Screening for Distress in *BRCA1/2* carriers: a prospective study

Identificação do distress *em portadores de* BRCA1/2*: um estudo prospetivo*

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Keywords
Hereditary Cancer; BRCA carrier; Psychological Distress; Predictive Factors; Risk perception.

Abstract

Introduction: The period of time elapsed after receiving a positive test result, has been previously associated with distress in BRCA1/2 carriers. However, there is a need for reliable instruments and prospective data on distress and perception of risk by those carriers, given the significant increase in demand for BRCA1/2 testing.
Aim: To validate and implement in clinical practice, an instrument for the detection of distress and analysis of risk perception, in individuals that test positive for a BRCA1/2 test.
Materials and Methods: We conducted a prospective study to design and test an instrument (Distress and Risk Perception Questionnaire-DRP) to evaluate distress and risk perception by BRCA1/2 carriers. Predictive factors for clinically relevant distress, were also explored.
Results: One hundred and seventy consecutive, newly diagnosed BRCA1/2 carriers were included (pre-test phase: 21 and test: 149). Distress was measured with the distress thermometer (DT) and DRP, both applied, by telephone, one month after test disclosure. Clinically relevant distress was observed in 40% of the cases. Being a female (OR male vs female=0.37; 95%CI=0.10-1.09) and index patient (OR index vs relative=3.93; 95%CI=1.13-18.37) were independent predictors for distress after adjusting for personal history of cancer. The risk perception was high and no significant correlation with distress was observed with either DT or DRP (Spearman correlation coefficient<0.1 and p>0.05 in both).
Conclusion: DRP is a new scale, easy to administer by telephone, which measures distress and risk perception in BRCA1/2 carriers. Gender and type of genetic screening (being an index patient or a relative) may play a role in the short-term emotional impact of a positive BRCA test result.

Palavras-chave
Cancro hereditário; portador BRCA; stresse psicológico; fatores preditivos; perceção de risco.

Resumo

***Introdução**: O* distress *identificado em portadores de mutações BRCA1/2 foi previamente associado ao período de tempo decorrido desde o conhecimento do resultado do teste. Atendendo ao aumento da procura para realizar testes genéticos, são necessários dados prospetivos sobre o* distress *e a perceção de risco nos portadores de variantes patogénicas BRCA1/2.*
***Objectivo**: Desenvolver e validar um questionário dirigido para medir o* distress *e a perceção de risco em portadores de BRCA1/2.*
***Materiais e Métodos**: Neste estudo, de carater prospetivo, foi elaborado e testado um instrumento (questionário de* distress *e perceção de Risco - DPR) que avalia o* distress *e a perceção de risco em portadores de BRCA1/2. Foram também explorados fatores preditivos para o* distress *clinicamente relevante.*
***Resultados**: Foram analisados cento e setenta portadores de BRCA1/2 recém diagnosticados (21 na fase pré-teste e 149 na fase teste), identificados de forma consecutiva. Mediu-se o* distress *com o termómetro de* distress *(TD) e com o DPR, ambos aplicados através de entrevista telefónica, um mês após a comunicação dos resultados do teste genético. Em 40% dos casos observou-se* distress *clinicamente relevante; o género feminino (OR masculino* vs *feminino=0,37; 95%CI=0,10-1,09) e a situação*

de ser o primeiro familiar a ser testado (doente índex) (OR índex vs *familiar=3,93; 95%CI=1,13-18,37) foram identificados como fatores preditores independentes para o* distress*. A perceção de risco individual e familiar foi alta e não se observou correlação significativa desta com o* distress*, medido tanto com o TD como com o DPR (coeficiente de correlação Spearman<0,1 e p>0,05 em ambos).*

***Conclusão**: O questionário DPR é uma escala nova, fácil de administrar por via telefónica, que mede o* distress *e a perceção de risco em portadores BCRA1/2. As doentes mulheres e a situação de primeiro familiar a ser testado (doente índex) são fatores preditores do impacto emocional, a curto prazo, de um resultado positivo no teste genético BCRA1/2.*

