RESEARCH ARTICLE

Surgical Risk Factors of Patients with Operable Gist

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Introduction: Gastrointestinal stromal tumors (GIST) are the most frequently mezenchimale tumors of the gastrointestinal tract. This study aims to analyze the results after surgical treatment of GIST and identify key risk factors influencing postoperative course of these patients in order to discover the most effective therapeutic methods to significantly improve postoperative course of these patients. **Methods**: We retrospectively reviewed the medical records of all patients who underwent surgical removal of GISTs from 2004-2014. Patient demographics, criterion for admission, surgery, complications, secondary dissemination, histopathological data and clinical course were analized following patient survival at 12, 24, 36 and to 60 months postoperatively. Statistical analysis was performed using the MedCalc software program, and survival analysis was done by Kaplan Meyer. **Results**: During this period we analyzed a total of 28 cases, including 13 males and 15 females with age from 33 to 80 years (median, 61). The tumor was located in the stomach (15 cases; 53%), small intestine in ten cases (36%) and other sites in three patients (11%). Multivariate analysis revealed that tumor size (P <0,05), criterion for admission (P<0,05) and secondary dissemination (P<0,05) are independed prognostic factors. **Conclusions**: Factors like: age and sex of patients, size and tumor site, presence or absence of metastasis, are prognostic risk factors with significant differences in the evolution of patients with operable GIST. The small number of patients and retrospective nature of the study have created difficulties in the estimation where we concluded the need of a prospective multicentric study.

Keywords: gastrointestinal stromal tumors, survival, prognosis, surgical resection

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Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasm of the gastrointestinal system, with an annual incidence estimated at 1.5 / 100.000 [1-5]. The tumor typically occurs in the stomach or small intestine, infrequently in the colon, rectum and esophagus, and rarely outside the gastrointestinal tract [3,6]. The most common clinical presentation of these tumors is gastrointestinal bleeding (with acute hematemesis, melaena or chronic anemia). They may cause intestinal obstruction, abdominal pain, weight loss or a palpable mass, otherwise can be incidentally detected during a surgical intervention or an endoscopic/radiological procedure. It is recognised that the treatment of these tumors is multidisciplinary and the surgery is often necessary [7]. Surgical resection is currently the golden standard in the management of GISTs [3,8]. Complete resection with negative margins is the main goal of surgery. The way surgery is managed and other therapeutic actions are made influence very much the progress of this tumor. However, recurrence is common, and the 5 years survival rate after complete resection ranges from 40% to 65% [9]. Today there is a constant and multicentric concern to discover the best methods and principles of treatment especially for tumors, in order to improve the prognosis of these patients [10]. These efforts are hampered by the low incidence of these lesions and the difficulty of obtaining representative batches.

The primary aim of the present study was to report our experience in patients who underwent a surgical resection for GIST tumor in the 1st Surgical Department of Mureş County Hospital and to correlate our results with other studies published in the field. Another objective was to identify the main risk factors influencing prognosis and further development of these patients, in order to discover the most effective methods or therapeutic protocols that could significantly improve the chances for survival or the quality of life in GISTs patients.

Materials and Methods

We retrospectively investigated patients who underwent a surgical procedure for GISTs in the 1st Surgical Department of Mureş County hospital between 2004 and 2014. We reviewed data from the early postoperative period, investigating the outcomes in the late postoperative period and we analyzed the factors that influenced survival among patients who had surgery for GISTs. We reviewed demographic data, criterion for admission, surgery, complications, secondary dissemination, histopathological data and clinical course from hospital archives and computerized database. We obtained postoperative data on 28 patients by telephone. All contacted persons were informed of the nature and importance of the study and the privacy it offers.

Patients selected for this study were divided into six groups:
- I Group- criterion for admission to two groups: emergency and programming.

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- II Group- tumor site with three subgroups: stomach, intestine and other sites.
- III Group- tumor diameter: 0- 10 cm, 11- 20 cm and 21- 30 cm.
- IV Group - presence or absence of metastases.
- V Group- radical or palliative surgery.
- VI Group- indolent (probably benign) or malignant GIST (for probably benign GIST we consider: intestinal tumors: maximum diameter ≤ 2 cm and and no more than 5 mitoses per 50 HPFs; gastric tumors: maximum diameter ≤ 5 cm and no more than 5 mitoses per 50 HPFs).

