Patient Burden of Illness Associated With Desmoid Tumors

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BACKGROUND

- Desmoid tumors (DT)—also known as desmoid-type fibromatosis or aggressive fibromatosis—are rare, locally aggressive, fibroblastic soft-tissue tumors that are characterized by infiltrative growth and a tendency to recur.[1,2,3]
- DTs are associated with significant symptom and physical function burden that can impact patients' overall health-related quality of life.[2,4,5]
- The course of DT is unpredictable, as spontaneous regression, long-lasting stable disease, and disease progression can occur.[2,6-8]

OBJECTIVE

- To review the epidemiology; clinical, humanistic, and economic burden; and available treatments for DT.

METHODS

- Literature database searches for English-language articles from November 2011 to November 2021 were conducted in PubMed, EMBASE, and the Cochrane Library.
  - Articles on disease description and its presentation; epidemiology; clinical, humanistic, and economic burden; treatment; and guidelines were included.
- Conference abstracts published from 2015 to 2022 were also reviewed; in addition, the bibliographies of identified literature reviews and key studies were reviewed to identify additional seminal studies published before 2011.

RESULTS

- A total of 541 publications were identified from the searches, and 60 were selected for inclusion in the evidence base for this review.

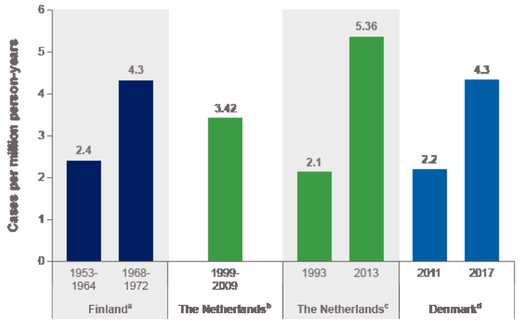
DIAGNOSTIC CHALLENGES

- Because of the morphologic heterogeneity and variable characteristics of DT, patients are confronted with diagnostic challenges:
  - **Delays in diagnosis:** The inability to recognize symptoms can result in diagnosis delays. Most patients interviewed in a United Kingdom study reported delays in diagnosis.[4] They experienced a long diagnostic trajectory within primary and secondary healthcare to receive the correct diagnosis of DT.
  - **Misdiagnosis:** Based on pathologic similarities with other myofibroblastic diseases (e.g., sarcoma, gastrointestinal stromal tumor, nodular fasciitis, leiomyoma) and the low incidence of DT, cases are reported to be misdiagnosed following histologic analysis.[9-11] A French nationwide survey demonstrated that one-third of DT are misdiagnosed.[11] Some patients have reported receiving an initial diagnosis of "cancer" or "malignant sarcoma."[4]

EPIDEMIOLOGY AND RISK FACTORS

- Four primary studies[12-16] providing estimates on the incidence of DT were identified in the literature (Figure 1). An additional source (Orphanet Report Series, 2021) provides a summary of all reported estimates. No study evaluating the prevalence of DT was identified. Likewise, no epidemiological study of DT in the United States (US) was identified. Most DT cases appear in the age range of 20-40 years, and cases among females are 2.2 to 3.9 times the number of cases among males. [12,13,15,16]
- One study[12] reported a 5-year mortality rate of 7 per 1,000 (95% confidence interval, 3-16) among Danish patients with DT compared with 5 per 1,000 (95% confidence interval, 4-7) in a healthy matched cohort.
- Several risk factors for the development of DT are cited in the literature: trauma (DT develops following surgical trauma[2,17]), estrogen and pregnancy (DT increases during pregnancy and in women taking hormonal contraceptives,[3] and adenomatous polyposis coli (APC) gene mutations (patients with the APC mutation may have up to a 30% risk of developing DT).[3,18,3,19]

Figure 1. Incidence of DT in European Countries Reported in Primary Studies



Sources: [a]Reitamo et al.[15]; [b]Nieuwenhuis et al.[13]; [c]van Broekhoven et al.[16]; [d]Anneberg et al.[12]

Note: Data from the Orphanet report[14] are not included in this figure because the data represent an average of various primary sources.

HUMANISTIC BURDEN

DT has a broad negative impact on patients, with deterioration reported in physical, social, and emotional functioning domains (Table 1).[4,20-22]

ECONOMIC BURDEN

No studies evaluating direct or indirect costs of patients with DTs were identified in the literature. Healthcare resource utilization of patients with DT from the Danish Sarcoma Database (2009-2018) was reported to be substantially higher than that in a comparison cohort of the general population.[12]

- Within 3 years after the index date, patients with DT had, on average, 1 inpatient and 7.1 outpatient visits as well as 7.5 days in the hospital compared with an average of 0.8 inpatient and 0.1 outpatient visits and 0.8 days in the hospital in the comparison cohort.[12]
- DT impacts employment and job productivity. In a survey conducted among French patients with DT, 26% stopped working, and 10% worked part time (Table 1).[4,25]

GUIDELINES AND CURRENT TREATMENTS

There are currently no Food and Drug Administration–approved treatment options specifically indicated for patients with DT.