Introduction

Pathogenic mutations in *BRCA1/2* genes explain most of the known cases of hereditary breast and ovarian cancer.[1-3] These carriers are also at risk for prostate and pancreatic cancer and, for *BRCA2* carriers, also for gastric cancer, multiple myeloma and other neoplasia.[4,5] Intensive surveillance, chemoprevention and/or prophylactic surgeries are recommended to *BRCA1/2* carriers with the main goal of preventing cancer morbidity and mortality.[6]

Testing for *BRCA1/2* pathogenic variants should be preceded by appropriate genetic counselling. During counselling, advantages and disadvantages of testing, including the possible adverse psychological outcomes should be discussed. Genetic counselling regarding *BRCA1/2* testing is a complex process that may not always fulfil patients' needs.[7, 8] Even for index patients and their relatives with positive test results, uncertainty looms and is perceived as a limitation, justifying implementation of surveillance and preventive procedures.[6, 9] Indeed,[8] realizing its status as a *BRCA1/2* carrier may have an emotional impact affecting the patient, her/his family and her/his social context.[10-12] Previous studies have shown that the psychosocial outcomes following *BRCA1/2* testing vary according to the previous individual and family experiences of each patient as well as with the time elapsed after disclosure of the test result.[10-19] Distress increases shortly after receiving results and returns to pretesting levels over time. Time is relevant not only for carriers but also for individuals with inconclusive results and non-carriers of *BRCA1/2* mutations.[14,16] The possibility of positive results of *BRCA1/2* testing eliciting anxiety, depression or guilt was previously described.[14,16,20,21] Possible causes are the possibility of having transmitted the cancer predisposing variant to their offspring and due to other family, marital and reproductive issues,[11-13] as well as issues of access to health care and insurance. There is little information, however, about that impact emotional distress may have in the understanding and adherence to specific risk-reducing management plans proposed to *BRCA* carriers. A previous study reported that not only breast cancer genetics knowledge but also cancer--specific distress were significantly associated with adherence to recommended risk reducing plan.[22]

Women are overrepresented in previous studies of distress, and even studies that included men had very low numbers of confirmed carriers.[23,24] With the recognition that *BRCA1/2* men also have higher cancer risks,[24] and need specific surveillance guidelines,[25] the number of male candidates for *BRCA* genetic screening is increasing. More information is needed about the psychological impact of *BRCA1/2* testing in male carriers.

Instruments for identification of the impact of cancer risk assessment have been previously described.[26, 27] Distress, a vital measure in psycho-oncology,[28-31] was also studied and patients with a positive *BRCA1/2* test result had distinct questionnaire results from patients with negative or inconclusive tests.[26] For this subgroup of individuals, a reliable instrument allowing for the systematic identification of distress is needed to manage adequate psychosocial support. In this study, our primary objectives were to develop and validate a short instrument, possible to apply by telephone, to evaluate the prevalence of distress one month after the disclosure of a positive *BRCA1* or *BRCA2* test result. The instrument included questions about risk perception. An exploratory objective was the analysis of predictive factors for clinically relevant distress, in this population.

Materials and Methods

Institutional approval – This study was approved by the Ethics Committee of Instituto Português de Oncologia de Lisboa Francisco Gentil (Study number IPOLFG, UIC/634).

Study design and participants – This was a prospective, cross-sectional study conducted in the family cancer clinic of the Instituto Português de Oncologia de Lisboa, a tertiary cancer centre, that provides

counselling for several public and private health institutions of Southern Portugal, under a multidisciplinary program. The study population comprised all consecutive *BRCA1/2* carriers identified from April 2011 to April 2014 aged 18 and older, capable of expressing free consent, regardless of gender and previous cancer history. All subjects had received pre- and post-testing genetic counselling and were carriers of a deleterious *BRCA1/2* mutation.

Study procedures – Subjects were invited to participate in this study, after the post-test counselling visit. Those willing to participate signed the informed consent form. A structured telephone interview was conducted by the research nurses one month after disclosure of the positive *BRCA1* or *BRCA2* test result. Research genetic nurses were trained on competences in communication through telephone interviews by a certified psychologist.