For each group of patients we have carried out in a first stage of analysis preliminary statistical overview. Based on the results obtained from this analysis we selected for further study and establish the main risk factors statistically significant prognostic criteria that may influence the operated patients with GIST. Statistical analysis was performed using MedCalc Software program (Version 12.3.0 bvba, Mariakerke, Belgium). Data were expressed as (%) or median (range). Survival was calculated by the Kaplan-Meier [K.M] method. We considered $p < 0,05$ to be statistically significant. The study was approved by the local ethics committee.

Results
Age and gender
In the present study 28 cases of GIST were diagnosed between 2004- 2014. The age of all the patient ranged from 33 to 80 years, with the median age of 61 years. Of the 28 patient, 13 (46%) were men, and 15 (54%) were women (figure 1).

Admission methods
Eight patients (29%) were admitted by emergency in our hospital and twenty (71%) of them came by appointment (p=0,0005; HR 0,2537 with 95% CI 0,06830 to 0,9427; HR 3,9410 with 95% CI 1,0607 to 14,6423)(figure 2).

Surgical therapy
The surgical strategy has been adopted depending on patient's condition on admission. Ten patients (36%) underwent palliative surgery and eighteen patients (64%) had radical intervention (p=0,0009; HR 0,2687 with 95% CI 0,08145 to 0,8865; HR 3,7214 with 95% CI 1,1280 to 12,2774) (figure 3).

Metastasis
A small number of patients 9 (32%) had metastases at the time of surgery (p= 0,0020; HR 0,2936 with 95% CI 0,08370 to 1,0299; HR 3,4059 with 95% CI 0,9710 to 11,9468) (figure 4).
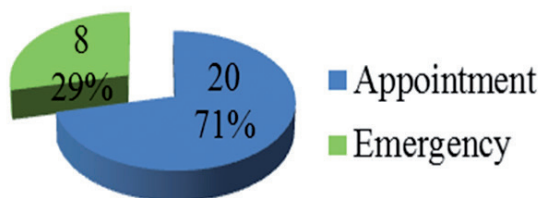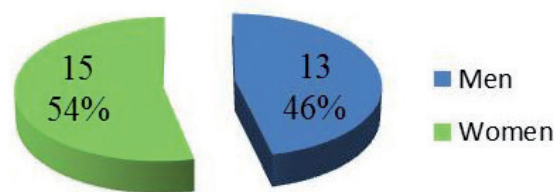

Fig. 1. Case distribution depending on gender

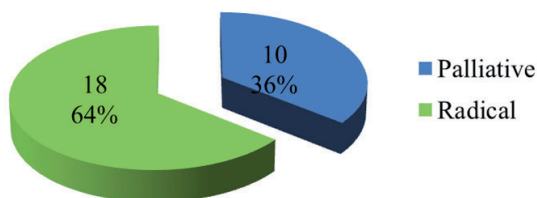Fig. 2a. Distribution depending on the admission criteria

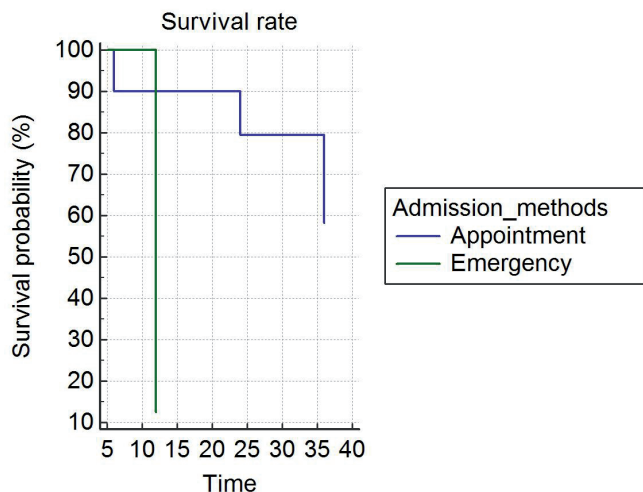Fig. 3a. Distribution depending on the type of surgery

