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ORIGINAL ARTICLE *Clinical haemophilia*

Distress in patients with bleeding disorders: a single institutional cross-sectional study

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Introduction: Distress may affect a patient's ability to cope with and manage disease. **Aim:** To report distress prevalence in adult patients with bleeding disorders and determine whether specific clinical and health characteristics, including disease severity and employment status, are associated with distress. **Methods:** Patients who visited a Haemophilia Treatment Centre (HTC) between January 1st, 2012 through February 28th, 2014 and who completed a distress screen, pain screen and questionnaire were evaluated cross sectionally. Distress was measured by the National Comprehensive Cancer Network Distress Management Tool, which allowed patients to rate recent distress on a 0–10 point scale. A rating of five or more was categorized as high distress. Pain was measured by the Brief Pain Inventory Short Form, which asked patients to rate pain types on 0–10 point scales. Patients reported employment and other demographic and behavioural information on the questionnaire. Primary diagnosis, age, HIV and HCV status were abstracted from medical records. Adjusted logistic regression was used to identify distress associations. **Results:** High distress prevalence among 152 patients with bleeding disorders was 31.6%. Unemployment, disability, greater depressive symptoms and higher pain were associated with high distress in multivariable models. Bleeding disorder diagnosis, race/ethnicity, HIV/HCV status and on-demand treatment regimen were not associated with high distress. **Conclusion:** Distress among patients with congenital bleeding disorders followed at a comprehensive HTC was high and similar to that reported among patients with cancer. Future research should determine whether distress impacts clinical outcomes in patients with bleeding disorders as demonstrated in other chronic disorders.

Keywords: depression, distress, haemophilia, pain, quality of life, United States

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Introduction

Distress is a multifactorial unpleasant experience that may or may not accompany a psychiatric syndrome. It can affect a patient's ability to cope with and manage disease which, in turn, may affect health outcomes. For example, among patients with chronic diseases like diabetes or arthritis, distress is associated with poorer medication regimen adherence, glycemic control, physical and general health, functional impairment and higher health care costs [1–5]. Persons with bleeding disorders may be particularly susceptible to distress because they must often practice regular self-care and disease management to reduce bleeding frequency, joint damage and mortality risk. They may be subject to disease-related distress due to pain, HIV and/or HCV infection, medical and treatment expenses, social stigma, burdensome self-care demands and other factors related to having a chronic health condition [6–8]. If patients with bleeding disorders experiencing distress are less likely to follow treatment plans or seek care, as occurs in distressed patients with diabetes and arthritis, consequences could include increased complication risk, poorer health outcomes and even premature death.

Qualitative studies suggest that patients with bleeding disorders may be prone to distress [6,7] but it is

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uncertain how much distress patients experience at any given time and unclear whether distress is caused primarily by the bleeding disorder. It is natural to believe that patients with more severe disease or more complicated clinical consequences may be more likely to report distress. However, other life circumstances like unemployment, which may or may not be influenced by a bleeding disorder diagnosis, could also influence distress. Understanding how clinical disease and non-clinical factors influence distress might help focus patient treatment and care plans.

Patients and physicians may be apprehensive to discuss distress. Patients may feel uncomfortable raising concerns with their provider about distressing practical, family, or emotional problems. Providers may not consider asking about distress, may be unsure of how to treat distress, or may make their own assumptions about patients' distress levels [9,10]. Systematically, screening for distress offers patients a way to report distress, gives the ability to quantify distress and allows clinicians to plan for and provide effective treatment.

We began screening for distress in adults attending the Emory University Haemophilia Treatment Centre (HTC) in 2012 as an additional way to assess the patient's needs during the visit. Inasmuch as there is no standard or endorsed way to screen for distress in patients with bleeding disorders, and the social worker and psychiatrist supporting the HTC also supported the cancer centre, we used a screening tool originally designed to measure distress in patients with cancer and already in use in the cancer centre. To better understand patient distress overall, we undertook an analysis of accumulated patient distress information. The aims of this paper are to (i) quantify distress in patients with bleeding disorders who attend our clinic and (ii) determine whether specific clinical and health characteristics, including disease severity and employment status, are associated with distress. We hypothesized that patients with severe haemophilia would report higher distress.

Patients and methods

Study cohort

The cohort consisted of adult patients with bleeding disorders who attended the HTC anytime between January 1st, 2012 through February 28th, 2014 for an annual visit and who completed a written distress screen, pain screen and clinic questionnaire as part of their routine visit. The screens and questionnaire were included in the informational packet the patient received upon checking in and were typically completed in the waiting room. If a patient completed all three forms multiple times during the time period, only the most recent data were included. The analysis was approved by the Emory University Institutional Review Board.