Patient measurements – Socioeconomic and demographic data were collected from patients' clinical notes. Variables assessed were age, gender, marital status, number of children and occupational status.[32]

Distress Thermometer (DT)- – This is a universal measure to evaluate distress in cancer patients. It is a single-item, 11-point range scale (ranging from 0 "no distress" to 10 "extreme distress"), used as a self-report measure of psychological distress.[33-35] DT is validated in the Portuguese population.[35] The symptoms list was not used since it would be difficult to use it by telephone. During telephone interviews patients were asked to give the number (0-10) that best described how distressed they had been in the previous week, including the day of the interview. In the Portuguese population, a DT score above 4 indicates clinically relevant distress level.[35]

Distress and Risk Perception Questionnaire (DRP) – DRP is a 13 item self-report measure that evaluates two dimensions: psychological distress and risk perception concerning disease status and individualized risk-management plan. We developed the DCRP because there was the need to have a short questionnaire that could be easily answered through a telephone interview. Psychological distress in DRP comprises three scales: anxiety, depression and loss of emotional control. Each scale has 3 items, all with a 5 position Likert type response (appendix 1). These 9 items correspond to a short version of the Mental Health Inventory Questionnaire (MHI) that has been used to evaluate psychological distress in populations without a psychiatric diagnosis (24 items) and emotional well-being (14 items). MHI is validated for the Portuguese population.[36] The other dimension of DRP, risk perception concerning disease status and individualized risk-management plans,[6] comprises 4 items also with a 5 position Likert type response each (appendix 1). In DRP each item was scored in a scale ranging from 1 to 5; the global score for each dimension was obtained by the sum of the scores from the respective items. Distress score ranges from 9 "no distress" to 45 "extreme distress" and the risk perception score ranges from 4 to 20, with higher values corresponding to better risk perception.

Pre-test phase: validation of DRP questionnaire – We conducted a pre-test phase between September 2010 and March 2011 in a sample of 21 individuals to assess the internal consistency and construct validity of DRP. Cronbach's alpha was calculated for each subscale and dimension separately and all obtained values were above 0.80, showing adequate internal consistency. Spearman rank correlation coefficient was used to evaluate the convergent and discriminant validity. Convergent validity was deemed to be acceptable if convergent correlations (i.e., correlation between items that should theoretically be related to each other) were above 0.4. For discriminant validity there should be a difference of at least 10 decimal points between the convergent and discriminant correlations (i.e., correlation between items that should not be related). The results obtained were similar to the ones reported for the original longer Portuguese version of the MHI questionnaire[36] and were in compliance with the pre-specified acceptance conditions. Concurrent validity was evaluated by comparison to DT with reliable results (Spearman's rank correlation coefficient = 0.86). A DRP distress score above 21 was the optimal cut off value found by Receiver Operating Characteristic (ROC) curve analysis for identification of individuals with clinically relevant distress (sensitivity=100%; specificity=91%).

Statistical methods

Descriptive statistics was used for socio-demographic and clinical characterization of the sample and for description of the distress and risk perception score measures. The correlation between risk perception and distress levels was evaluated using the Spearman rank correlation coefficient. We conducted

an exploratory analysis using logistic regression in order to identify independent predictors of clinically relevant distress (DT score>4 or DCRP score distress>21). The factors evaluated were age (≤50 *vs* >50 years-old), gender, prior cancer diagnosis (yes *vs* no), type of genetic screening (index proband *vs* other familial), and offspring (yes *vs* no). The unadjusted OR refer to the results of the univariate logistic regression analysis. Factors with statistically significant associations (p<0.10) on univariate analysis were then analysed using multivariable logistic regression to identify independent risk factors. We calculated the Variance Inflation Factors (VIF) to check for multicollinearity and the Durbin-Watson (DW) statistics to test for correlated residuals. In all cases VIF values were below four and the DW statistics were close to two with non-significant associated p-values, thus indicating no multicollinearity or autocorrelation issues. All tests were two-sided and a significance level of 5% was considered unless otherwise specified. As there were no missing values no imputation methods were required. The analysis was conducted using R.[37]

Results

One hundred and forty nine out of 177 eligible new consecutive identified *BRCA1/2* carriers were included in this study. Reasons for exclusion were logistical reasons (n=22), death (n=2), patient refusal (n=1) and progressive symptomatic disease preventing participation (n=3).

