had a primary tumor, the rest complaining of tumor relapses after apparently radical surgical interventions(4 cases - first recurrence; 1 case - second recurrence), 2 patients addressing to our clinic after surgical exploration of the primitive retroperitoneal tumor and palliative interventions in other hospitals. Of the 41 patients, only 35 (85.36%) were operated, the remainder refusing a surgical intervention or being considered inoperative due to the advanced tumor stage or due to significant comorbidities counterindicating the operation (4 cases - 9.75% of all cases). The most frequently operated age group was that of the most frequently affected patients, followed by that of 21-30 years. Some of patient and tumor characteristics are summarized in *Table 1*.

The most frequent symptom bringing the patient to the doctor was pain, in 78.04% of cases, followed by digestive complaints (54% of patients) and the perception of a tumor in 29.26% of cases. Digestive complaints consisted of: intestinal transit change in 11 cases (acceleration, slowing or absence of intestinal transit), vomiting - 5 patients, inappetence - 5 cases, dysphagia - 1 case. In 9 patients general signs were noticed: weight loss between 2 and 5.67 kg/month unaccompanied by appetite alteration, profuse sweat - 1 case. More seldom, manifestations of vascular involvement like edema were remarked - 7.31% of patients, symptoms related to neurologic involvement (motor and sensitive deficits of lower limbs) - 9.75% of patients, urinary manifestations- haematuria, anuria - 4.87% of patients. The persistence of the symptomatology until patient presentation to the doctor varied from 1 week to 4 years. For sarcomas, in the majority of cases, the symptomatic period until patient addressed to our clinic had been more than 6 months.

From the diagnostic tools that were used, abdominopelvic CT with contrast media, MRI and abdominopelvic echography have proved of special value in specifying retroperitoneal tumor presence, localization, vascular and visceral involvement. Although MRI was a less frequently used investigation (in only 5 cases), it represented a high accuracy investigation, in all cases evidencing the tumor and its concomitent metastases and in one case even suggesting tumor histopathologic type. The degree of use of abdominopelvic echography has decreased in favour of CT. CT with contrast media offers consistent detail on tumor relationship to vascular and visceral structures. Preoperative diagnosis of tumor vascular involvement has been applied in 29 cases, of which: in 26 cases based on CT, in 2

Table 1. *Patient and primitive retroperitoneal tumor characteristics*

Operated patients with retroperitoneal tumors	**Number** 35	**Histopathologic benign tumor types**	**Number**
- with primary tumor	30	serous cysts	2
- with a recurrence	5	lipomas	1
		myxoid fibrous lipoma	1
		benign mesenchymal proliferation	1
		inflammatory connective tissue proliferation	1
Follow-up period of operated patients	(months)	tumor dimension	
medium	36,65	medium	15,11 cm
median	29,5	median	15 cm
extreme values	1,34-143	extreme values	2-30 cm
Gender	Number	Vascular involvement	
- masculine	18	- with vascular involvement	19 cases
- feminine	17	- no vascular involvement	16 cases
		Type of blood vessel involvement	Number
		- only arterial	2
		- only venous	1
		- both arterial and venous	16
Histopathologic types of malignant tumors	Number	Visceral involvement	Number
sarcomas	16	- with visceral involvement	29
carcinomas	5	- without visceral involvement	6
malignant lymphomas	3		
malignant - undetermined	2		

cases- only on MRI and in one case based on both CT and echography. In 34.61% of cases (9 patients), medical imaging (CT) has overestimated (5 patients) or underestimated (4 cases) the degree of vascular involvement ascertained intraoperatively. Tumor dimension (maximal diameter), as determined by pre-operative imaging, has correlated well with the actual tumor size discovered intraoperatively, with a correlation index of 0.877.

The majority of operated tumors were malignant (74.3% of operated tumors), benign/malignant ratio being of 1/ 4.34. A substantial percent of 8.6% of undetermination of the histopathologic type can be remarked. Histopathologic types of benign tumors were: serous cysts - 2 cases, lipoma-1 case, myxoid fibrous lipoma - 1 case, a benign mezenchymoma, one case of inflammatory proliferation of connective tissue. Between malignant tumors, sarcomas have predominated, representing 61% of the malignant tumors (16 cases), followed by carcinomas (19% cases), lymphomas (12% cases) and undetermined malignant tumors (37.5% cases) (*Table 1*). The most frequent types of sarcoma were : unclassified sarcomas - 37.5% cases, fibrosarcomas - 31.3% of sarcomas, those of G3 type being predominant. The most of operated tumors were larger than 10 cm (88.6% cases), in 60% cases having between 15 and 30 cm. Medium tumor size was of 15.11 cm, with extreme values of 2 and 30 cm. The majority of sarcomas had a maximum diameter of more than 10 cm.