Data sources: distress screening tool

The National Comprehensive Cancer Network (NCCN) Distress Management Tool is a one-page document that measures recent distress and sources of distress [11]. Patients were asked to circle a number on a distress thermometer that best described how much distress they experienced during the past week. The thermometer ranged from 0 ('no distress') to 10 ('extreme distress'). Following NCCN guidelines, we defined high distress as a score of five or higher [12]. We classified a rating of 1–4 as mild/moderate distress and 0 as no distress. The distress screening tool also asked patients to identify from a problem checklist whether any of 38 specific concerns among five different categories were recently problematic or not.

Data sources: pain screening tool

Each patient self-reported pain using the Brief Pain Inventory Short Form that measured both pain intensity and interference in the patient's life [13]. Patients used a diagram to shade in body parts where they felt pain. Patients then used a scale that ranged from 0 ('no pain') to 10 ('pain as bad as you can imagine') to rate their average pain. Each patient also rated how much pain interfered with their general activity in the past day using a scale that ranged from 0 ('does not interfere') to 10 ('completely interferes'). Pain was categorized as none (score = 0); some (1–4); and high (5–10) and interference as none (score = 0); some (1–4); and substantial (5–10).

Data sources: clinic questionnaire

A clinic questionnaire collected information about the patient's health and behaviours. Patients reported crutch use, physical activity, current ability to participate in daily life activities [14], current employment status, number of school/work days missed in the past year due to their bleeding disorder, average alcohol consumption, current tobacco use and recent depressive mood frequency. Depressive mood frequency was ascertained using the Patient Health Questionnaire-2 (PHQ-2) [15], which consists of two questions: 'Over the past 2 weeks, how often have you been bothered by little interest or pleasure in doing things?' and 'Over the past 2 weeks, how often have you been bothered by feeling down, depressed, or hopeless?' Patients were asked to check 'not at all' (0), 'several days' (1), 'more than half the days' (2), or 'nearly every day' (3) to both. The numbered responses to these two questions were then added together to create a total score that could range from 0 to 6. A total score of 3 or more is typically deemed the optimal cut-point for identifying those who may need further depression screening [15].

Data sources: medical records

Date of birth, age, race/ethnicity, primary diagnosis, baseline factor activity level, the use and frequency of factor taken for prophylaxis (factor replacement prescribed at least once weekly for bleeding prevention) and HIV and HCV antibody positive status for each patient were collected from electronic medical records. We classified patients with primary diagnoses of haemophilia A or B as having mild, moderate, or severe disease based on their documented factor level (>5%, 1–5% and <1% respectively).

Statistical analysis

Cohort characteristics were described overall and for each distress category. Unadjusted logistic regression was used to calculate OR and 95% CIs describing the association between the characteristic and high distress compared to no/mild/moderate distress. Distress was also examined as a continuous outcome in linear regression models. Adjusted logistic regression models that controlled for possible confounders were used to examine whether diagnosis or employment were associated with high distress. We deemed a variable to be a confounder if it was related both to high distress and diagnosis or employment in our cohort. In adjusted models, because the covariates depression and pain were collinear, we ran two models; one including depression and the other including pain. We tested for interactions. Venn diagrams examined overlap between distress, depressive symptoms, pain and unemployment/disability. Correlation coefficients describing the relationship between various pain rankings (0–10 scales) and distress (0–10 scale) were calculated using Spearman rank coefficients. Test for trend *P*-values was performed using the Cochran–Armitage test. In sensitivity analyses, we ran logistic regression models comparing highly distressed patients (i) to mild/moderately distressed patients and (ii) to patients who reported no distress. All analyses were done using SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

Cohort descriptives

There were 478 unique adult patients who came to the HTC at least once between January 1st, 2012 and February 28th, 2014 for an annual comprehensive visit. Of these, 260 (54%) completed at least one distress screen during that period and had data available for analysis. There were 168 patients who completed all three forms on the same day and 152 patients who fully completed the distress screen. Nearly three-quarters of the patients identified as White race (Table 1). The average patient age was 39.8 years and ranged from 20 to 82 years. Most were male (70%) and had haemophilia (68%). Hepatitis C and HIV prevalence in the cohort was 36% and 14% respectively. Three-quarters of the patients reported at least some pain on average (mean = 3). Of these, the most commonly reported pain areas included the knee (41%), ankle (35%), back (30%), elbow (26%) and shoulder (23%). Of patients with severe haemophilia ($n = 57$), over half (58%) were being prescribed prophylaxis at the time of their visit.

Distress descriptives

Nearly one-third of the patients reported high distress while an additional 40% reported mild/moderate distress (Fig. 1). Mean distress score was 3.2. Each patient on average identified five recent concerns from the 38 problem checklist. The most commonly reported concerns were pain (47%), sleep (36%), fatigue (35%), worry (34%) and insurance/financial problems (32%). The least reported concerns were mouth sores (1%), fevers (2%), ability to have children (4%) and diarrhoea (4%). Only 19% of the patients reported that none of the 38 problems were recently concerning.