Socio-demographic and clinical characterization

Table 1 shows the socio-demographic and clinical characteristics of the 149 individuals included in the study. There was a predominance of women (81%). The overall median age at the time of inclusion in the study was 43 years, being 42 (range: 21-74) in women and 44 (range: 25-73) years in men.

Sixty-seven individuals (45%) had a previous cancer diagnosis, 14 more than 5 years prior to inclusion in the study and the remaining 53 within a 5 year period. The remaining 82 carriers (55%) were healthy at risk and had previously consented on pre-symptomatic *BRCA1/2* diagnosis. Fifty four carriers (36%) had consented on genetic *BRCA1/2* screening as index patients (the first family relative to be tested in one family) and the others as relatives of patients previously tested and positive for a BRCA1/2 mutation. Only 42 participants (28%) had no offspring and most (68%) were professionally active. Regarding occupational status only 9% were non-qualified workers.

Table 1 – Socio-demographic and clinical characteristics

	N (%)
Age	
Median [min-max]	43 [21-74]
Age ≤50 years	103 (69%)
Age >50 yeas	46 (31%)
Sex	
Female	120 (81%)
Male	29 (19%)
Marital status	
Married or with a partner	82 (55%)
Single, divorced, widowed	46 (31%)
Unknown	21 (14%)
Offspring	
No	42 (28%)
Yes	106 (71%)
Unknown	1 (1%)
Number of children, median [min-max]	1 [0-6]
Number of daughters, median [min-max]	1 [0-3]
Number of sons, median [min-max]	0 [0-4]
Occupational status	
Student	6 (4%)
Unemployed	5 (3%)
Retired	10 (7%)
Employed	102 (68%)
Qualified worker[a]	33 (22%)
Intermediate level profession[b]	56 (38%)
Non-qualified worker[c]	13 (9%)
Unknown	26 (17%)
Prior cancer diagnosis	
Yes	67 (45%)
No	82 (55%)
Type of genetic screening	
Index patient	54 (36%)
Relatives of index patients	95 (64%)

[a] Profession related to military, political and management positions and scientific activities [10].
[b] Civil service and commercials, administrative, security, qualified agriculture, forest and fishing workers, qualified industry workers [10].
[c] Non-qualified workers and machine and technical operators [10].

Evaluation of distress and risk perception

Table 2 presents the descriptive summary of the scores concerning the DT and all dimensions and subscales of the DRP measure instrument. The mean observed distress scores were 3.1 (SD 2.7) and 20.1 (SD 7.9) for DT and DRP instruments, respectively. Fifty percent of the individuals reported a DT score≤2 and a distress score measured by DRP≤18; in both cases these values are below the cut-off for clinically relevant distress levels (above 4 for DT and above 21

Table 2 – Descriptive summary for Distress and Risk Perception

Dimensions and subscales	Mean	SD	Min	Max	Median	IQR
Distress – DT	3.1	2.7	0	10	2	[1-5]
Distress – DRP	20.1	7.9	9	41	18	[13-25]
Anxiety	7.4	2.8	3	15	7	[5-9]
Depression	6.5	2.9	3	15	6	[4-8]
Loss of emotional control	6.3	2.8	3	14	6	[4-8]
Risk Perception – DRP	18.7	1.9	11	20	20	[18-20]

DT – Distress Thermometer; DRP - Distress and Risk Perception Questionnaire; SD – Standard deviation; IQR – Interquartile range [25% quartile – 75% quartile] Minimum and maximum possible scores for each dimension/subscale: Distress – DT: 0-10; Distress – DRP: 9-45; Anxiety: 3-15; Depression: 3-15; Loss of emotional control: 3-15; Risk Perception about individualized risk-reducing plans: 4-20.

for DRP). Forty-two (28%) and 60 (40%) individuals were found to have clinically relevant distress when evaluated by the DT and DRP scale, respectively. Those carriers were evaluated in the clinic and 28 of them (19%) were confirmed as having criteria for specialized psychological-social support, and were appropriately referred.

As for risk perception observed in our sample (mean 18.7; SD 1.9; median 20) (Table 2) no significant correlation could be demonstrated between the risk perception and the distress levels, either evaluated by DRP (correlation coefficient=-0.047; p-value=0.5731) or DT (correlation coefficient= 0.041; p-value=0.6202).