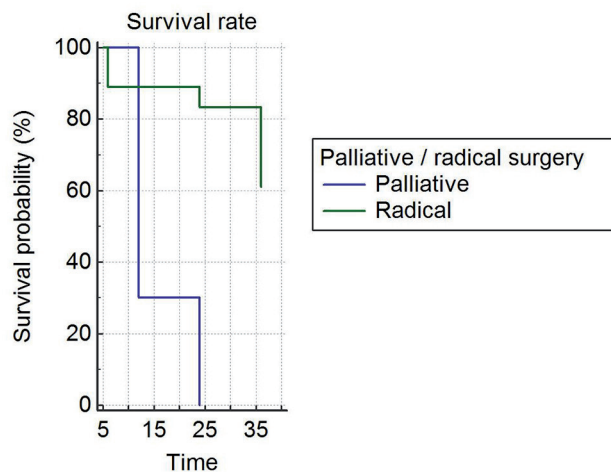Fig. 2b. K. M analysis based on admission criteria

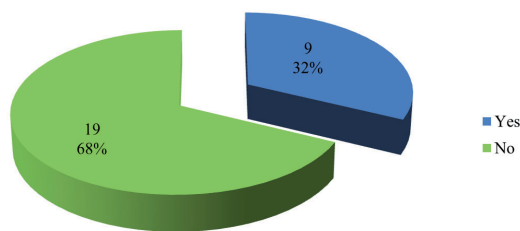Fig. 3b. K. M analysis depending on the type of surgery

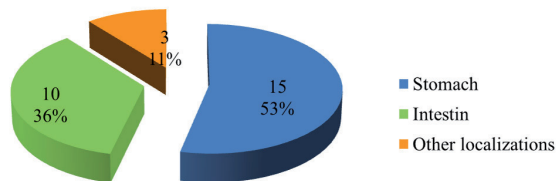Fig. 4a. Distribution depending on the metastasis

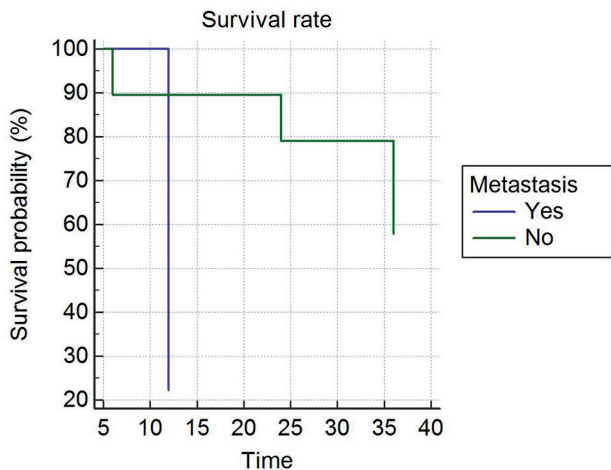

Fig. 5a. Distribution depending on tumor localization

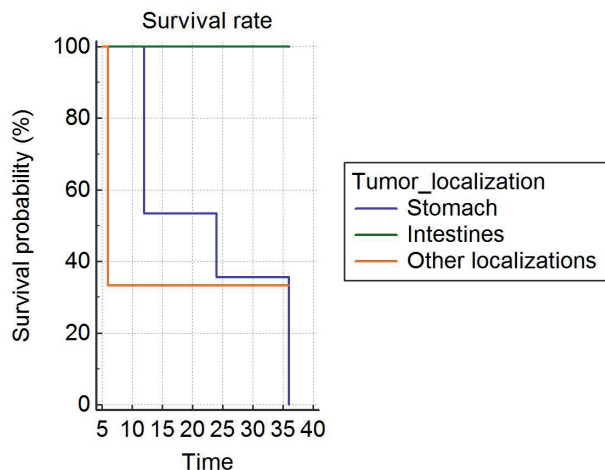Fig. 4b. K. M analysis based on the presence/ absence of metastases