In 34 cases the surgical intervention was classical and in one case there was a laparoscopic intervention. The preferred surgical approach was median laparotomy in 29 cases, in the remainder of the cases infracostal (3 cases), left pararectal (1 case) and lumbar incisions (1 case) being performed. Radical resection was possible in only 37% of cases, in the majority of the situations tumor biopsy being accomplished (46% cases) *(Fig. 1)*. In the remainder of the cases tumor debulking-11% of patients and simple exploratory laparotomy-6% patients were done. Radical excision was most frequently possible in the case of sarcomas and it was most rarely achieved in lymphomas, undetermined histopathologic type and undetermined malignant tumors *(Fig. 2)*.

In 100% of operated cases, vascular involvement by the tumor has constituted the reason for the impossibility of radical excision. In 54.54% of these cases vascular involvement has represented the sole impediment of unresecability, in the remainder of the situations, along with vascular causes, multiple organ involvement by the tumor, invasion into vertebral column and concomitent hepatic metastases have also contributed. Statistically, resecability has depended significantly only on the presence or not of vascular involvement, presentation as primary/recurrent tumor and has been higher in female patients. Only in 19 cases there was a real direct vascular involvement by the tumor in the form of invasion, compression, dislocation, or inclusion. In 16 cases there was a double, arterial and venous direct involvement, in 2 cases - only arterial and in 1 case only venous involvement *(Table 1)*.

In the attempt to achieve a radical excision, in 22.9% of operated cases (9 patients) resections of organs along with the primary tumor were done. The most frequently sacrificed organ was the kidney (30% of cases), followed by the

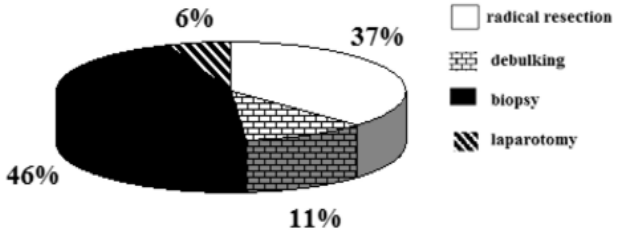

Figure 1. *Types of surgical interventions in the treatment of primitive retroperitoneal tumors*

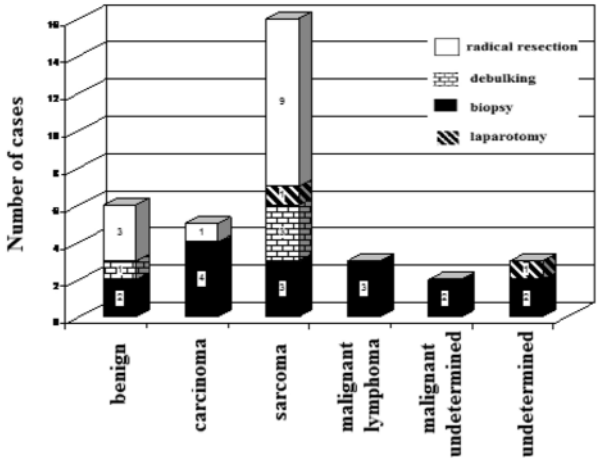

Figure 2. *Surgical interventions practiced for different histopathologic tumor types*

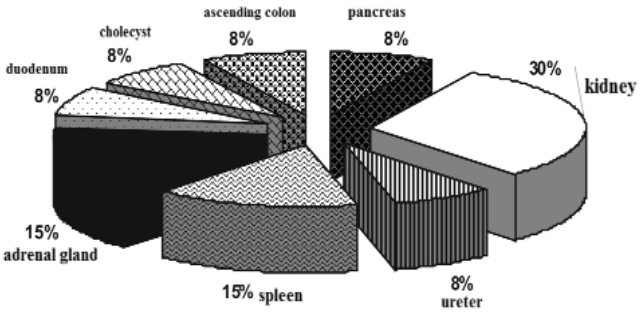

Figure 3. *Organs resected en bloc with the tumor*

adrenal gland (15% of cases) and the spleen (15% of cases). Other resected organs were: the ureter, pancreas, duodenum, ascending colon, gall bladder *(Fig. 3)*.

In 20% of the operated cases there were intraoperative complications of either haemorraghic nature or related to digestive tube lesions. An important intraoperative haemmorhage has been caused by: inferior cava vein lesion (1 case) which necessitated suture with separate threads, haemmorhage from tumor

Table 2. *Local and regional complications after retroperitoneal tumor surgery*

Local and regional complications	Number of cases
Hepatoenteric fistula with choleperitoneum external biliary fistula	1
High flow rectovaginal fistula, with vaginal and ureteral necrosis, uroperitoneum	1
Cholecystogastric anastomosis dehiscence with peritonitis	1
Intestinal subocclusion	2
Lumbosacral plexus fiber lesion with sensitive and motor deficit	1
Lower limb edema	1
Profound thrombophlebitis	1
Proctorrhagia from sigmoid polyps	1
Upper digestive haemorrhage	1