Table 3 – Predictive factors for clinically relevant distress scores during the month after disclosure of a positive *BRCA1/2* test (univariate analysis)

Variable	*n*	Distress measure instrument: DT			Distress measure instrument: DRP		
		DT>4 N (%)	OR (95% CI)	p	DRP>21 N (%)	OR (95% CI)	p
Gender							
Male	29	4 (14%)	0.35 (0.10-0.97)	0.0424	5 (17%)	0.25 (0.08-0.64)	0.0032
Female (ref)	120	38 (32%)	1		55 (46%)	1	
Age							
>50 years	46	15 (33%)	1.36 (0.63-2.89)	0.4264	18 (39%)	0.93 (0.45-1.89)	0.8497
≤50 years	103	27 (26%)	1		42 (41%)	1	
Prior cancer diagnosis							
Yes	67	20 (30%)	1.16 (0.56-2.38)	0.6837	30 (45%)	1.41 (0.73-2.73)	0.3107
No	82	22 (27%)	1		30 (37%)	1	
Type of genetic screening							
Index	54	20 (37%)	1.95 (0.94-4.07)	0.0730	26 (48%)	1.67 (0.84-3.30)	0.1404
Relative	95	22 (23%)	1		34 (36%)	1	
Offspring[a]							
Yes	106	32 (30%)	1.38 (0.62-3.27)	0.4379	46 (43%)	1.53 (0.73-3.31)	0.265
No (ref)	42	10 (24%)	1		14 (33%)	1	

DT – Distress Thermometer; DRP – Distress and Risk Perception Questionnaire

[a] One subject without information concerning offspring was not included in this analysis.

Fig 1A – Boxplot of Distress Thermometer (DT) distress score by gender

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Fig 1B – Boxplot of Distress and Risk Perception Questionnaire (DRP) distress score by gender

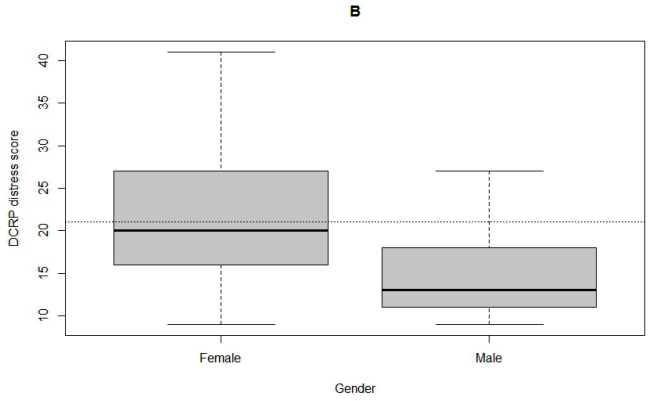

Fig 1C – Boxplot of Distress Thermometer (DT) distress score by type of genetic screening

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Fig 1D – Boxplot of Distress and Risk Perception Questionnaire (DRP) distress score by type of genetic screening

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Horizontal dotted lines indicate the cut-off values above which the distress level becomes clinically relevant.

Exploratory analysis of the predictors for clinically relevant distress

In preliminary descriptive analysis distress scores were consistently higher in women than in men and in index patients as opposed to non-index cases (Figures 1A-B and 1C-D). Nevertheless, in univariate analysis, gender was the only factor significantly associated with clinically relevant distress, with a reduction of 65% to 75% in the odds in men compared to women (DT instrument: Unadjusted OR=0.35; 95%CI 0.10-0.97. DCRP instrument: Unadjusted OR=0.25; 95% CI: 0.08-0.64) (Table 3). A trend for an association between type of genetic screening and clinically relevant distress was observed for DT, with an increase of 95% of the odds of distress in index cases compared to non-index cases (Unadjusted OR=1.95; 95% CI 0.94-4.07) (Table 3).

In order to control for a potential confounding effect between gender and type of genetic screening (in females 43% were index cases and in males only 10%) and prior cancer diagnosis (52% in females and 17% in males) we also conducted a multivariable analysis considering these variables (Table 4). All the other variables were well balanced between genders. This multivariable analysis confirmed gender (DCRP score) as an independent factor for clinically relevant distress after adjusting for type of genetic screening and prior history of cancer (OR male *vs* female=0.26; 95% CI 0.08-0.71). In the multivariable analysis based on the DT score, type of genetic screening was an independent factor (OR index *vs* familial=3.93; 95% CI 1.13-18.37) and there was a trend for lower odds of distress in men (OR male *vs* female=0.37; 95% CI 0.10-1.09).