Fig. 5b. K. M analysis depending on tumor localization

Tumor localization

Tumors were most commonly located in the stomach (n=15; 53%), followed by the intestines (n=10; 36 %) and other localizations (n=3; 11%) - (p=0,007; HR 1,4117 with 95% CI 0,2908 to 6,8520; HR 6,7296 with 95% CI 1,8358 to 24,6687; HR 0,7084 with 95% CI 0,1459 to 3,4383; HR 4,7671 with 95% CI 1,3057 to 17,4048; HR 0,1486 with 95% CI 0,04054 to 0,5447; HR 0,2098 with 95% CI 0,05746 to 0,7659) (figure 5).

Tumor size

Tumors varied greatly in size from 1 cm to 30 cm, the mean size of primary tumors was 9 cm (p= 0,0044; HR 1,6667 with 95% CI 0,1752 to 15,8555; HR 4,3790 with 95% CI 0,7442 to 25,7685; HR 0,6000 with 95% CI 0,06307 to 5,7080; HR 2,6274 with 95% CI 0,5276 to 13,0841; HR 0,2284 with 95% CI 0,03881 to 1,3438; HR 0,3806 with 95% CI 0,07643 to 1,8953) (figure 6).

Malignant / indolent (benign characteristics) GIST

Two patients had indolent and twenty six patients had malignant GIST.

P=0,0636; HR 3,2333 with 95% CI 0,2845 to 36,7402; HR 0,3093 with 95% CI 0,02722 to 3, 5145 (figure 7).

Discussions

It is found that the incidence of GIST tumors in surgical services is low but raises particular interests for diagnosis and treatment for everyone. Although lately the possibili-

ties of early diagnosis of GIST patients increasingly improved, there remain cases that present advanced forms of evolution or complications. These issues point out several studies to find factors influencing the prognosis of patients with GIST. In our study we found that these factors influence in different way the evolution and prognosis of patients.

In this context we can say that the admission criteria of hospitalized patients had a significant impact on the evolution and prognosis of their survival. Following K.M estimation, patients that are admitted and operated under emergency conditions have a significantly weaker outcome than patients admitted and operated electively (p<0,05).

Another factor which is significantly influencing the evolution in patients with operated GIST in this study is related to the type of surgery. Patients who received radical surgery regardless of the location of the tumor had a significantly better evolution (p<0,05) to patients who for various reasons surgeries were performed palliative purposes only. Also patients with metastases in the evolutionary stage of tumor, regardless of their location had much weaker evolution compared to patients without metastases. Practically all patients with metastases died in the first 12 months after surgery. Meanwhile in patients who had surgery without any metastasis we could find survivals over 5 years. These issues are obvious and available in K.M evolutionary curves (p<0,05).

It is interesting that the postoperative evolution in this patients is affected differently by tumor location and its diameter.
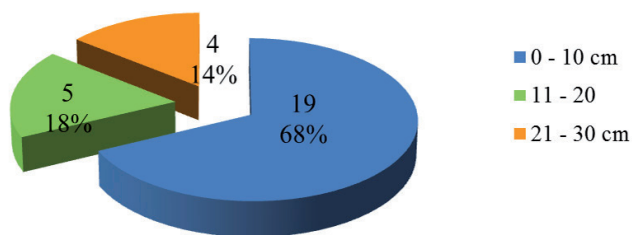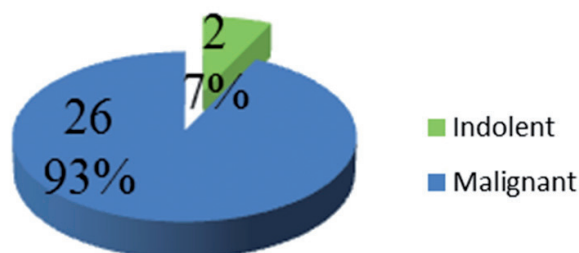
Fig. 6a. Distribution depending on tumor size

