Clinicopathological Characteristics And Prognostic Factors For The Recurrence Of Abdominal Desmoid Tumors: Analysis Of 113 Patients From Two Chinese Hospitals

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Research

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Abstract

Background and purpose: Abdominal desmoid tumors (ADTs) are rare soft-tissue neoplasms that have a relatively high local recurrence rate. The purpose of the present study was to delineate the clinicopathologic features and explore the prognostic factors of ADTs.

Methods: From January 2000 to January 2019, patients with ADTs who underwent macroscopically complete resection at the China National Cancer Center were included in the study. The clinicopathologic characteristics and follow-up data were carefully collected and reviewed. Prognostic factors such as age at presentation, sex, tumor location, tumor size and tumor proximity to nerves or vasculature were analyzed, and recurrence-free survival was analyzed with these factors.

Results: A total of 113 patients with ADTs were assigned to the abdominal wall group (n = 66) or abdominal cavity group (n = 47) according to the tumor site. Abdominal wall DTs and intra-abdominal DTs demonstrated distinct clinicopathological features and prognoses. During a median 61-month follow-up period, twelve (10.2%) patients had local recurrence. According to the univariate and multivariate analyses, intra-abdominal tumors, large tumors, and positive margins were independent risk factors for poor prognosis.

Conclusion: Compared with intra-abdominal DTs, abdominal wall DTs demonstrate different clinicopathological features and a better prognosis. Under the premise of ensuring negative margins during the first surgical procedure, patients with abdominal wall DTs can obtain satisfactory prognoses through radical resection.

Introduction

Desmoid tumors (DTs), also known as aggressive fibromatosis, are rare clonal proliferating tumors that may arise from mesenchymal stem cells\(^1,2\). Although DTs have no potential for metastasis or malignancy, the lesions show local aggressiveness to surrounding structures and exhibit a propensity to recur, leading to a high local recurrence rate and significant functional impairments and morbidity\(^3-5\). Consequently, surgeons choose more aggressive treatment strategies, including radical surgical resection\(^6-8\), radiotherapy\(^9,10\), systemic therapy\(^11-13\) and neoadjuvant radiation with or without chemotherapy\(^14,15\). However, due to the rarity of DTs and their recognized unpredictable natural history, optimal treatment management strategies have not been well established.

DTs can occur anywhere in the body and cause different clinical symptoms. According to their distribution, they can be classified as extra-abdominal, abdominal wall, and intra-abdominal types. Intra-abdominal DTs may cause intestinal obstruction, fistulization or dysuria, and extra-abdominal DTs may result in neuropathic pain\(^16\). Currently, a large number of studies have suggested that age, surgical margin, tumor location, tumor size, and adjuvant radiotherapy are clinicopathologic prognostic factors associated with recurrence\(^17-20\). However, it has been shown that DTs located in the abdominal wall and
abdominal cavity are relatively minimally invasive and have a relatively low recurrence rate. Different desmoid tumors may have different biological make-ups and different genes, which indicates that abdominal DTs (ADTs) may represent a different disease from DTs in the girdle, head, neck, extremity or other parts of the body. In addition, data on the management of ADTs are limited, and prognostic factors are not specific. Therefore, we conducted a double-center study and enrolled 113 patients from two different Chinese hospitals, aiming to delineate the clinicopathologic features and determine the prognostic factors for recurrence-free survival (RFS) in ADTs after macroscopic complete surgical resection.

Patients

From January 2000 to January 2019, a total of 343 patients who underwent surgical resection and were pathologically diagnosed with DTs from two different Chinese institutions were retrospectively reviewed. The inclusion criteria were as follows: (1) patients with DTs of the abdominal wall or abdominal cavity; (2) patients undergoing macroscopically complete surgical resection (R0 or R1); and (3) patients who received surgical resection as the initial treatment. Patients with unclear microscopic margin status of resection or those who were lost to follow-up were excluded. According to the above criteria, the remaining 113 patients were analyzed and formed the basis of the present study: 102 patients were from the Cancer Hospital Chinese Academy of Medical Sciences, and 11 patients were from Beijing Hospital. The study protocol was approved by the ethics committee of the National Cancer Center, and all patients signed an informed consent form before the study.

