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Report

The characteristics of cyclical and non-cyclical mastalgia: a prospective study using a modified McGill Pain Questionnaire

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Summary

Breast pain (mastalgia) is a common condition (usually classified as cyclical or non-cyclical) the characteristics of which have never been studied using a standardized pain instrument. We have modified the short form of the McGill Pain Questionnaire (SF-MPQ) for the measurement of mastalgia, and have administered it to 271 women with breast pain and without breast cancer. The mean pain-rating index (sum of 15 descriptors of SF-MPQ) was similar between cyclical and non-cyclical pain, and was 12.0 (of 45) for the entire group. When compared to similar studies of pain at other sites, this falls in the same range as chronic cancer pain, and just below the pain of rheumatoid arthritis. Mean %VAS (visual analog scale) was 45.12 and mean %PPI (present pain index) was 39.9. Most women described their pain as 'heavy, aching and tender,' and these descriptors were given significantly higher ratings by women with cyclical pain. In women with non-cyclical mastalgia, the overall pain severity was related to the size of the painful area, and the steadiness of the pain, and the affective components were more prominent than in women with cyclical mastalgia. Thus, cyclical and non-cyclical mastalgia show some differences in their characteristics with substantial overlap. The total breast pain score was most efficiently estimated by a combination of the VAS, the PPI, and the quality of life questions ($R^2 = 0.96$). Studies of breast pain should include both groups to better understand and characterize these differences, particularly with regard to a possible connection with breast cancer risk.

Introduction

Mastalgia (breast pain) is a common complaint, which affects an estimated 10–30% of women, although accurate population based figures are not available. A significant minority of women (2–5%) experience moderate or severe mastalgia, with its burden of pain and suffering, and attendant impact on quality of life. Breast pain is only rarely a symptom of breast cancer [1], but nonetheless deserves rigorous investigation for several reasons. Firstly, the etiology of breast pain remains unclear. Postulated mechanisms include altered ratios of fatty acid esters [2], higher basal prolactin levels [3], increased prolactin response to stimulation [4, 5], and high dietary fat [6]. However, the biologic mechanisms leading to pain remain unknown. Secondly, no satisfactory treatment exists: the most commonly prescribed medications (danazol and bromocriptine) are often poorly tolerated and provide temporary relief [7]. Tamoxifen has been used, but has potentially serious side effects [8], and progesterone treatment has had mixed results [9, 10]. Finally, there are data suggesting a link with breast cancer risk. These come from two sources: two case-control studies which showed an association between breast cancer occurrence and cyclical mastalgia [11, 12] and two studies of mammographic parenchymal patterns, which described an association between high risk mammographic patterns and cyclical mastalgia [13, 14]. The measurement of pain was very variable in these studies, and was retrospective in all except one [12].

Further prospective investigations of mastalgia will require an instrument for the reproducible measurement of breast pain. There has been some discussion in the literature as to the appropriate method of

measuring breast pain; most authors have used a visual analog scale, and some have advocated the use of pain diaries [15]. The descriptors that most accurately describe the pain, their contribution to the overall perception of pain, and to overall quality of life impact, have never been measured. Many authors do, however, refer to the fact that the pain must be accurately classified and described in order to develop algorithms for diagnosis and treatment, and begin to investigate the etiology of this troubling and common condition.

There has also been some discussion in the literature regarding differences between cyclic and non-cyclic mastalgia, and most clinical classifications distinguish between these two forms [16]. It has been suggested that the etiology of cyclic and non-cyclic breast pain differ, with the cyclic variety having more of an overlap with premenstrual syndrome, and therefore a hormonal etiology [7, 16]. Presumably because of distinctions like this, both of the case-control studies of mastalgia and breast cancer risk mentioned above excluded women with non-cyclic mastalgia [11]. The true etiologic and biologic difference between these two forms of mastalgia remains an open question however, and differences in the characteristics of the cyclical and non-cyclical breast pain have not been systematically examined using a standard pain instrument.

We have performed a prospective study of women with breast pain in order to better define the characteristics of the pain, and its impact on quality of life. We have modified the short form of the McGill Pain Questionnaire (SF-MPQ) [17], and have administered it to 271 women without dominant breast lesions, seen at the Breast Care Center of University Hospital, Syracuse, NY. The main intent of the study was to establish whether or not cyclic and non-cyclic breast pain has distinct characteristics. To differentiate these characteristics it was necessary to develop a standard pain instrument, designed specifically for the breast.