Table 3. *General complications after retroperitoneal tumor surgery*

General complications	Number of cases
Jaundice	2
Arrhythmia-paroxysmal atrial fibrillation	1
Hepatic failure	1
Respiratory failure	1
Septic shock	1
MSOF	1
Death	1

bed after complete tumor excision or from hypervascularized tumor during biopsy, managed by meshes, haemostatic sponges or powder. Precocious postoperative complications rate (during the first month postoperatively) has been of 34.28%, 28.57% of complications being in the first week postoperatively. Between the major complications, we can remark especially anastomotic dehiscences, managed by surgical reinterventions (*Table 2* and *3*). Surgical reintervention rate was of 14.28% and mortality rate in the first postoperative month-2.86%.

5-year survival rate for all operated patients was of 14%, 50% of these patients having a medium survival of 10 months postoperatively *(Fig. 4)*. Instead, 5-year global survival rate estimation for radically operated patients was of 34%, 50% of these patients surviving 35 months postoperatively, having a significantly higher survival than the patients with biopsy, simple laparotomy and debulking interventions *(Fig. 5)*. Between unradical surgical interventions there were no significant differences in the 5-year global survival rate. From the big number of variables subjected to statistical analysis, predictors of a significantly higher global 5-year survival rate have proved to be: lack of tumor vascular involvement *(Fig. 6)*, higher duration of the surgical operation, more than 120 minutes versus shorter interventions, the absence of patient significant comorbidities, female gender (males having a 3.23 higher risk of death than females) *(Fig. 7)*, presence of recurrences or metastases *(Fig. 8)*, adjuvant radio- and chemotherapy, histopatholgic type other than "undetermined", that has been associated with a 5.75 higher risk of death than the other histopathologic types. All the other variables, related to the tumor, patient or the type of surgical intervention have not proved to be significant predictors in the global survival analysis of these patients. In the group of radically operated patients the estimation of the 5-year free-disease survival rate was of 49.5%, with a 5-year recurrence rate of 50.5% *(Fig. 9)*. Female gender was associated with a 16.15 lower risk of recurrence comparatively with male gender. In operated patients, 1 to 3 recurrences were recorded that appeared from 4 to 42 months postoperatively. In 22.9%

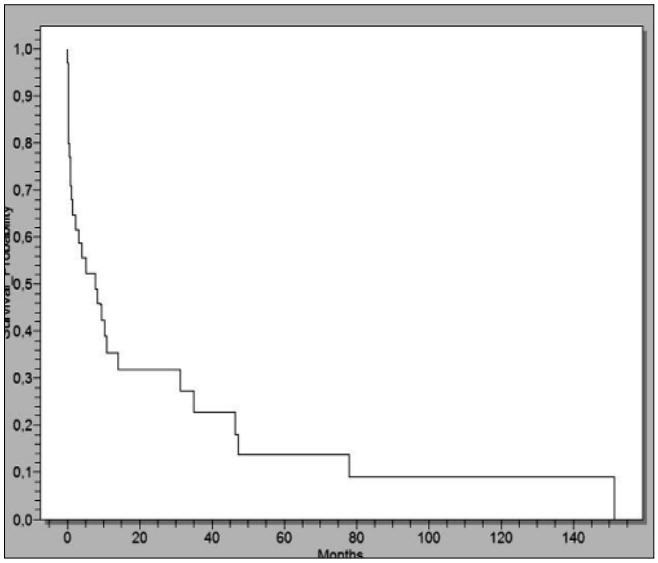

Figure 4. *5-year survival for the entire group of operated patients with primitive retroperitoneal tumors*

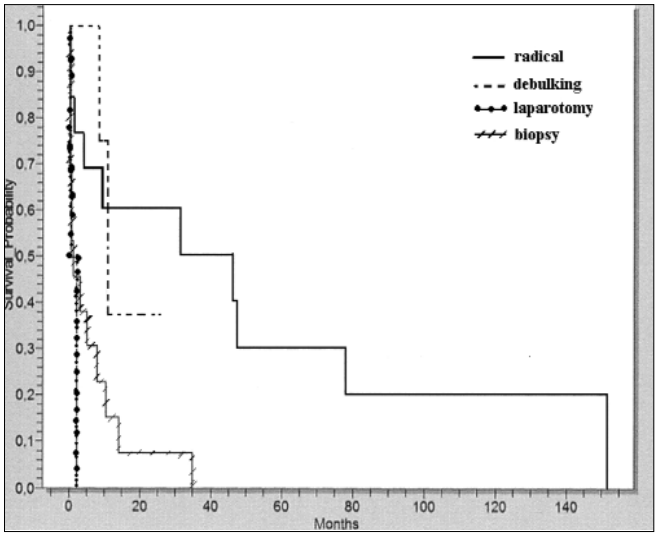

Figure 5. *5-year overall survival for operated patients depending on the type of surgical intervention*