Unadjusted associations between high distress vs. no/mild/moderate distress

In unadjusted analyses, patients who were unemployed or disabled, reported higher depressive symptoms, reported having to limit school/work/recreational activities due to pain, loss of motion, or weakness, used crutches, had current pain, reported some or high pain on average and who reported that pain interfered substantially with their daily activities were more likely to report high distress (Table 2). A prescribed on-demand infusion schedule was not associated with high distress compared to prophylaxis among patients with severe haemophilia (OR = 1.33, 95% CI = 0.43–4.18). Patients who exercised between 1 and 4 times per week were less likely to report high distress compared to patients who exercised less than once a week. High distress prevalence did not vary significantly by age (OR = 1.01, 95% CI = 0.99–1.04 for each 1 year increase) nor by gender, race, alcohol consumption, or HIV or HCV status. Patients who reported high distress missed more work and school days in the past year when compared with patients who had low or no distress (mean = 29 days vs. 3 days).

Patients reporting high distress identified more concerns from the 38 problem checklist when compared with other patients (mean = 10 vs. 3 problems)

Table 1. Demographic, clinical, functional and pain characteristics of the cohort (n = 152).

	Mean (SD)	*N* (%)
Demographic		
Age in years	39.8 (15.3)	152 (100.0)
Male sex		107 (70.4)
Race		
White		111 (74.0)
Black or African-American		33 (22.0)
Other		6 (4.0)
Employment status		
Working full-time		66 (45.8)
Student, part-time, retired, homemaker		38 (26.4)
Unemployed		17 (11.8)
Disabled		23 (16.0)
Average alcohol consumption		
None		70 (48.3)
<1 drink a week		42 (29.0)
1–4 drinks per week		25 (17.2)
5 or more drinks per week		8 (5.5)
Current tobacco use		31 (21.2)
Clinical		
Primary diagnosis		
Haemophilia A, severe		50 (33.1)
Haemophilia A, moderate		12 (7.9)
Haemophilia A, mild		21 (13.9)
Haemophilia B, severe		7 (4.6)
Haemophilia B, moderate		1 (0.7)
Haemophilia B, mild		12 (7.9)
VWD type 1 or PFD		33 (21.9)
Other VWD		15 (9.9)
HIV positive		21 (13.8)
HCV antibody positive		55 (36.2)
Functional		
PHQ-2 score	0.9 (1.5)	
0–2		129 (88.4)
3–6		17 (11.6)
No. of days work/school missed in past year because of bleed	10.5 (53.6)	141 (100.0)
How often exercise (>30 min)		
Less than once a week		64 (45.4)
Between 1 and 3 times a week		41 (29.1)
Between 3 and 4 times a week		23 (16.3)
5 or more times a week		13 (9.2)
Current activity level		
Unrestricted school/work/rec		75 (56.8)
Unrestricted school/work and limited rec		29 (22.0)
Limited school/work/rec		19 (14.4)
Limited school/work/rec and self-care		6 (4.6)
Requires assistance for school/work, no rec		3 (2.3)
Currently use crutches		17 (12.0)
Pain		
Pain anytime today		68 (53.1)
Pain on average	3.0 (2.6)	
None (0)		34 (25.6)
Some (1–4)		62 (46.6)
High (5–10)		37 (27.8)
Pain has interfered with daily activity in last 24 h	2.8 (3.1)	
None (0)		50 (37.6)
Some (1–4)		46 (34.6)
A lot (5–10)		37 (27.8)

VWD, von Willebrand disease; PFD, platelet function defect; PHQ-2, Patient Health Questionnaire.

(Fig. 2). The specific problems most associated with high distress were pain, getting around and all problems listed in the ‘emotional’ category: depression, fears, nervousness, sadness, worry and loss of interest.

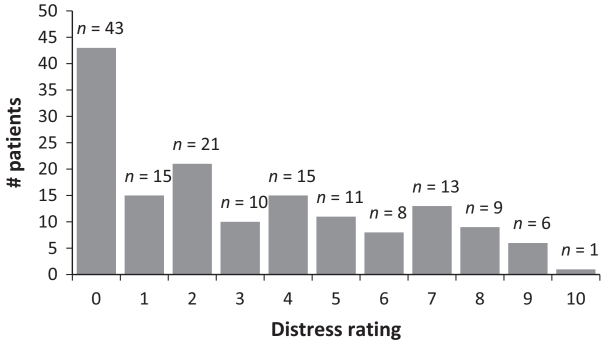

Fig. 1. Distress rating (n = 152).

Ankle pain was mostly associated with high distress when compared with other body areas; 57% of highly distressed patients reported ankle pain while only 25% of no/mild/moderate distressed patients did so. Patients who reported high pain levels (pain scores ≥5) to questions about pain were significantly more likely to report high distress. Patients who reported that pain had substantially interfered in their daily lives were significantly more likely to report high distress in both linear and logistic regression models. The correlation coefficients comparing pain and interference rankings (0–10 scale) to distress ranking (0–10 scale) showed slight positive correlations (all coefficients between 0.35 and 0.57). High distress, high depressive symptoms, high pain and unemployment/disability were occasionally reported together but not always (Fig. 3).