Clinical data collection

In the present study, clinical data were collected based on electronic records and included age at diagnosis, sex, body mass index (BMI), comorbidities, previous abdominal surgery, admission status, tumor location, tumor size, tumor stage, surgical resection margins, and tumor proximity to important blood vessels or nerves. In addition, the surgical outcomes, including the duration of operation, intraoperative blood loss, postoperative complications, and postoperative hospital days, were also collected and reviewed. Tumor site was categorized as intra-abdominal or abdominal wall. Retroperitoneal lesions were considered extra-abdominal DTs and were excluded. Surgical margin and tumor size were examined by two pathologists specializing in gastroenteric tumors, and the microscopic margin status was considered positive if the tumor was identified in the pathological specimen to be less than 0.5 cm from the edge of the inkblot. According to the patient's general condition and the radiologist's experience, adjuvant radiation with a median overall dose of 55 Gy was recommended. The patients received a follow-up survey every 1-2 years via outpatient visits or telephone until recurrence, death or December 31, 2019. Local recurrence was the main endpoint and was diagnosed by physical computed tomography (CT) scans or magnetic resonance imaging (MRI).

Statistical analysis
All data were analyzed using the Statistical Package for the Social Sciences (SPSS version 24.0, IBM Corp., Armonk, NY, United States). Quantitative data were expressed as the mean ± standard deviation, and the two groups were compared with paired Student's t-tests and Mann–Whitney U-tests for independent values for normally and nonnormally distributed values, respectively. Qualitative data and ordinal data are presented as the number of cases and percentages, and the groups were compared using χ² tests or Mann–Whitney U-tests, as appropriate. The local RFS time was defined as the time interval between the date of pathological diagnosis and recurrence. RFS rates were analyzed by the Kaplan-Meier method and were compared between the subgroups with the log-rank test. In addition, the Cox proportional hazards regression model was used to perform multivariate analysis to identify the independent prognostic factors. A P value of <0.05 was considered statistically significant.

Results

Clinical and pathological characteristics

All patients successfully underwent macroscopically complete surgical resection (Figure 1A, 1B), and there were no deaths during the perioperative period. Table 1 describes the clinical and pathologic characteristics of the 113 patients included in this study in detail. The median age at first diagnosis was 36 years (range 15-71), and the cohort was predominantly female (73.5%, n = 83). The average body mass index (BMI) was 22.6 ± 3.1 kg/m². Most patients (89.4%, n = 101) had primary tumors, and the median tumor size was 5.5 cm (range 1.4-30). The common symptoms were abdominal pain (14.2%, n = 16), changes in bowel habits (5.3%, n = 6), obstructions (2.7%, n = 3), anemia (2.7%, n = 3), and hydronephrosis (1.8%, n = 2). Resection margins were positive in 10 (8.8%) patients, and adjuvant radiotherapy was performed in 9 (8.0%) patients after surgery. The surgical outcomes and postoperative complications are listed in Table 2. The mean operation time and intraoperative blood loss were 138.5 ± 83.6 min (range 40-360) and 70.6 ± 114.4 ml (range 10-400), respectively. A total of 21 (18.6%) patients experienced postoperative complications, and the most common complication was chronic pain (7.1%, n = 8), followed by wound infection (6.2%, n = 7), anastomosis leakage (3.5%, n = 4), ileus (2.7%, n = 3), incisional hernia (1.8%, n = 2) and neurological problems (0.9%, n = 1).