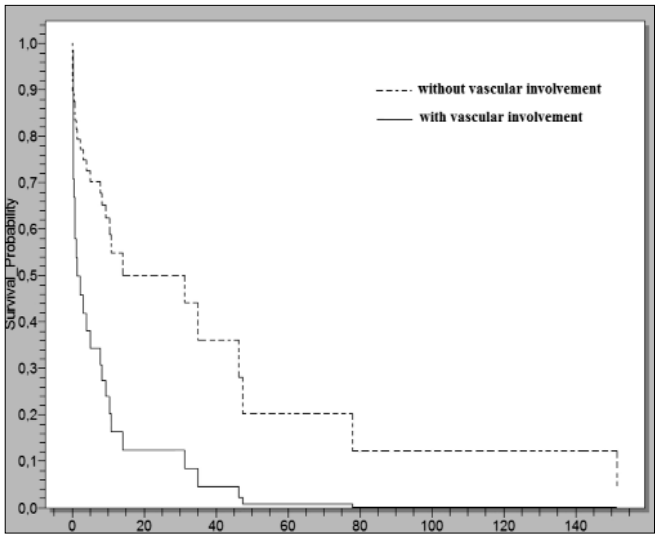

Figure 6. *Patient survival probability in case of vascular involvement by the tumor*

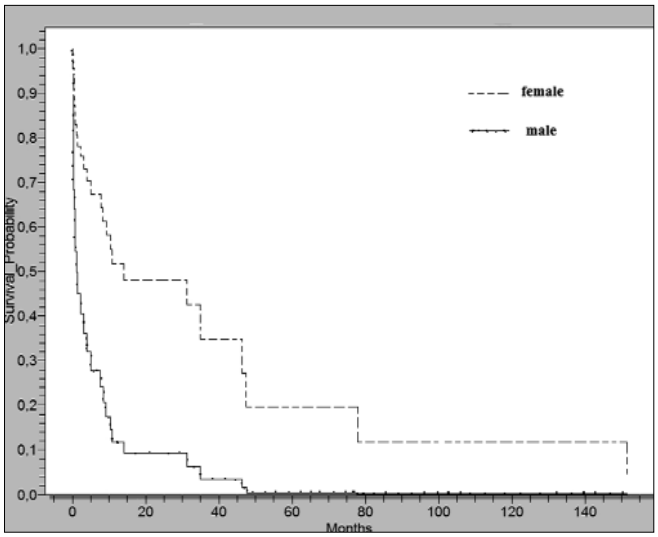

Figure 7. *5-year survival rate of operated patients is different for the two genders*

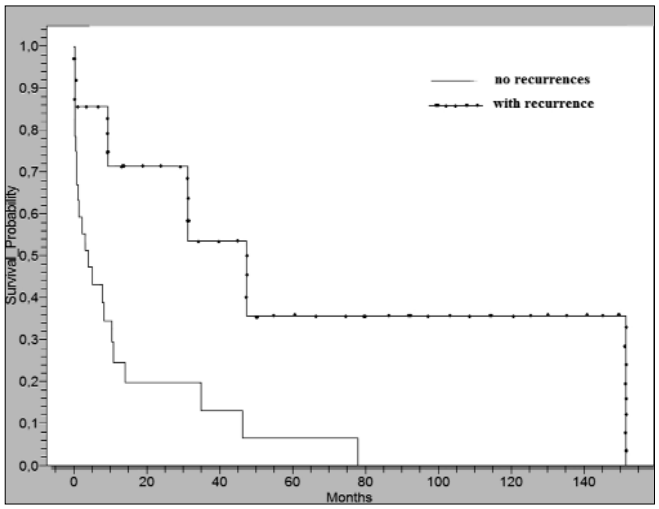

Figure 8. *The paradox of recurrences*

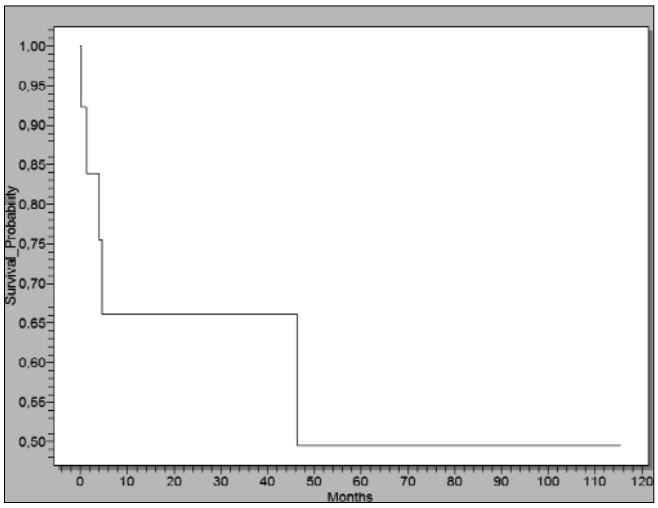

Figure 9. *5-year free-disease survival rate for operated patients (Kaplan-Meier estimation)*

patients metastases have also been recorded, the majority in the retroperitoneum, but also pulmonary, hepatic, ganglionic, parietal abdominal and peritoneal.