Discussion

In this study the prevalence of clinically relevant distress during the month after disclosure of a positive *BRCA1/2* test result was 40%. Female gender and undergoing index testing were identified as predictive

Table 4 – Predictive factors for clinically relevant distress scores during the month after disclosure of a positive *BRCA1/2* test (multivariable analysis)

Variable	Model A Distress measure instrument DT			Model B Distress measure instrument DRP		
	OR	95%CI	p	OR	95%CI	P
Gender						
Male	0.37	0.10-1.09	0.0960	0.26	0.08-0.71	0.0131
Female	1			1		
Prior cancer diagnosis						
Yes	0.44	0.07-1.15	0.1106	0.79	0.27-2.19	0.6574
No	1			1		
Type genetic screening						
Index	3.93	1.13-18.37	0.0468	1.57	0.55-4.69	0.4026
Relative	1			1		

DT – Distress Thermometer; DRP – Distress and Risk Perception Questionnaire
Model A: Variance Inflation Factors: gender=1.06, prior cancer diagnosis=3.31, type genetic screening=3.31; Durbin-Watson statistic=2.05, p-value=0.766
Model B: Variance Inflation Factors: gender=1.06, prior cancer diagnosis=2.34, type genetic screening=3.32; Durbin-Watson statistic=2.05, p-value=0.766

factors for distress. We also observed that even distressed carriers were able to retain information about individualized risk reducing plans.

We developed a new measure, the DRP, given the lack of available instruments validated for the Portuguese population evaluating both distress and risk perception. There is also a need for short but reliable questionnaires that can be applied during telephone interviews. Indeed, other questionnaires are longer and not so easily applied by digital means, although they measure other dimensions besides Distress.[26, 27]

The prevalence of clinically relevant distress dropped to 28% when considering the results obtained with the DT instrument. The apparent discrepancy between DT and DRP is related either with the different sensitivity of the measures or with the different time periods these instruments refer to. Interviews were conducted one month after test disclosure but DT evaluates distress during the last 7 days while DRP evaluates distress for the whole month after test disclosure. Our results are in line with the previous observations that distress is influenced by time elapsed after test disclosure, decreasing to pre-test levels with time.[10, 14, 16] Even though we did not study pre-test levels, our data suggests that as much as 40% of carriers experienced clinically relevant distress at any time during the first month after disclosure of the test result. This proportion decreases to 28% in the last 7 days of the covered timeframe. Although most of these carriers declined psychological support, 28 (19%) were referred to psychological observation after review of these results.

Our sample consisted of women, aged less than 51 years, actively employed and with at least one child. Concerning predictive factors for distress we found some differences between the DT and DRP: when analyzing DRP, female gender was the only factor significantly associated with distress after adjusting for type of genetic screening and for prior cancer diagnosis. This may be explained by the known association of *BRCA1/2* gene mutations with female cancers, together with their impact on femininity.[16] With DT besides female gender, a trend for a higher distress among index patients was also observed. These predictive factors for distress measured with DT (index cases and female gender) may be related with the time needed to integrate the complex genetic information in the individual and family dynamics. The emotional impact of an adverse life event such as the disclosure of a high cancer risk arouses coping strategies of avoidance.[38-40] These strategies predominate during the early stage when the emotional intensity of the life event is highest.[41] Previous data reveal that, after a few weeks, these mechanisms lose their dominance, and other factors such as the search for information and the need to share it with others start to emerge.[10] Index cases should communicate or allow communication of information about the genetic risk to relatives.[42] This might be a possible explanation for the association found between type of genetic screening and distress in DT (evaluates distress during the last week in a

4 week period) but not in DRP (which evaluates distress during the whole 4 week period). Effective risk perception may have contributed to overcome the lower proportion of clinically relevant distress observed when using DT.[43] Nevertheless, we could not demonstrate any significant correlation between risk perception and distress, probably because there were no identifiable patients with low level of risk perception.