Adjusted associations between high distress vs. no/mild/moderate distress

Higher average pain, higher depressive symptoms and unemployment were all independently associated with high distress in multivariable logistic regression models (Table 3). Being disabled and having mild haemophilia (either A or B) were associated with high distress after controlling for pain but not after controlling for depression. Adjusted results were similar when distress was analysed as a continuous outcome variable (as opposed to a dichotomous variable) in linear regression models.

Sensitivity analysis

When we compared (i) highly distressed patients to mild/moderately distressed patients and (ii) highly distressed patients to patients reporting no distress, results were generally similar to our reported results although CIs were slightly wider, as expected due to smaller sample sizes.

Discussion

Nearly one-third of patients with bleeding disorders reported high distress and an additional 40% reported

Table 2. Unadjusted associations between high distress (≥5) vs. no (0) or mild/moderate (1–4) distress and various health characteristics ($n = 152$).

	Distress category*			
	None *N* (column %)	Mild/Mod *N* (column %)	High *N* (column %)	Unadjusted OR (95% CI)
Demographic				
Age in years				
18–30	20 (46.5)	21 (34.4)	13 (27.1)	1.0
31–45	12 (27.9)	22 (36.1)	15 (31.3)	1.39 (0.58–3.32)
46–83	11 (25.6)	18 (29.5)	20 (41.7)	2.18 (0.93–5.06)
Gender				
Male	31 (72.1)	40 (65.6)	36 (75.0)	1.0
Female	12 (27.9)	21 (34.4)	12 (25.0)	1.39 (0.64–3.02)
Race				
White	29 (69.0)	49 (80.3)	33 (70.2)	1.0
Black or African-American	11 (26.2)	9 (14.8)	13 (27.7)	1.54 (0.69–3.45)
Other	2 (4.8)	3 (4.9)	1 (2.1)	0.47 (0.05–4.20)
Employment status				
Working full-time	19 (45.2)	31 (55.4)	16 (34.8)	1.0
Student, part-time, retired, home	19 (45.2)	15 (26.8)	4 (8.7)	0.36 (0.11–1.16)
Unemployed	1 (2.4)	4 (7.1)	12 (26.1)	7.50 (2.29–24.54)
Disabled	3 (7.1)	6 (10.7)	14 (30.4)	4.86 (1.77–13.33)
Average alcohol consumption				
None	18 (45.0)	26 (45.6)	26 (54.2)	1.0
<1 drink a week	11 (27.5)	20 (35.1)	11 (22.9)	0.60 (0.26–1.39)
1–4 drinks per week	9 (22.5)	9 (15.8)	7 (14.6)	0.66 (0.24–1.79)
5 or more drinks per week	2 (5.0)	2 (3.5)	4 (8.3)	1.69 (0.39–7.35)
Current tobacco use				
No	37 (90.2)	47 (78.3)	31 (68.9)	1.0
Yes	4 (9.8)	13 (21.7)	14 (31.1)	2.23 (0.98–5.06)
Clinical				
Primary diagnosis				
Haemophilia A or B severe	18 (41.9)	22 (36.1)	17 (36.2)	1.0
Haemophilia A or B moderate	3 (7.0)	6 (9.8)	4 (8.5)	1.05 (0.28–3.87)
Haemophilia A or B mild	7 (16.3)	10 (16.4)	16 (34.0)	2.22 (0.91–5.38)
VWD type 1 or PFD	9 (20.9)	16 (26.2)	8 (17.0)	0.75 (0.28–2.00)
Other VWD	6 (14.0)	7 (11.5)	2 (4.3)	0.36 (0.07–1.78)
HIV				
No	38 (88.4)	54 (88.5)	39 (81.3)	1.0
Yes	5 (11.6)	7 (11.5)	9 (18.8)	1.77 (0.69–4.54)
HCV				
No	31 (72.1)	40 (65.6)	26 (54.2)	1.0
Yes	12 (27.9)	21 (34.4)	22 (45.8)	1.82 (0.90–3.67)
Functional				
PHQ-2 score				
0–2	40 (97.6)	59 (100.0)	30 (65.2)	1.0
3–6	1 (2.4)	0 (–)	16 (34.8)	52.8 (6.72–414.72)
No. of days work/school missed in past years				
0	33 (82.5)	39 (67.2)	33 (76.7)	1.0
1–5	5 (12.5)	9 (15.5)	4 (9.3)	0.62 (0.19–2.04)
>5	2 (5.0)	10 (17.2)	6 (14.0)	1.09 (0.38–3.16)
How often exercise (>30 min)				
Less than once a week	15 (38.5)	22 (38.6)	27 (60.0)	1.0
Between 1 and 3 times a week	13 (33.3)	19 (33.3)	9 (20.0)	0.39 (0.16–0.94)
Between 3 and 4 times a week	5 (12.8)	14 (24.6)	4 (8.9)	0.29 (0.09–0.95)
5 or more times a week	6 (15.4)	2 (3.5)	5 (11.1)	0.86 (0.25–2.91)
Current activity level				
Unrestricted school/work and rec	28 (73.7)	32 (58.2)	15 (38.5)	1.0
Limited school/work/rec	9 (23.7)	23 (41.8)	22 (56.4)	2.75 (1.26–6.02)
Requires assistance	1 (2.6)	0 (–)	2 (5.1)	8.00 (0.68–94.22)
Currently use crutches				
No	39 (97.5)	54 (94.7)	32 (71.1)	1.0
Yes	1 (2.5)	3 (5.3)	13 (28.9)	9.45 (2.87–31.06)
Pain				
Pain anytime today				
No	28 (68.3)	22 (44.9)	10 (26.3)	1.0
Yes	13 (31.7)	27 (55.1)	28 (73.7)	3.50 (1.52–8.05)