Discussions

Although very rare, primitive retroperitoneal tumors generate a special interest due to the associated extremely low global and free-disease survival, the complexity of the surgical treatment and the high rate of recurrence after a radical operation that constitutes a frequent cause of death. The limited number of cases and the retrospective character of the studies on these tumors is a major limiting factor of the statistical power of the results reported by various centres. To accumulate a higher number of cases, statistical analysis is performed on long periods of time, impeding the attempt to make a comparison between cases and among centres, if we take into account the dynamics in the imaging techniques, histopathological interpretations or in the surgical experience that naturally occur in time. The very low incidence of these tumors has been an obstacle for randomized trials concerning different forms of therapies, bringing an explanation for the lack of a concord, a unanimously accepted diagnosis, treatment and follow-up protocol in these cases (16,25,27,29,30).

In our study, the majority of patient characteristics (relatively equal involvement of the two genders, with a slight predominence in women, the most frequent affected age category), but also many tumor characteristics (the major frequency of sarcomas, impressing dimensions, vascular and visceral involvement) are simmilar to the reports of the majority of authors (2,12). Although the second affected age category was of 61-70 years, however, the second most

operated age group was that of 21-30 years. The most frequent tumors were malignant, with a malignant/benign ratio of 4.3/1, superposable over specific literature data (2,6). Sarcomas predominated, but a particularity of the analysed group was the higher percent of carcinomas relatively to lymphomas. The finding of a significant 8.6% percent of undetermined histopathologic tumors, but also of malignant undetermined forms (8%) underlines the difficulty of histopathologic identification of these extremely heterogenous, yet very simmilar tumors. The impossibility of histopathologic differentiation of these tumors represents an aditional impediment to a specific adequate treatment (12). In future, the identification of specific tumor markers for various histopathologic forms (as already observed by us for chondrosarcomas where there is an increase in alkaline phosphatase activity during tumor activity), as well as the large scale use of genomic and molecular techniques will significantly improve the management of these tumors, but also will allow a faster diagnosis and even the implementation of population screening. A preoperative histopathologic tumor type determination would be ideal, because it would allow the avoidance of unnecessary surgical interventions. In our group of patients, CT-guided core-needle biopsy was performed in only two cases, in one the histopathologic diagnostic being confirmed by the analysis of tumor resection piece and in the other-the diagnostic being uncertain. The limited use of preoperative core-needle biopsy is explained by the risks associated with this manoeuvre, but also by the incomplete character of information brought by this investigation. A tumor of a large size can present several histopathologic characteristics through its different sectors and preoperative core-needle biopsy can be misleading (6). However, the diagnosis of malignant lymphomas by these techniques, without a useless aggressive surgical intervention would be desirable (33). Currently, there are numerous imaging clues regarding the various histopathologic types, such as the degree of CT attenuation, the types of MRI signal, captation of contrast media or spontaneous contrast (4,34), but the exploitation of these information has not been integrated into clinical thinking yet. In our study, in the majority of cases, the preoperative diagnostic of tumor has been made on CT, echography and MRI data. We discovered that in cases where radical resection was not possible the main cause has been tumor vascular involvement. The discovery that in 34.61% of cases there was a certain degree of discordance between the level of vascular involvement shown by imaging data and the intraoperative reality impedes us to classify as unoperative a tumor based only on imaging data. Surgical strategy is dependent on acquiring detailed imaging data in several planes and on 3-D reconstructions, as accurate as possible, to gain insight into tumor vascular and visceral relationships. The final diagnosis of primitive retroperitoneal tumor, as well as of histopathologic type, can be achieved only by surgical intervention with the complete examination of the tumor resection piece. There is an important difficulty in examining surgical margin limits, because, in such tumors having more than 10 cm diamters, the work of the histopathologist becomes overwhelming. The finding that ''undetermined '' histopathologic type [where radical excision along with a complete tumor resection piece examination were impossible, as also described by other centres (17)] is associated with a 5.75 times higher risk of death than benign type, becomes a stimulus to search methods to improve histopathologic identification, that could also increase the prognostic of these patients.