According to the tumor sites, 113 patients were assigned to the abdominal wall group (n = 66) or the intra-abdominal cavity group (n = 47). Figure 2 shows the distribution of various tumor sites in the abdominal cavity, including stomach (n = 2, 4.3%), pancreas (n = 1, 2.1%), duodenum (n = 2, 4.3%), small intestine mesentery (n = 25, 53.2%), ileocecal mesentery (n = 7, 14.9%), transverse mesentery (n = 8, 17.0%) and sigmoid mesentery (n = 2, 4.3%). The proportion of female patients in the abdominal wall group was significantly higher than that in the intra-abdominal group (93.9% vs. 44.7%, P<0.001). In contrast, the proportion of patients aged 35 years or older was significantly higher in the intra-abdominal group than in the abdominal wall group (91.5% vs 63.6%, P=0.001). There were more patients with a previous history of cesarean section in the abdominal wall group than in the intra-abdominal group (34.8% vs 6.4%, P<0.001). In addition, patients with lesions in the abdominal wall were less likely to present with clinical symptoms than patients with intra-abdominal lesions (13.6% vs 40.4%, P = 0.001).
The number of patients in the intra-abdominal group with lesions greater than 10 cm was significantly higher than that in the abdominal wall group (27.7% vs. 7.6%, \( P = 0.011 \)), and the lesions in the intra-abdominal group were mostly adhered to important nerves or vasculature (42.6% vs. 13.6%, \( P = 0.001 \)). In terms of surgical outcomes, the abdominal wall group had a significantly shorter operation time (98.7 ± 50.0 min vs. 194.5 ± 90.3 min, \( P<0.001 \)) and a lower amount of intraoperative blood loss than the intra-abdominal group (24.1 ± 41.1 ml vs. 136.0 ± 149.4 ml, \( P<0.001 \)).

**Survival analysis**

The median follow-up interval was 61 months (range 9-250). Only 2 patients died at the last follow-up, and no patient died due to recurrence or complications caused by ADTs. During the whole follow-up period, a total of 12 patients developed recurrence after surgery with or without adjuvant radiotherapy: 2 (16.7%) cases of recurrence were found in patients presenting with intra-abdominal DTs, and 10 (83.3%) cases of recurrence were found in patients presenting with abdominal wall DTs. The estimated 5- and 10-year RFS rates for the entire cohort were 92.8% and 89.8%, respectively (Figure 3). It is worth noting that recurrence was still observed in one patient beyond 10 years. In addition, none of the 12 patients who were admitted with recurrent disease experienced recurrence during follow-up after surgical resection combined with or without radiotherapy.

According to the univariate analysis, tumor location, tumor size, and margin status significantly affected RFS (\( P<0.05 \)). A significantly higher rate of local recurrence was associated with abdominal wall DTs, a tumor size >10 cm, and an R1 margin status (Figure 4A-C). According to the multivariate analysis, RFS was significantly affected by tumor location (HR: 8.407; 95% CI, 1.649-42.865; \( P = 0.010 \)), tumor size (HR: 17.437; 95% CI, 3.648-83.346; \( P<0.001 \)) and margin status (HR: 8.045; 95% CI, 2.388-27.099; \( P = 0.001 \)).

**Discussion**

DTs are clinically rare soft-tissue neoplasms of clonal myofibroblastic tumors that originate from musculoaponeurotic structures, fascial planes and ligaments throughout the body\(^{[1,2]}\). Although DTs have no potential for metastasis or malignancy, the lesions show local aggressiveness to surrounding structures and exhibit a propensity to recur, and the local recurrence rate can be as high as 17.6%-30.7% \(^{[16,21,23,27]}\). According to the distribution of DTs, lesions can be classified as extra-abdominal, abdominal wall, and intra-abdominal types. The biological behaviors of DTs in different parts of the body are different, and previous studies have demonstrated that the prognosis of ADTs is significantly better than that of extra-abdominal DTs\(^{[25,21,23,27]}\). To further delineate the clinicopathologic features and prognostic factors of this rare tumor, we conducted a double-center retrospective study to provide a reference for clinical work.