(continued)

Table 2. (continued)

	Distress category*			
	None *N* (column %)	Mild/Mod *N* (column %)	High *N* (column %)	Unadjusted OR (95% CI)
Pain on average				
None (rating = 0)	18 (48.7)	10 (19.6)	6 (13.3)	1.0
Some (rating = 1–4)	13 (35.1)	34 (66.7)	15 (33.3)	1.49 (0.52–4.28)
High (rating = 5–10)	6 (16.2)	7 (13.7)	24 (53.3)	8.62 (2.84–26.15)
Pain has interfered with daily activity in last 24 h				
None (rating = 0)	22 (61.1)	21 (40.4)	7 (15.6)	1.0
Some (rating = 1–4)	8 (22.2)	23 (44.2)	15 (33.3)	2.97 (1.08–8.15)
A lot (rating = 5–10)	6 (16.7)	8 (15.4)	23 (51.1)	10.09 (3.57–28.52)

VWD, von Willebrand disease; PFD, platelet function defect; PHQ-2, Patient Health Questionnaire.
*No distress is distress rating = 0, mild/moderate distress is rating of 1–4, and high distress is rating ≥5.

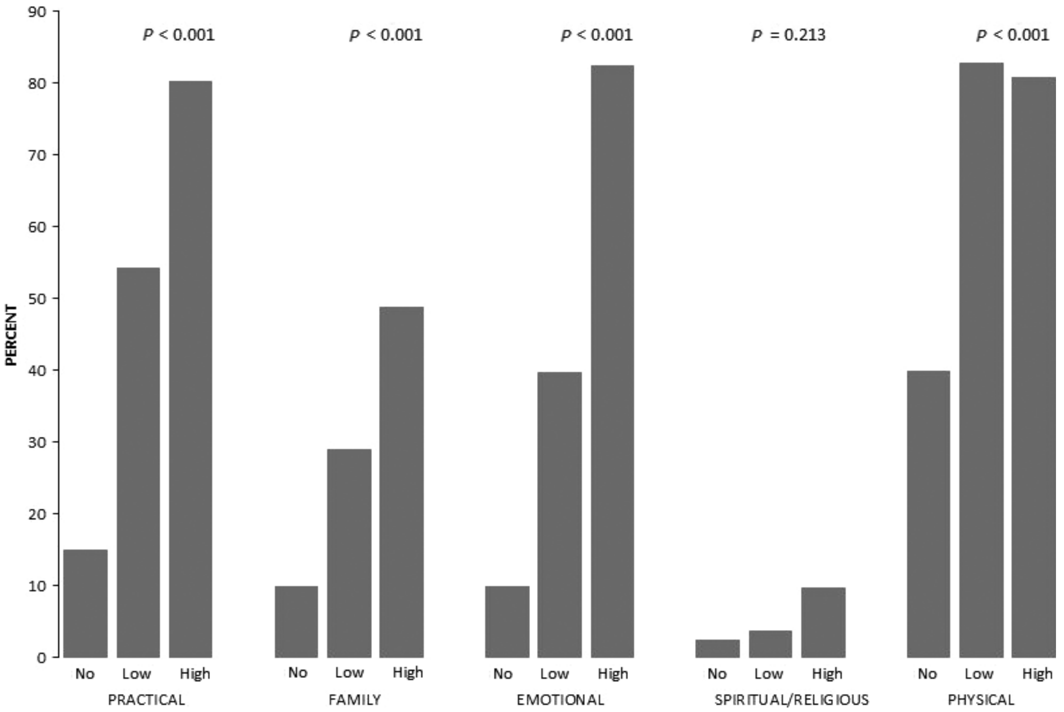

Fig. 2. Per cent of patients who reported experiencing at least one specific problem among five categories by no (0), mild/moderate (1–4) and high distress (≥5) with *P*-value for trend test.