The preferred surgical approach was median laparotomy, that offers a maximum exposure of these gigantic tumors (12). It is already known that a small incision, even though more esthetic, can offer a false impression of unresecability (3,17). The small rate of tumor resecability has been registered in the context of vascular involvement of: inferior vena cava, aorta, illiac vessels, celiac trunk, mesenteric arteries, renal and splenic vessels, portal vein, as reported by others (5). In the past, vascular involvement by the tumor was considered one of the counterindications of surgical resection. In many centres, now, it is already accepted that in case of vascular involvement by retroperitoneal tumors, ample multiple vascular sacrifices followed by complex arterial and venous reconstructions must be done. The effectuation of such vascular resections, permitting the accomplishment of radicality, does not decrease survival rate of operated patients by comparison with those with no vascular involvement (16,18,32). That is why we consider that the establishment of specialized centres for multidisciplinary treatment of retroperitoneal tumors (as we can already find in some countries for sarcomas), with the obligatory presence of a vascular surgeon, but also of urologists, surgeons specialized in digestive operations, neurosurgeons (in case of tumor invasion into the conjugation holes), radiotherapists (to apply intraoperative radiotherapy in selected cases) in the surgical team is strongly required. The lack of vascular synthetical grafts, special suture materials and even of extracorporeal circulation systems, justify why, in such cases, not only the lack of a vascular surgeon specific experience represents a limitation, but, even more, the lack of a satisfactory endowment for the surgical management of these tumors is a major obstacle.

5-year survival rate for all operated patients (radically and unradically) was low, of 14% at 5 years, at the lower limit of the interval reported in specialized literature (2,8,33). No significant difference between the survival rates for the patients with benign or malignant tumors has been noticed, because the resecability of these tumors has not been different. Even an apparently innocent histopathologic type, due to the presentation at an advanced stage, with vascular and visceral affection can be associated with an unfavourable prognostic. The only factor that has fundamentally improved survival rate has been represented by radical resection, even with the price of visceral sacrifices. The reported resection rate of organs adjacent to the tumor by different centres varies between 30 and 93% (2,12). 5-year survival rate for radically operated patients was of 34%, significantly higher than that of patients with non-radical interventions. The lack of a a significant difference between the survival rates of the patients where biopsy, debulking or simple exploratory laparotomy have been done, urges us to consider as unadvisable such operations that additionaly associate specific complications, bringing physical,

moral and material costs to the patient and hospital. The observation of a lower five-year survival rate for patients with significant associated comorbidities justify the rigurous selection of the cases that should be operated. Instead, patient age has not influenced survival rate. Although the number of female patient has been slightly higher, masculine gender has been associated with a 3.23 higher risk of death than feminine gender in which resecability was more often possible. We could not find many simmilar observations in the reports of other centres. We have not been able yet to identify factors to explain such a significant difference between the survival of the two sexes in the group analysed by us.

In the group of patients with long surgical interventions, of over 120 minutes, there was a surprisingly higher survival rate than in the case of short surgical interventions, although we had expected a contrary finality due to associated complications. In fact, the longer operations represented radical interventions, already found to be a major element to increase the survival rate of these patients. The rate of perioperative complications and precocious postoperative mortality are simmilar to those given by other centres (25). Vascular involvement, impeding the achievement of a radical intervention, represented a predictor of a shorter survival of these patients, as others have noticed too. We found a recurrences paradox. The univariate statistical analysis apparently suggested that the occurrence of a recurrence increased overall survival for these patients. In fact, a longer survival makes possible the expression of relapses and metastases, the high tendency to recurrence of both the malignant and of the benign retroperitoneal tumors following radical interventions being already known.

Until now, the efficacy of complementary treatments has been questionable in the case of such tumors, because of the impossibility of conducting randomized trials and due to the variability in cancer treatment between different institutions and geographic areas (24-27). In our study, the patients having access to an oncological centre with direct acccess to these types of therapies and to experienced medical staff in applying complementary treatments, we discovered a higher overall survival for patients with adjuvant association of both chemo- and radiotherapy (being offered to patients with malignant lymphomas, carcinomas, but also for some sarcomas). Instead, neoadjuvant radiotherapy, as well as prior patient exposure to a toxic environment for sarcoma patients, appeared to decrease operated patient survival rate.

Other variables related to the patient, tumor (histopathologic type, dimension, grading), the number of resected organs, intra- and postoperative complications, reintervention rate, hospitalization period, the period of postoperative stay in the ICU, have not proved to be predictors in the overall survival analysis of operated patients. The 49.5% rate of free-disease survival for radically operated patients, with a high 5-year recurrence of 50.5%, is comparable to the results provided by other institutions, with local relapse rates varying between 40 and 82% (5,8,12,24) and 5-year free-disease rates of 55 to 78% (2). Relapses occur especially in the first two years. The occurrence of recurrences even after a considerable time period postoperatively urges us to a long follow-up of radically operated patients, even if isolatedly they may appear cured. In the case of the first recurrence a radical excison was possible, but for the following local relapses this has not been possible anymore, confirming the finding of other centres (16). The rate of metastazing of 22.9% for the group studied by us is simmilar to that of 20-30% reported in literature. Along with retroperitoneal, liver and pulmonary metastases (an already mentioned metastazing pattern), we also found bone, ganglia, parietal abdominal and peritoneal metastases.