Methods

The SF-MPQ was modified for the breast (see below). It was administered to women being seen at the Breast Care Center of University Hospital, Upstate Medical University, in Syracuse, New York. The questionnaire was approved by the Institutional Review Board, and was then administered to 450 women, of whom 54 had been diagnosed with breast cancer, and 125 had no breast pain within the past 3 months. The remaining 271 women who completed the questionnaire, and described some breast pain over the preceding 3 months, are the subject of this report. A preliminary verbal screen was used to exclude non-breast pain. All patients underwent appropriate clinical evaluation, including physical examination, mammography, and if indicated, ultrasonography, to exclude malignancy as a cause of breast pain. All women had subsequent follow-up visits to confirm the absence of breast cancer.

Our breast pain questionnaire (BPQ) based on modifications of the SF-MPQ is available at http://apkarianlab.northwestern.edu. The first 11 BPQ descriptors characterize the sensory dimensions of breast pain (throbbing, shooting, stabbing, sharp, cramping, gnawing, burning, aching, heavy, tender, splitting) with the next four being affective descriptors (tiring, sickening, fearful, punishing). Each dimension had four possible scores (0–3), yielding a possible maximal score of 33 for the sensory descriptors, 12 for the affective descriptors and a possible minimum score of 0 for both. The questionnaire also assessed the pain intensity by a visual analog scale and by the McGill present pain index. These elements of the BPQ directly replicate the first portion of the SF-MPQ. A question regarding the chronicity of the pain (periodic, intermittent, steady) was taken from the long form of the MPQ. We then added a breast specific segment, which addressed the temporal properties of the pain: cyclicity, number of painful days per month, and relationship to menstrual cycle. The location of the pain was ascertained on breast drawings, which replaced the whole body drawing in the original MPQ. A set of quality of life questions were designed using criteria outlined by Williams [18], to reflect issues directly related with breast pain: effect on sexual activity, use of pain medicine, presence of other pains, effect on sleep and work.

We calculated a set of *summary pain measures*: the %sensory component (%sensory) was the sum of the scores for each sensory descriptor divided by 33, calculated as a percentage. For example, for a woman who described moderate shooting pain but all other sensory components were absent, had a raw sensory score of 2, and her %sensory score was $(2/33)*100$. Similarly, the % affective score was calculated as the sum of scores of the affective descriptors as a percentage of the maximal affective score. %Qtotal is the sum of the sensory and affective scores, calculated as

a percentage, with appropriate weighting, since there were 11 sensory and four affective descriptors. %PPI was the present pain index of the SF-MPQ (mild, discomforting, distressing, horrible, excruciating) expressed as a percentage of a five-point scale. %VAS is the visual analog scale expressed as a percent value. %QOL consisted of the score for quality of life questions. The %totalBP was the final summary value and equaled (%Qtotal) + (%PPI) + (%VAS) + (%QOL).

We also calculated values for *ancillary components of pain*: chronicity of pain, duration of pain in months, number of painful days and most painful day per menstrual cycle in patients with cyclic pain, size of painful area (calculated from the breast sketch), use of medications for pain, presence of other pains.

Step-wise linear regression was used to identify predictors of total breast pain, and to examine differences in the pattern of cyclic versus non-cyclic pain. Principal components factor analysis was used to examine the clustering of the sensory and affective dimensions and their summary measures. Factor analysis and correlation analysis was used to examine the inter-relationship of *summary pain measures* and *ancillary components of pain* for cyclic and non-cyclic pain groups.

Results

The study subjects ranged in age from 16 to 81 years (mean 46.2). Of these, 254 women were premenopausal, and 13 were postmenopausal.

Overall pain ratings

The mean pain-rating index (sum of 15 descriptors of SF-MPQ) was 12.02 (of a possible maximum of 45) for all women with breast pain. The mean rating for the sensory component was 9.90 (out of 33), and for the affective component was 1.15 (of 12). Mean %VAS was 45.12 and mean %PPI was 39.9 (2.0 on the absolute 0–5 PPI scale).

Sensory and affective descriptors in cyclic and non-cyclic pain

One hundred and thirty-four women characterized the pain as cyclic, whereas 152 women described non-cyclic pain. The mean age of the cyclic group was 41 years, and that of the non-cyclic group was 50 years.