We further divided ADT patients into an intra-abdominal DT group and an abdominal wall DT group to compare the clinicopathological features and prognosis factors of the two groups. Consistent with previous literature\(^{[8,23,28]}\), the present study revealed that compared to patients with intra-abdominal DTs,
the majority of patients with abdominal wall DTs were young women with a history of cesarean section. Our study also found that the tumor size of patients with intra-abdominal DTs was significantly larger than that of patients with abdominal wall DTs, and most of these patients presented with corresponding clinical symptoms upon first diagnosis. This may be due to the insidious nature of intra-abdominal DTs and the absence of obvious special clinical symptoms at the initial stage. As the tumor gradually increases and compresses the surrounding organs, it causes abdominal pain, ileus, hydronephrosis and other clinical symptoms[29]. Furthermore, we also found that the lesions in the intra-abdominal group were more likely to adhere to important nerves or vasculature than the lesion in the abdominal wall group, which may also be due to the insidious nature of intra-abdominal DTs, and the local aggressiveness of the tumor was more serious at the time of diagnosis.

Prognostic factors affecting the survival of DT patients have been previously reported. He et al. reported that younger age, extra-abdominal sites, a large tumor size and a close or positive margin status are independent prognostic factors for RFS in patients with DTs[27]. In addition, Mullen et al. reported that margin status was a significant prognostic factor for postoperative relapse in DT patients undergoing surgical resection[21]. Our study targeted ADTs, and the results showed that an intra-abdominal site, a large tumor size and R0 resection were all independent predictors for RFS in DT patients. Previous studies have demonstrated that the long-term prognosis of patients with abdominal wall DTs is significantly better than that of patients with intra-abdominal DT[28,30]. Wilkinson et al. reported the prognosis of 50 patients with abdominal wall DTs who underwent surgical resection. Within a median follow-up period of 5 years, the local recurrence rate was only 8% (4/50). Of these 46 disease-free patients, 13 were pregnant without complications due to abdominal mesh repair or tumor recurrence[28]. Consistent with previous literature reports, this study revealed that the RFS rate of patients with abdominal wall DTs was significantly better than that of patients with intra-abdominal DTs, and only 3% (2/66) of patients with abdominal wall DTs had local recurrence during follow-up. However, the local recurrence rate of patients with intra-abdominal DTs was 23.1% (10/47), and the tumor size was greater than 5 cm in all 10 patients with recurrence, of whom 4 patients had tumors larger than 10 cm. In addition, of the 10 patients with recurrence in the intra-abdominal DT group, 5 had positive margins after surgery. We believe that unlike abdominal wall DTs located on the body surface, due to the rarity of DTs and the absence of special clinical symptoms in the initial stage, lesions in the abdominal cavity are already large at the time of diagnosis and are closely related to the surrounding important nerves or vasculature. To preserve organ function as much as possible, it is difficult to achieve radical resection, which results in a significantly higher local recurrence rate. Furthermore, the muscular and fascial defects of the abdominal wall caused by radical resection can be repaired with synthetic or biological mesh, providing a reliable technical guarantee for R0 resection in abdominal wall DTs[31,32].

There were several limitations to the present study. First, it was a retrospective study; thus, the bias from patient selection and information collection was unavoidable. Second, the period of our study was within a span of nearly 20 years, the treatment strategies for DTs have been changing, and the early pathological reports are not as normative as they are now. This led to a lack of vital information, such as
data regarding SMA, β-catenin, Desmin, and Ki-67, in some patients and made it difficult to evaluate their value in predicting prognosis.

**Conclusion**

Compared with extra-abdominal DTs, ADTs have a better prognosis because only 9.7% of patients experience recurrence within 10 years after macroscopically complete surgical resection. Moreover, abdominal wall DTs and intra-abdominal DTs demonstrate distinct clinicopathological features and prognoses. Under the premise of ensuring negative margins during the first surgical procedure, patients with abdominal wall DTs can obtain satisfactory prognoses through radical resection.

**Declarations**

**Acknowledgements**

We would like to thank all participants for their contributions in data collection.