Conclusions

1. Primitive retroperitoneal tumors constitute a very difficult area of general surgery, associating a poor prognosis with high recurrence rates and low overall and free-disease survival rates for operated patients.
2. Both our experience, as well as that of other centres, supports the conclusion that radical excision represents the most important factor that can increase overall and free-disease survival rate for these patients. Surgeon's target must be radicality and in achieveing this goal, he/she must not fear of the: large, even gigantic tumor dimension, histopathologic type, patient age, multiple visceral and vascular involvement, complex organ and vessel resections, intra- and postoperative complications, reinterventions for management of complications, these factors being statistically found insignificant in operated patient survival. An adequately trained, multidisciplinary surgical team, including a vascular surgeon, with an appropriate material and equipment basis, experienced in retroperitoneal tumor surgery, can successfully handle ample, high complexity operations and can solve possible ensuing complications associated to such radical, even aggressive interventions.
   As long as there is no multidisciplinary team, appropriately provided both with a material and a human base for complex vascular interventions, vascular involvement by retroperitoneal tumors remains an essential predictor of a poor survival for these patients, being responsible for unradicality.
3. 3-D medical imaging reconstructions based on data from several planes are essential to determine tumor relationship to vascular and visceral structures preoperatively.
4. In our study we could not test the signficance of a compartment surgery, as other authors have recommended. However, in profile literature, very different views on the amplitude of surgical aggressiveness still persist. Our statistical analysis suggests that non-radical interventions such as debulking and simple laparotomy have to be abandoned, because they do not increase survival, but can associate fearful surgical complications.
5. Even after a radical intervention, the necessity of a prolonged rigurous follow-up persists, due to the high risk of tumor recurrence.
6. The establishment of a national database for the

follow-up of these patients becomes mandatory, to evaluate the results of different types of surgical therapies by comparison with unoperated patients, the effects of complementary treatments, for the identification of risk factors, of screening methods, as well as for an accurate expression of overall and free-disease survival over a long period following the initial operation.