mild/moderate distress. Having severe or moderate haemophilia was not associated with distress nor was HIV or HCV sero-positivity. We had hypothesized that patients with severe haemophilia would report the highest distress. Although patients with severe and moderate haemophilia were more likely to report limited activity, crutch use, HIV and/or HCV seropositivity, prophylaxis use, disability, or unemployment when compared with patients with other diagnoses, they were not more likely to report high distress. In fact, some of our results suggest that patients with mild haemophilia were most likely to experience high distress. It is not clear if any association between mild haemophilia and high distress is simply due to statistical over-adjustment [16], is true only in our study population, or represents a genuine finding. If true, one theory is that mild haemophilia may not significantly impact a patient until adulthood, which could result in self-perception changes and a perceived loss of functional capacity in later life thereby leading to distress while patients with severe haemophilia may have gradually adjusted to their disease and disability over a lifetime. Alternatively, patients with mild haemophilia may have received less social support or feel disconnected from haemophilia community resources. Cancer research has shown that distress in cancer patients is not exclusively related to the disease severity, stage, prognosis, treatment, or time since

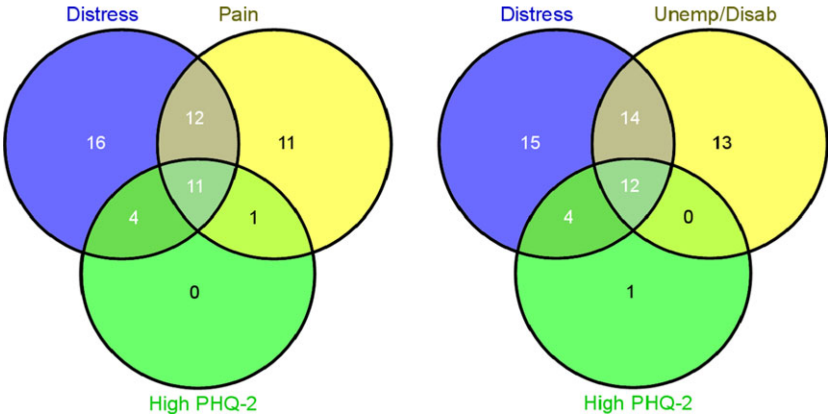

Fig. 3. Distribution of high distress, high pain and high depressive symptoms among patients who reported at least one ($n = 55$)* and distribution of high distress, unemployment or disability and high depressive symptoms among patients who reported at least one ($n = 59$)^. *One hundred and twenty-eight patients were not missing distress, pain, or depressive symptoms information and of these, 55 patients reported at least high distress, high pain, or high depressive symptoms. ^One hundred and fourty patients were not missing distress, employment, or depressive symptoms information and of these, 59 patients reported at least high distress, unemployment or disability, or high depressive symptoms.

Table 3. Multivariable associations between high distress (≥ 5) vs. no (0) or mild/moderate (1–4) distress and various health characteristics.

	Adjusted OR (95% CI)	
	Model 1 (n = 126)	Model 2 (n = 138)
Predictor		
Diagnosis		
Severe/moderate haemophilia	1.0	1.0
Mild haemophilia	6.87 (1.53–30.78)	3.28 (0.69–15.58)
Other bleeding disorders	2.10 (0.45–9.79)	1.23 (0.28–5.38)
Employment		
Work full-time	1.0	1.0
Student, part-time, retired, homemaker	0.49 (0.11–2.14)	0.34 (0.08–1.45)
Unemployed	6.15 (1.28–29.45)	6.53 (1.23–34.68)
Disabled	6.20 (1.54–24.92)	3.77 (0.81–17.48)
Pain on average		
0 (no pain)	1.0	
1–4 (low pain)	1.37 (0.35–5.34)	
5–10 (high pain)	5.64 (1.26–25.32)	
Depression score (PHQ-2)		2.25 (1.49–3.42)
Age	1.00 (0.97–1.04)	1.01 (0.98–1.05)
Race		
White	1.0	1.0
Black or African-American or other	1.23 (0.34–4.41)	1.15 (0.32–4.09)
HIV		
No	1.0	1.0
Yes	0.85 (0.18–4.07)	0.92 (0.19–4.49)
HCV		
No	1.0	1.0
Yes	1.38 (0.37–5.19)	1.05 (0.28–3.96)

PHQ-2, Patient Health Questionnaire.

diagnosis [17–19]. In the cancer field, it is believed that other factors like perceived social support may better predict distress [20]. Employment may represent social support which is consistent with our finding a negative association between employment and distress [21,22].