Table 1. Sensory and affective characteristics of cyclical and non-cyclical mastalgia

	cyclic	Non-cyclic	*p* value
Number of subjects	134	152	
Mean age	41 years	50 years	0.00000
%Sensory	28	31	0.1
%Affective	6.6	12.6	0.02
Individual descriptors*			
Burning	0.3	0.6	0.002
Aching	1.6	1.3	0.01
Heavy	1.1	0.8	0.02
Tender	1.9	1.5	0.0001
Sickening	0.1	0.3	0.04
Fearful	0.2	0.6	0.002
%VAS	44.84	45.32	0.9
%PPI	38.52	41.01	0.2
%QOL	28.68	26.09	0.4

*Only descriptors with significantly different scores between cyclical and non-cyclical groups are presented.

Table 1 shows the characteristics of the two groups of patients, the total sensory and affective scores, and the VAS, PPI and QOL scores. The total breast pain score of the two groups was similar (135.9 for cyclic and 140.1 for non-cyclic pain). Both groups rated the sensory descriptors heavy, aching and tender with the highest scores, but scores for all three parameters were significantly higher for women with cyclic pain. Scores for burning (sensory), sickening, and fearful (affective) pain were significantly higher in the non-cyclic group, resulting in a significantly higher mean % affective score for non-cyclic pain. Thus cyclical pain has a stronger sensory component, whereas non-cyclical pain has a more pronounced affective component. There was no difference in the %VAS, %PPI, and %QOL among women with cyclical and non-cyclical pain.

Principal components factor analysis was used to further characterize the subjective perceptual properties of cyclical and non-cyclical breast pain. Figure 1 shows the two-factor mappings for the two groups. The non-cyclical pain descriptors are separated into two distinct clusters: one cluster is comprised of tender, aching and heavy (these have the strongest loadings), the remaining descriptors clustering separately. On the other hand, cyclical breast pain is comprised of many more clusters: with a main cluster made up of sharp, shooting, and stabbing (with strongest loadings), another by heavy,aching, and