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References

1. Mirilas P, Skandalakis JE. Surgical anatomy of the retroperitoneal spaces - part I: embryogenesis and anatomy. Am Surg. 2009;75(11):1091-7.
2. Strauss DC, Hayes AJ, Thomas JM. Retroperitoneal tumours: review of manegement. Ann R Coll Surg Engl. 2011;93(4): 275-80.
3. Setlacec D, Proca E, Popa C. Tumorile retroperitoneale primitive. Bucureşti: Editura Medicală; 1986.
4. Merran S, Karila-Cohen P, Vieillefond A. [Primary retroperitoneal tumors in adults]. J Radiol. 2004;85(2 Pt 2):252-64. [Article in French]
5. Xu YH, Guo KJ, Guo RX, Ge CL, Tian YL, He SG. Surgical management of 143 patients with adult primary retroperitoneal tumor. World J Gastroenterol. 2007;13(18):2619-21.
6. Angelescu N. Tratat de Patologie Chirurgicală. Bucureşti: Editura Medicala; 2003.
7. Schwartz, Shires, Spencer, Daly, Fisher, Galloway. Principiile Chirurgiei, Seventh Edition. Bucureşti: Editura Teora; 2005.
8. Sinescu I, Gluck G, Harza M. Urologie Oncologică. Bucureşti: Editura Universitară "Carol Davila"; 2006.
9. Popescu I, Lucan M. Tratat de Chirurgie. VolI. Urologie. Bucureşti: Editura Academiei Române; 2007.
10. Gatita CE, Georgescu I, Nemes R. Difficulties in diagnosis of primitive retroperitoneal tumors. Current Health Sciences Journal. 2010;36(3):1-5.
11. Lazar AM, Straja ND, Bratucu E.. An unusual sarcomatous retroperitoneal metastasis. A rare case-report with a brief literature review. Chirurgia (Bucur) 2012;107(1):108-14.
12. Virseda Rodríguez JA, Donate Moreno MJ, Pastor Navarro H, Carrión López P, Martínez Ruiz J, Martínez Sanchiz C, et al. Primary retroperitoneal tumors: review of our 10-year case series. Arch Esp Urol. 2010;63(1):13-22.
13. Bratu O, Madan V, Rusu F, Ilie C, Mischianu D, Barla R, et al. The mangement of primitive retroperitoneal tumors - problems of clinical, imagistic diagnosis, and treatment. J Med Life. 2008; 1(3):334-42.
14. Gronchi A, Casali PG, Fiore M, Mariani L, Lo Vullo S, Bertulli R, et al. Retroperitoneal soft tissue sarcomas: patterns of recurrence in 167 patients treated at a single institution. Cancer. 2004;100(11):2448-55.
15. Mendenhall WM, Zlotecki RA, Hochwald SN, Hemming AW, Grobmyer SR, Cance WG. Retroperitoneal soft tissue sarcoma. Cancer. 2005;104(4):669-75.
16. Hueman MT, Herman JM, Ahuja N. Management of retroperitoneal sarcomas. Surg Clin North Am. 2008;88(3): 583-97, vii.
17. Vasile I, Vîlcea D, Nemeş R, Curcă T, Paşalega M, Calotă F, et al. Primary retroperitoneal tumors - diagnostic and therapeutic difficulties Chirurgia (Bucur). 2005;100(1):27-33. [Article in Romanian]
18. Song TK, Harris EJ Jr, Raghavan S, Norton JA. Major blood vessel reconstruction during sarcoma surgery. Arch Surg. 2009; 144(9):817-22.
19. Santos CE, Correia MM, Thuler LC, Rosa BR, Accetta A, de Almeida Dias J, et al. Compartment Surgery in Treatment Strategies for Retroperitoneal Sarcomas: A Single-center experience. World J Surg 2010;34(11):2773-81.
20. Gronchi A, Pollock R. Surgery in retroperitoneal soft tissue sarcoma: a call for a consensus between Europe and North America. Ann Surg Oncol. 2011;18(8):2107-10. Comment on Ann Surg Oncol. 2011;18(8):2136-42.
21. Bonvalot S, Miceli R, Berselli M, Causeret S, Colombo C, Mariani L, et al. Aggressive surgery in retroperitoneal soft tissue sarcoma carried out at high-volume centers is safe and is associated with improved local control. Ann Surg Oncol. 2010;17(6):1507-14.
22. Gronchi A, Lo Vullo S, Fiore M, Mussi C, Stacchiotti S, Collini P, et al. Aggressive surgical policies in a retrospectively reviewed single - institution case series of retroperitoneal soft tissue sarcoma patients. J Clin Oncol. 2009;27(1):24-30. Epub 2008 Dec 1.
23. Lewis JJ, Leung D, Woodruff JM, Brennan MF. Retroperitoneal soft-tissue sarcoma: analysis of 500 patients treated at a single institution. Ann Surg. 1998;228(3):355-65.
24. Windham TC, Pisters PW. Retroperitoneal sarcomas. Cancer Control. 2005;12(1):36-43.
25. Lehnert T, Cardona S, Hinz U, Willeke F, Mechtersheimer G, Treiber M, et al. Primary and locally recurrent retroperitoneal soft-tissue sarcoma: local control and survival. Eur J Surg Oncol. 2009;35(9):986-93. Epub 2009 Jan 12.
26. Chen CQ, Yin L, Peng CH, Cai Y, Li YF, Zhao R, et al. Prognopstic factors of retroperitoneal soft tissue sarcomas: analysis of 132 cases. Chin Med J (Engl). 2007;120(12):1047-50.
27. Porter GA, Baxter NN, Pisters PW. Retroperitoneal sarcoma: a population-based analysis of epidemiology, surgery, and radiotherapy. Cancer. 2006;106(7):1610-16.
28. Meşină C, Vasile I, Vîlcea ID, Paşalega M, Pârvănescu H, Calotă F, et al. Soft tissue sarcoma - problems of diagnosis and treatment. Chirurgia (Bucur). 2010;105(2):257-66. [Article in Romanian]
29. Pisters PW. Resection of some ~ but not all ~ clinically uninvolved adjacent viscera as part of surgery for retroperitoneal soft tissue sarcomas. J Clin Oncol. 2009;27(1):6-8. Epub 2008 Dec 1.
30. Raut CP, Swallow CJ. Are radical compartmental resections for retroperitoneal sarcomas justified? Ann Surg Oncol. 2010; 17(6):1481-4.
31. Nathan H, Raut CP, Thornton K, Herman JM, Ahuja N, Schulick RD, et al. Predictors of survival after resection of retroperitoneal sarcoma: a population-based analysis and critical appraisal of the AJCC staging system. Ann Surg. 2009;250(6): 970-6.
32. Schwarzbach MH, Hormann Y, Hinz U, Leowardi C, Böckler D, Mechtersheimer G, et al. Clinical results of surgery for retroperitoneal sarcoma with major blood vessel involvement. J Vasc Surg. 2006;44(1):46-55.
33. Tambo M, Fujimoto K, Miyake M, Hoshiyama F, Matsushita C, Hirao Y. Clinicpathological review of 46 primary retroperitonal tumors. Int J Urol. 2007;14(9):785-8.
34. Nishino M, Hayakawa K, Minami M, Yamamoto A, Ueda H, Takasu K. Primary retroperitoneal neoplasms: CT and MR imaging findings with anatomic and pathologic diagnostic clues. Radiographics. 2003;23(1):45-57.