**Availability of data and materials**

The datasets used during the current study are available from the corresponding author upon reasonable request.

**Ethics approval and consent to participate**

The study protocol and informed consent form were consistent with the recommendations of the Declaration of Helsinki and approved by the ethics committee of the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College approved this study.

**Consent for publication**

Not applicable

**Competing interests**

The authors declare that they have no conflict of interest

**Authors’ contributions**

(I) conception and design: JWL and SCZ; (II) administrative support: JWL, XSW and ZXZ; (III) provision of study materials or patients: SCZ and ZS ; (IV) collection and assembly of data: ZS and SCZ (V) data analysis and interpretation: JWL and SCZ. All authors read and approved the final manuscript.

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Tables

**Table 1.** Clinicopathological characteristics of 113 patients with ADT
| Characteristic                        | Overall  | Abdominal wall | Abdominal cavity | $P$  |
|--------------------------------------|----------|----------------|------------------|------|
|                                      | (n = 113)| (n = 66)       | (n = 47)         |      |
| Gender                               |          |                |                  | 0.001|
| Male                                 | 30 (26.5)| 4 (6.1)        | 26 (55.3)        |      |
| Female                               | 83 (73.5)| 62 (93.9)      | 21 (44.7)        |      |
| Age (years)                          |          |                |                  | 0.001|
| $\geq$ 30                            | 85 (75.2)| 42 (63.6)      | 43 (91.5)        |      |
| $<$ 30                               | 28 (24.8)| 24 (36.4)      | 4 (8.5)          |      |
| BMI (kg/m², mean ± SD)               |          |                |                  | 0.711|
| Preoperative albumin (g/L, mean ± SD)| 39.0 ± 3.2| 39.3 ± 3.2    | 38.9 ± 3.3      | 0.409|
| Admission status                     |          |                |                  | 0.356|
| Primary                              | 101 (89.4)| 57 (86.4)     | 44 (93.6)        |      |
| Recurrent                            | 12 (10.6)| 9 (13.6)       | 3 (6.4)          |      |
| Previous cesarean section history    |          |                |                  | 0.001|
| Yes                                  | 26 (23.0)| 23 (34.8)      | 3 (6.4)          |      |
| No                                   | 87 (77.0)| 43 (65.2)      | 44 (93.6)        |      |
| Symptoms                             | 28 (24.8)| 9 (13.6)       | 19 (40.4)        | 0.001|
| Abdominal pain                       | 16 (14.2)| 9 (13.6)       | 7 (14.9)         |      |
| Changes in bowel habits              | 6 (5.3)  | 0 (0)          | 6 (12.8)         |      |
| Obstruction                          | 3 (2.7)  | 0 (0)          | 3 (6.4)          |      |
| Anemia                               | 3 (2.7)  | 0 (0)          | 3 (6.4)          |      |
| Hydronephrosis                       | 2 (1.8)  | 0 (0)          | 2 (4.3)          |      |
| Tumor size (cm)                      |          |                |                  | 0.011|
| 0-5                                  | 39 (34.5)| 23 (34.8)      | 16 (34.0)        |      |
| 5-10                                 | 56 (49.6)| 38 (57.6)      | 18 (38.3)        |      |
| $\geq$ 10                            | 18 (15.9)| 5 (7.6)        | 13 (27.7)        |      |
| Margin status                        |          |                |                  | 0.368|
| R0                                   | 103       | 62 (93.9)      | 41 (87.2)        |      |
| Characteristic                        | Overall (n = 113) | Abdominal wall (n = 66) | Abdominal cavity (n = 47) |
|--------------------------------------|-------------------|-------------------------|--------------------------|
| Adjuvant RT                          | 0.864             |                         |                          |
| Yes                                  | 0.001             |                         |                          |
| No                                   | 0.001             |                         |                          |
| Adjacent to nerves/vascular          | 0.001             |                         |                          |
| Yes                                  | 0.001             |                         |                          |
| No                                   | 0.001             |                         |                          |