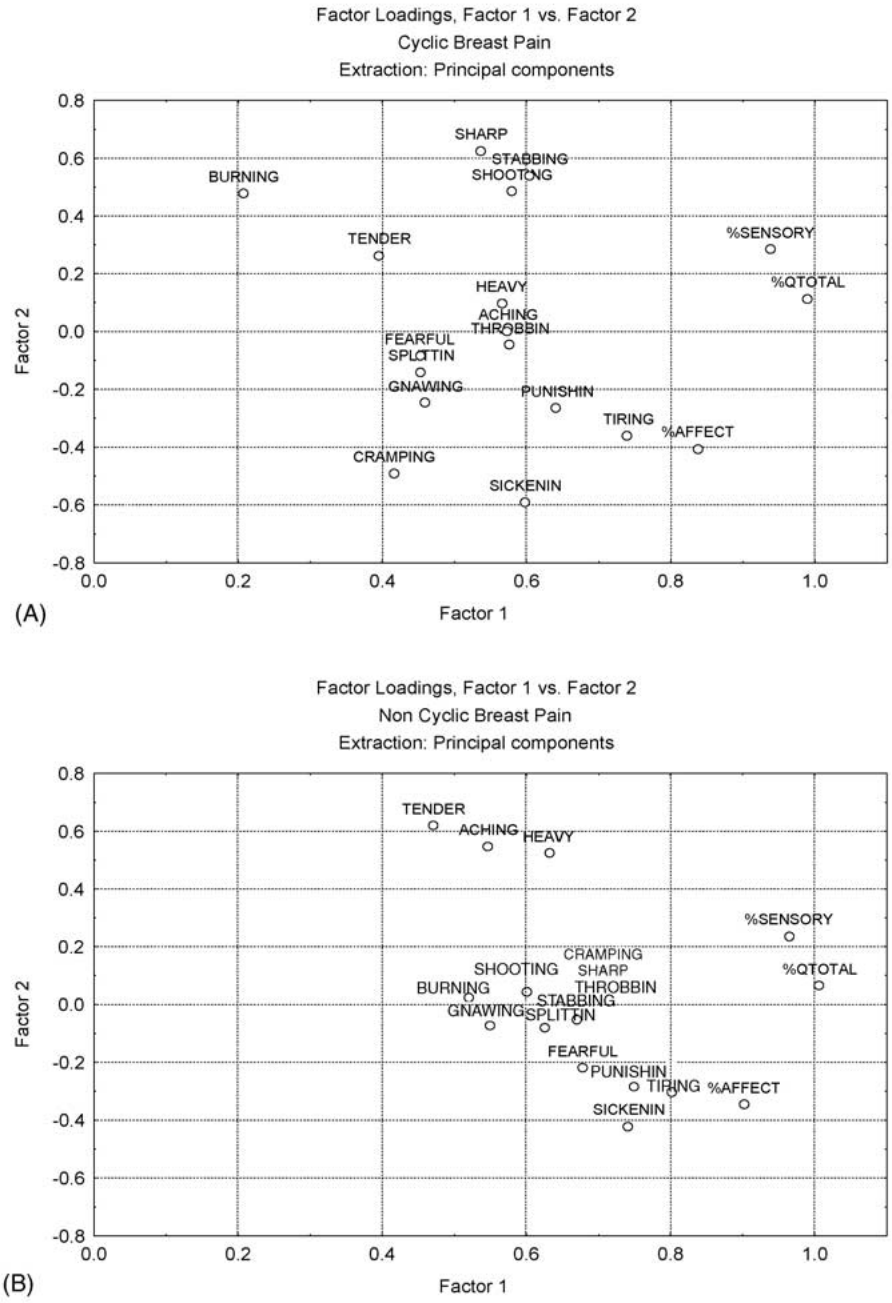

Figure 1. Principal components two factor analysis for 15 descriptors of pain, taken from the SF-MPQ as well as their relative relationship to the overall sensory, affective and total (Qtotal) pain ratings. In (A) these measures are presented for all women with cyclical breast pain. In (B) the same measures are shown for women with non-cyclical breast pain.

throbbing, a third by fearful, splitting, and gnawing, while burning and tender remain distinct dimensions. The factor analysis, therefore suggests that the subjective perception of cyclic breast pain is of higher dimensionality and thus more complex than non-cyclic breast pain.

Contribution of ancillary components to summary pain measures

The distribution of the most painful day of the cycle and of the number of painful days, is shown in Figure 2. The majority of women with cyclical pain described the most painful day as being between day