As previously described[14,16,20] cancer specific distress in this population probably depends on the concerns about medical surveillance, prophylactic surgeries, communication of results to family members and reproductive decisions. Transmission of a clear risk reducing plan may help to divert the focus from negative information (being the carrier of a characteristic associated with high risk for cancer) to coping.[42]

No difference in distress was observed between cancer survivors and individuals undergoing pre--symptomatic testing. This may be explained by the sense of familiarity with cancer[8,42] observed in some *BRCA1/2* families: even non-affected individuals deal with cancer in their close relatives (mothers, sisters, aunts and cousins) since very young ages. This familiarity may lead to the acquisition of adaptive mechanisms and skills that help to deal better with cancer related information,[43] like, in this specific setting, a positive *BRCA1/2* test result.

Few studies with small numbers have evaluated the impact of *BRCA1/2* testing in men. Both distress and self-perception of risk have been reported as increased in male *BRCA1/2* carriers.[24,44] Cancer risks have been recognized for these carriers[4,24] but, with the possible exception of prostate cancer[25] clear evidence is lacking concerning benefits of surveillance. To our knowledge, this study is the first description of the association between gender (being lower for men) and distress after the disclosure of a positive *BRCA1/2* test. Distress was previously identified[38] in male *BRCA1/2* carriers up to 4 years after test disclosure, but data was retrospectively collected.[23] Our data adds to evidence that males have specific needs regarding genetic testing.[21, 44]

Conclusion

In conclusion, we validated a short questionnaire easy to implement in clinical practice to screen for distress and risk perception after disclosure of a *BRCA1/2* positive test. No correlation was observed between risk perception and the level of distress. Being a female and an index patient were the only factors associated with clinically relevant distress.

As a future recommendation, and besides the implementation of the DRP instrument in the routine practice of genetics clinics, the authors reinforce the need for larger prospective studies, that should address if short term distress predicts adverse psychological outcomes, in individuals that test positive for *BRCA1/2* testing.

The strengths of our study are its prospective design and the inclusion of a consecutive sample, minimizing selection bias. The shorter scale for Distress identification was validated by phone, allowing for widespread use in a time when candidates for cancer genetic testing are increasing and posing a huge burden on genetic and family cancer risk services.

The limitations of this study are the small sample of *BRCA1/2* carriers included in the validation phase and the single-center methodology. Nevertheless, the pre-validation sample was representative of all the participants included, and data were collected by the same trained health professionals during structured interviews throughout the whole study. The generalizability of this single-center research may not be compromised, because our center is a referral center for genetic *BRCA* screening in our country. Long term distress was not measured neither the association between short and long term distress, but that analysis was beyond the scope of this study.

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Annex 1

Distress and risk perception questionnaire (drp)

Section 1. Distress

The questions below are about worries that you may have had after receiving your genetic test results. Please answer every question indicating whether you have experienced each emotion always, often, sometimes, almost never or never in the past week.

QUESTIONS	ANSWERS				
	Always	Often	Sometimes	Almost never	Never
1. During the past month, how often did you feel nervous or uneasy due to the result of the genetic diagnosis?					
2. During the past month, how often did you feel anxious or worried due to your test results?					
3. Did you feel depressed during the past month?					
4. During the past month, how often did you feel tense and angry?					
5. How often in the past month did you feel emotionally stable?					
6. During the past month how often did you feel that your life projects were in jeopardy?					
7. How often, during the past month, did you feel that everything that happened was the opposite of what you wished?					
8. In the past month how often did you feel down?					
9. During the past month, have you been, or have you felt under great pressure or stress?					

Section 2. Risk Perception

The questions below are about the information you were provide with about cancer risk in your family and about possible measures of individual risk management. Please answer every question indicating whether you think you have perceived the information provided: very well, quite well, fairly well, almost nothing or nothing.

QUESTIONS	ANSWERS				
	Very well	Quite well	Fairly well	Almost Nothing	Nothing
10. Did you perceive the cancer risk related with your positive test result?					
11. Did you understand how important it is to have an individualized risk reducing plan?					
12. Did you retain information about the risk-reduction strategies available (clinical and radiological surveillance, other exams and preventive surgeries)?					
13. Do you consider the information provided by the team to be adequate?					