Highly distressed patients with bleeding disorders reported more concerns from the problem checklist overall when compared with less distressed patients, and they were considerably more likely to report emotional concerns like depression, fears, nervousness, sadness and worry. Similarly, the PHQ-2, which measured depressive symptoms, was strongly associated with distress. Although almost all patients with high depressive symptoms (PHQ-2 $\geq$ 3) were also highly distressed (16 of 17), only 10% of the patients in the cohort had high depressive symptoms, while 32% had high distress, suggesting that something more than depression drives high distress. Since we did not formally and systematically evaluate each patient with depressive symptoms to confirm what proportion had a clinical depression diagnosis, it is not possible to differentiate distress and depression. One study found that patients with diabetes who were screened for distress had high levels of depressive symptoms, but were for the most part, not clinically depressed, and recommended that different interventions were needed for distressed but not clinically depressed patients with diabetes [23]. Patient responses from the distress tool when combined with depression screening and diagnostic tools could help bleeding disorder providers decide when to offer services targeting distress vs. depression.

The largest limitation to this analysis was the cross-sectional design. Our results cannot ascertain whether certain characteristics caused distress or the reverse. Second, our cohort may not represent the entire bleeding disorder population. Only half of clinic patients (260/478) presenting for an annual check-up completed a distress screen and had available data. However, there was no difference in diagnosis or race between those who did and did not complete a distress screen. Patients who completed a distress screen were older (39.5 vs. 34.0 years) and more likely to have HCV (35% vs. 19%) or HIV (13% vs. 7%) compared to patients who did not complete a screen.

There was no difference in distress scores between those who completed all three forms and those who completed only the distress form. Finally, the PHQ-2 provided limited information regarding depressive symptoms and could not diagnose depression. However, the PHQ-2's high sensitivity and lower specificity suggest that patients classified without depressive symptoms do not have depression [15,24,25]. A substantial proportion of patients without depressive symptoms reported high distress. Thus, our results support the interpretation that distress and depression are distinct despite the lack of adequate diagnoses among those with high depressive symptoms.

The distress tool we used has been widely applied and validated in the cancer setting [26–28]. The reported prevalence of high distress in the cancer patient population using the same tool and score cut-off has varied. High distress prevalence was 29% among 91 men with advanced stage prostate cancer [29], 34% among 286 breast cancer patients [17], 35% among 380 ambulatory cancer patients [28], 41% among 98 newly diagnosed lung cancer patients [30] and 47% among 520 adult melanoma patients [31]. Although direct comparisons are limited, our sample reported similar distress levels as that seen in patients with cancer.

Bleeding disorder patients may benefit from a tailored distress-screening tool with detailed and unambiguous questions about pain and questions about both disease and non-disease-related characteristics. A distress-screening tool was created exclusively for patients with diabetes and implemented nearly 20 years ago [3]. Findings from this study suggested that diabetes-related emotional distress, separate from general distress, was an independent and major contributor to poor medication adherence [3]. A revised diabetes distress tool was more recently created to differentiate between various types of diabetes-related distress [32]. A distress thermometer was also created to measure distress in parents of chronically ill children [33]. In both populations, patient responses were used to formulate treatment interventions based on specific problem areas.

Conclusion

Distress in this cohort was substantial, distinct from depressive symptoms, and associated with pain and disability. Importantly, patients with clinically less severe bleeding disorders were at risk for distress. Although further research is required to ascertain whether high distress is associated with poor outcomes in the bleeding disorders population, and if so, whether treating distress improves health outcomes, the current use of tools to screen for distress and depression may facilitate psychosocial assessment in a busy clinical practice.

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References

1 Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med* 2000; **160**: 3278–85.

2 Anderson RJ, Grigsby AB, Freedland KE *et al.* Anxiety and poor glycemic control: a meta-analytic review of the literature. *Int J Psychiatry* 2002; **32**: 235–47.

3 Polonsky WH, Anderson BJ, Lohrer PA *et al.* Assessment of diabetes-related distress. *Diabetes Care* 1995; **18**: 754–60.

4 Strine TW, Hootman JM, Okoro CA *et al.* Frequent mental distress status among adults with arthritis age 45 years and older, 2001. *Arthritis Rheum* 2004; **51**: 533–7.

5 Pandit AU, Bailey SC, Curtis LM *et al.* Disease-related distress, self-care and clinical outcomes among low-income patients with diabetes. *J Epidemiol Community Health* 2014; **68**: 557–64.

6 Barlow JH, Stapley J, Ellard DR. Living with Haemophilia and von Willebrand's: a descriptive qualitative study. *Patient Educ Couns* 2007; **68**: 235–42.

7 Dew MA, Ragni MV, Nimorwicz P. Infection with human immunodeficiency virus and vulnerability to psychiatric distress: a study of men with haemophilia. *Arch Gen Psychiatry* 1990; **47**: 737–44.

8 Carvalhosa AM, Henrard S, Lambert C, Hermans C. Physical and mental quality of life in adult patients with haemophilia in Belgium: the impact of financial issues. *Haemophilia* 2014; **20**: 479–85.