Table 2
Surgical outcomes of 113 patients with ADT

| Duration of operation (min, mean ± SD) | 138.5 ± 83.6 | 98.7 ± 50.0 | 194.5 ± 90.3 |
|----------------------------------------|--------------|-------------|--------------|
| Intraoperative blood loss (ml, mean ± SD) | 70.6 ± 114.4 | 24.1 ± 41.1 | 136.0 ± 149.4 |
| Postoperative complications             | 21 (18.6)    | 10 (15.2)   | 11 (23.4)    |
| Wound infection                         | 7 (6.2)      | 4 (6.1)     | 2 (4.3)      |
| Ileus                                   | 3 (2.7)      | 0 (0)       | 3 (6.4)      |
| Anastomosis leakage                     | 4 (3.5)      | 0 (0)       | 4 (8.5)      |
| Incisional hernia                       | 2 (1.8)      | 2 (3.0)     | 0 (0)        |
| Chronic pain                            | 8 (7.1)      | 6 (9.1)     | 1 (2.1)      |
| Neurological problem                    | 1 (0.9)      | 0 (0)       | 1 (2.1)      |
| Mortality                               | 0 (0)        | 0 (0)       | 0 (0)        |
| Postoperative hospital stay (day, mean ± SD) | 3.9 ± 3.8  | 3.2 ± 2.4  | 5.9 ± 6.3  |
Table 3
Univariate and multivariate analysis for recurrence-free survival of 113 patients with A DT

| Variables                                      | Local recurrence-free survival | Univariate analysis | Multivariate analysis | HR (95%CI) | P     | HR (95%CI) | P     |
|------------------------------------------------|--------------------------------|---------------------|-----------------------|------------|-------|------------|-------|
|                                                |                                | HR (95%CI)          |                       | P          |       | HR (95%CI) | P     |
| Gender: male/female                            | 0.480 (0.107–2.153)            | 0.338               |                       |            |       |            |       |
| Age>30 years                                    | 1.409 (0.472–4.208)            | 0.539               |                       |            |       |            |       |
| Tumor location: abdominal cavity/abdominal wall | 4.026 (1.397–18.013)           | 0.039               | 8.407 (1.649–42.865)  | 0.010      |       |            |       |
| Admission status: recurrent/primary            | 3.557 (0.985–12.850)           | 0.063               |                       |            |       |            |       |
| Previous cesarean section history: yes/no      | 0.742 (0.149–3.691)            | 0.716               |                       |            |       |            |       |
| Preoperative albumin                           | 0.976 (0.833–1.672)            | 0.443               |                       |            |       |            |       |
| Tumor size                                      |                                |                     |                       |            |       |            |       |
| 0-5cm                                          | Reference - Reference -        |                     |                       |            |       |            |       |
| 5-10cm                                         | 1.759 (0.418–7.410)            | 0.441               | 1.361 (0.314–5.903)   | 0.681      |       |            |       |
| ≥10 cm                                         | 5.743 (1.424–23.158)           | 0.014               | 17.437 (3.648–83.346) | 0.001      |       |            |       |
| Adjacent to nerves/vascular: yes/no            | 1.807 (0.897–9.670)            | 0.120               |                       |            |       |            |       |
| Margin status: R1/R0                           | 5.512 (1.783–14.889)           | 0.002               | 8.045 (2.388–27.099)  | 0.001      |       |            |       |
| Adjuvant RT: yes/no                            | 0.762 (0.099–5.849)            | 0.794               |                       |            |       |            |       |

Figures
Figure 1

A. The tumor underwent macroscopic complete resection B. The tumor has a hard texture, white cut surface and no necrosis
Figure 2

The distribution of various tumor sites in the abdominal cavity
Figure 3

Recurrence-free survival rate of the entire cohort
Figure 4

A. RFS according to tumor site B. RFS according to tumor size C. RFS according to margin status