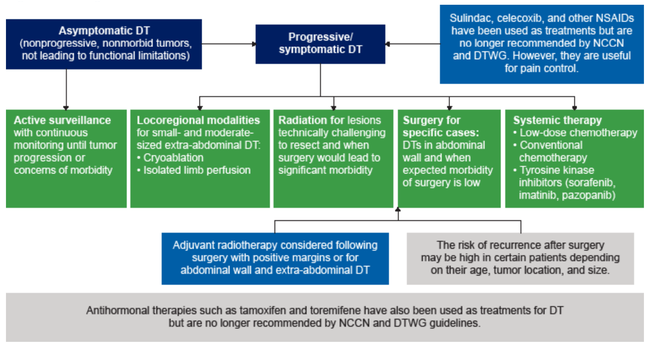
- Because of the highly variable presentation and symptoms of DT, treatment requires a highly individualized approach.[2-4,8]
- Two treatment guidelines provide guidance on the management of DT: the National Comprehensive Cancer Network (NCCN) Guidelines[26] and the Desmoid Tumor Working Group (DTWG) Guidelines.[7-8] Figure 2 presents key recommendations for the management of DT.

Table 1. Summary of Health-Related Quality of Life Studies in Desmoid Tumors

Study Design	Population	PRO Instrument(s)	Key Findings
Cross-sectional study[23]	DT (n = 102) and healthy controls (n = 102) Mean age, DT: 32.7 y; healthy controls: 32.5 y	EORTC QLQ-C30, GAD-7, and PHQ-9	Compared with healthy controls, patients with DT had statistically significantly lower global health status (81.43 ± 17.83 vs. 65.58 ± 22.64, respectively; $P < 0.0001$).
Qualitative study using concept elicitation and cognitive interviews[24]	Patients with localized or multifocal DT, N = 46 (n = 31 concept elicitation interviews: mean age, 44 y; n = 15 cognitive interviews: mean age, 45 y)	Gounder/Desmoid Tumor Research Foundation (DTRF) Desmoid Symptom/Impact Scale (GODDESS)	Most frequent reported symptoms across tumor locations: ▪ Disfigurement (81%) ▪ Nerve pain (71%) ▪ Decreased range of motion (68%) ▪ Muscle pain (65%) ▪ Fatigue (65%) Most frequent reported impacts on patients' lives: ▪ Fear (84%) ▪ Sleep disturbance (77%) ▪ Concern about lack of knowledge among healthcare providers (74%)
Longitudinal study of DART scores[21]	Patients with DT, N = 94 (152 completed DART screens), mean age: 40 y Patients with malignant sarcoma, N = 402 (2,422 DART screens), mean age: 56 y	DART, which includes PRO measures of physical symptoms (ESAS-r), depression (PHQ-9), anxiety (GAD-7), and social difficulties (SDI-21)	Persistent emotional distress associated with DT—including anxiety, depression, and poor well-being—were consistently worse in patients with DT than in patients with sarcoma. Living with DT is similar to living with a chronic disease with long periods of stabilization; the uncertainty associated with inconsistent growth patterns and the fear of progression and recurrence lead to high levels of anxiety.
Focus groups and patient interviews[4]	Adult patients with DT (N = 27); 2 focus groups (n = 14) and interviews (n = 13) Mean age at time of study: 39.5 y (range, 23-74)	EORTC QLQ-C30	Challenges reported by patients with DT: delayed/prolonged diagnosis, treatment uncertainty, treatment-related side effects, debilitating symptoms resulting in limitations in physical and psychosocial functioning, and financial challenges. Pain was the most debilitating symptom, with some patients becoming dependent on pain medications. DT affected relationships, social roles (resulting in isolation), functioning, finances, and employment (reduced ability to work or job loss). Financial strain is related to lost productivity and medical costs, including travel to medical visits.
Survey conducted by the French Patient Advocacy Group SOS Desmoid[25]	Patients with DT, N = 102 Median age: 41 y (range, 17-85)	Structured questionnaire created by patients of the association and reviewed by oncologists and pain doctors	▪ 65 patients (64%) reported pain; daily activity was affected in 14 cases, leisure activity in 12 cases ▪ Pain led to sleep disturbance in 48 cases (73%), irritability in 30 cases (46%), and anxiety in 10 cases (15%) ▪ 38 patients used analgesics (including NSAIDs in 14 patients and opioids in 9 patients) daily to manage pain ▪ Pain-related work disturbances included 17 patients (26%) who stopped working altogether and 7 (10%) who worked only part time due to pain

DART = Distress Assessment and Response Tool; DASH = Disabilities of the Arm, Shoulder and Hand; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer quality of life questionnaire C30; ESAS-r = Edmonton Symptom Assessment System-revised; GAD-7 = Generalized Anxiety Disorders-7; HRQOL = health-related quality of life; NSAID = nonsteroidal anti-inflammatory drug; PHQ-9 = Patient Health Questionnaire-9; PRO = patient-reported outcome; QOL = quality of life; TESS = Toronto Extremity Salvage score.

Figure 2. Managament of Desmoid Tumors



LIMITATIONS OF THE LITERATURE

- The number of publications on epidemiology, humanistic burden, and economic burden was limited, which considerably impaired the assessment for burden of the disease. Specifically, no epidemiological study in the US was identified, and no study evaluating the direct or indirect costs of patients with DT was identified.

CONCLUSIONS

- The substantial burden of illness of DT is related to misdiagnosis, morbidity (pain, and physical and functional limitations), and decreased quality of life (due to negative impacts on physical, emotional, and social domains). There is a high unmet need for treatments that target DT and are associated with improved quality of life for patients.

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