9 Keller M, Sommerfeldt S, Fischer C *et al.* Recognition of distress and psychiatric morbidity in cancer patients: a multi-method approach. *Ann Oncol* 2004; **15**: 1243–9.

10 Söllner W, DeVries A, Steixner E *et al.* How successful are oncologists in identifying patient distress, perceived social support, and need for psychosocial counselling? *Br J Cancer* 2001; **84**: 179–85.

11 National Comprehensive Cancer Network. Distress thermometer for patients. 2014. Available at http://www.nccn.org/patients/resources/life_with_cancer/pdf/nccn_distress_thermometer.pdf. Accessed July 9, 2014.

12 National Comprehensive Cancer Network. Distress management: clinical practice guidelines. *J Natl Compr Canc Netw* 2003; **1**: 344–74.

13 Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore* 1994; **23**: 129–38.

14 Lane H, Siddiqi AE, Ingram-Rich R, Tobase P, Scott Ward R; Universal Data Collection Joint Outcome Working Group, Hemophilia Treatment Center Network Study Investigators. Functional outcomes following ankle arthrodesis in males with haemophilia: analyses using the CDC's Universal Data Collection surveillance project. *Haemophilia* 2014; **20**: 709–15.

15 Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care* 2003; **41**: 1284–92.

16 Schisterman EF, Cole SR, Platt RW. Overadjustment bias and unnecessary adjustment in epidemiologic studies. *Epidemiology* 2009; **20**: 488–95.

17 Dabrowski M, Boucher K, Ward JH *et al.* Clinical experience with the NCCN distress

thermometer in breast cancer patients. *J Natl Compr Canc Netw* 2007; **5**: 104–11.

18 Graves KD, Arnold SM, Love CL, Kirsh KL, Moore PG, Passik SD. Distress screening in a multidisciplinary lung cancer clinic: prevalence and predictors of clinically significant distress. *Lung Cancer* 2007; **55**: 215–24.

19 Zabora J, BrintzenhofeSzoc K, Curbow B, Hooker C, Piantadosi S. The prevalence of psychological distress by cancer site. *Psychooncology* 2001; **10**: 19–28.

20 Hipkins J, Whitworth M, Tarrier N, Jayson G. Social support, anxiety and depression after chemotherapy for ovarian cancer: a prospective study. *Br J Health Psychol* 2004; **9**: 569–81.

21 Kavanaugh A, Han C, Bala M. Functional status and radiographic joint damage are associated with health economic outcomes in patients with rheumatoid arthritis. *J Rheumatol* 2004; **31**: 849–55.

22 Matthews S, Stansfeld S, Power C. Social support at age 33: the influence of gender, employment status and social class. *Soc Sci Med* 1999; **49**: 133–42.

23 Fisher L, Skaff MM, Mullan JT *et al.* Clinical depression versus distress among patients with type 2 diabetes: not just a question of semantics. *Diabetes Care* 2007; **30**: 542–8.

24 Lowe B, Kroenke K, Grafe K. Detecting and monitoring depression with a two-item questionnaire (PHQ-2). *J Psychosom Res* 2005; **58**: 163–71.

25 McManus D, Pipkin SS, Whooley MA. Screening for depression in patients with coronary heart disease (data from the Heart and Soul Study). *Am J Cardiol* 2005; **96**: 1076–81.

26 Hoffman BM, Zevon MA, D'Arrigo MC, Cecchini TB. Screening for distress in cancer patients: the NCCN rapid-screening measure. *Psychooncology* 2004; **13**: 792–9.

27 Grassi L, Johansen C, Annunziata MA *et al.* Screening for distress in cancer patients: a multicenter, nationwide study in Italy. *Cancer* 2013; **119**: 1714–21.

28 Jacobsen PB, Donovan KA, Trask PC *et al.* Screening for psychologic distress in ambulatory cancer patients. *Cancer* 2005; **103**: 1494–502.

29 Roth AJ, Kornblith AB, Batel-Copel L, Peabody E, Scher HI, Holland JC. Rapid screening for psychologic distress in men with prostate carcinoma: a pilot study. *Cancer* 1998; **82**: 1904–8.

30 Steinberg T, Roseman M, Kasymjanova G *et al.* Prevalence of emotional distress in newly diagnosed lung cancer patients. *Support Care Cancer* 2009; **17**: 1493–7.

31 Loquai C, Scheurich V, Syring N *et al.* Screening for distress in routine oncological care – a survey in 520 melanoma patients. *PLoS ONE* 2013; **8**: e668800.

32 Polonsky WH, Fisher L, Earles J *et al.* Assessing psychosocial distress in diabetes: development of the diabetes distress scale. *Diabetes Care* 2005; **28**: 626–31.

33 Haverman L, van Oers HA, Limperg PF *et al.* Development and validation of the distress thermometer for parents of a chronically ill child. *J Pediatr* 2013; **163**: 1140–6.