Fig. 7a. Distribuition depending on malignant or indolent GIST
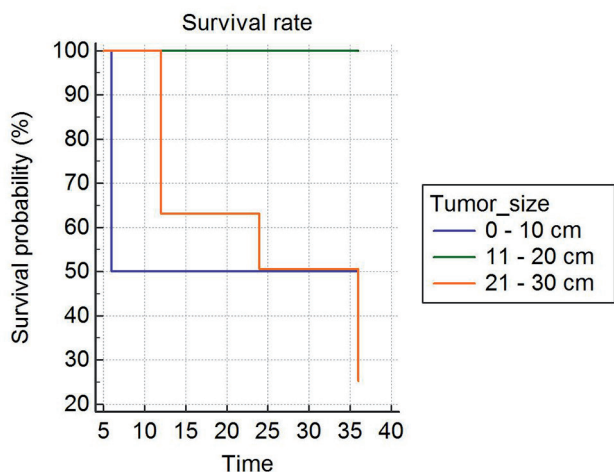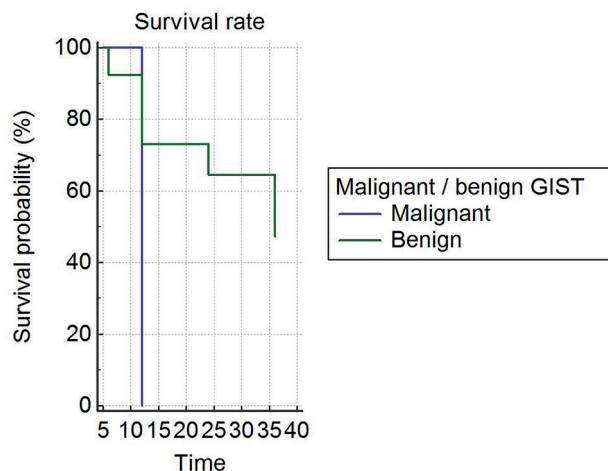

Fig. 6b. K. M analysis depending on tumor size

Fig. 7b. K.M analysis depending on probably benign/ malignant GIST

Depending on tumor localization we found that patients with small bowel GIST have statistically a better significant survival prognosis than patients with gastric or other locations (p<0,05)

In our opinion this evolution is due to the fact that tumors in the small intestine allow radical surgery more frequently than other sites such as stomach / retroperitoneum. But following HR with IC 95% of patients with GIST located in the small intestine and those with other sites (stomach, retroperitoneum), shows that a small number of cases especially those with retroperitoneal location might influence survival. Tumor diameter significantly influenced (p<0,05) postoperative evolution of patients. In this study group patients who had tumors between 10-20 cm had the best evolution compared to the other two groups.

This is explained by the fact that there are few cases in the group of 10- 20 cm diameter tumors so that a patient with a indolent GIST tumor exceed these dimensions but obviously influenced the analysis of this group. Besides these results from HR with 95% IC obtained from K.M estimates of the lot.

Another interesting aspect we found is related to the evolution of patients with indolent or malignant GIST is that the forecast made for survival difference is not statistically significant (p>0,06). This is clearly explained by only two cases of indolent GIST of which one died in the first

36 months after surgery for reasons beyond the GIST.

The small number of cases in our study group allowed us to accurately estimate risk and prognostic factors.

If the criterion for admission, type of surgery and the presence / absence of metastases the estimation did not create difficulties, for the diameter and location of the tumor, where three parameters of estimation were considered, the estimation was more difficult.

In this latter case, an estimation can significantly be influenced.

Likewise, the comparison between malignant and indolent GIST - where the patient's death with indolent GIST influenced surprisingly the estimation.

Conclusions

Patients admitted and operated in emergency with metastasis and palliative surgery have a poor prognosis compared to other patients.

The small intestine localization of the tumor, the size and benign histological character are favorable prognostic factors.

The small number of patients and retrospective nature of the study have created difficulties in the estimation where we concluded the need for a prospective multicenter study and include many cases a longer period of time.

It is useful to perform a prognostic score for these patients in order to improve their chances of survival. It will

be conducted on a large enough batch after a prospective study that includes other prognostic risk factors such as collateral disease, adjuvant treatment.

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