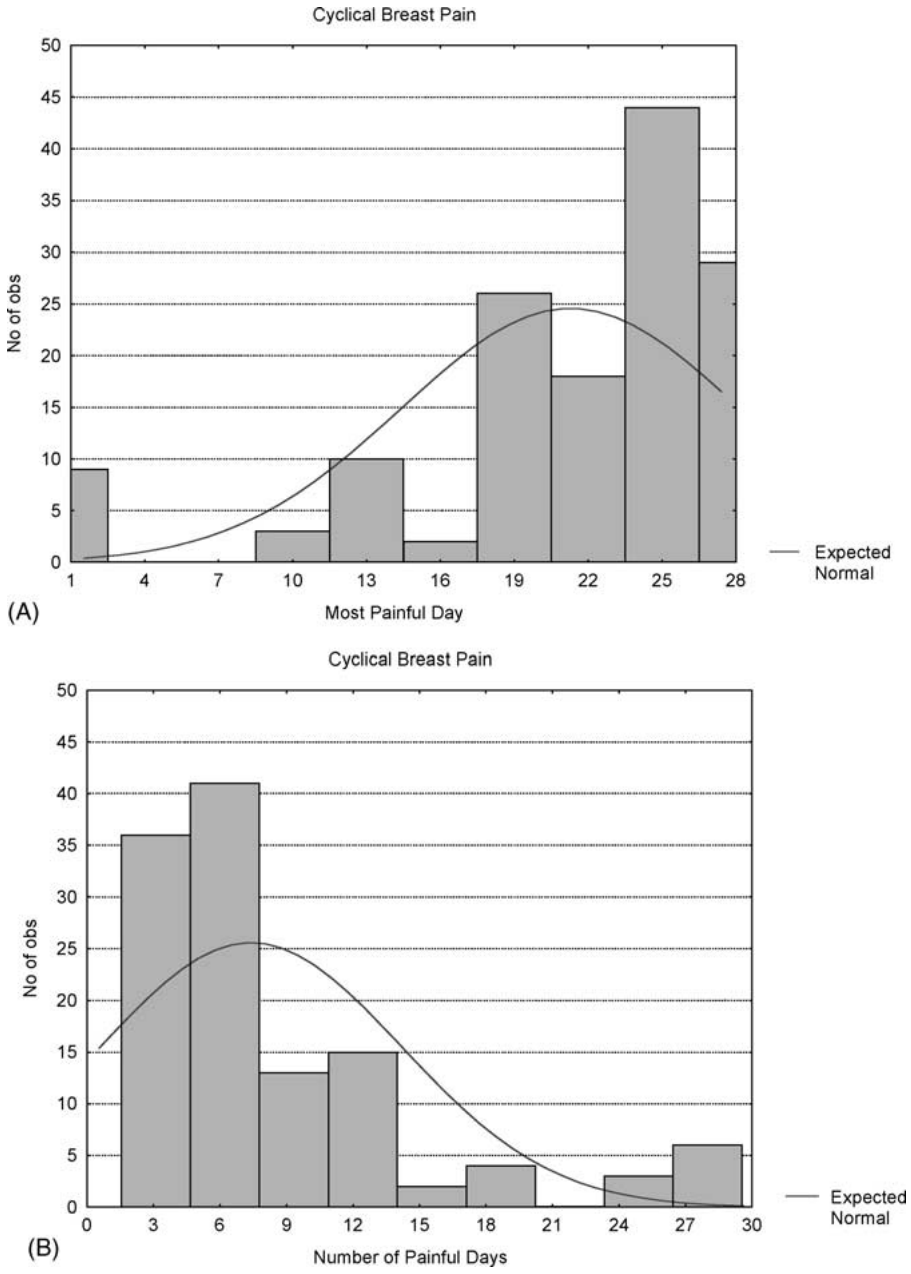

Figure 2. Cyclical mastalgia: most painful day of cycle (A) and number of painful days (B).

20 and 28 of the menstrual cycle, and pain lasted between 5 and 10 days for most women. Women who continued to experience pain through menstruation had the highest pain scores ($n = 8$, TotalBP was 173 ± 72). For those reporting most painful day in the middle third of the cycle ($n = 16$) had a mean score of 157 ± 63, and in the last third of the cycle ($n = 101$) the mean score was 130 ± 55. So although the majority of women report that their pain is greatest towards the end of the cycle, a minority who experienced their greatest pain in the early and mid-cycle actually have higher mean pain scores.

We then looked at the ancillary components of pain in relationship to the summary pain measures. Stepwise backwards elimination was used in linear regression models to identify the ancillary components

Table 2. Linear regression models exploring the contribution of ancillary components of pain to summary pain measures, for cyclic and non-cyclic mastalgia

Dependent variable	F-value for model	Significant ancillary components
Total breast pain score		
Cyclic	10.6	Worst day, medication, other pain
Non-cyclic	12.4	Steady, medication, other pain
%Sensory		
Cyclic	5.7	Steady
Non-cyclic	14.2	Steady
%Affective		
Cyclic	12.2	Steady
Non-cyclic	7.1	Steady
VAS		
Cyclic	<1	None
Non-cyclic	10.2	Steady, size of painful area
PPI		
Cyclic	7.8	Worst day
Noncyclic	6.2	Medication
QOL		
Cyclic	45.8	Worst day, medication, other pain
Non-cyclic	47.9	Steady, medication, other pain

Stepwise backward linear regression was performed, starting with the following explanatory variables: age, steady, periodic, brief, duration of breast pain in months, size of painful area, use of medications, and presence of other pains. For the models of cyclical pain, the number of painful days, and the worst day of the cycle was also used.

that were significant independent predictors of the summary pain measures (i.e., %sensory, %affective, %Qtotal, %VAS, %PPI, and %QOL). These analyses were performed separately for cyclical and non-cyclical pain, and are shown in Table 2. This multi-variate analysis showed a large overlap between cyclical and non-cyclical pain, with steadiness of pain, use of medications for pain, and the presence of other pains being important determinants. The major difference between cyclical and non-cyclical pain in these analyses was that for non-cyclical pain, the size of the painful area is significant, whereas for cyclical pain the most painful day contributes significantly to total pain score (i.e., pain early in the cycle being worst).

Figure 3 examines the relationship between the size of the painful area and the summary pain measures using univariate correlation analysis. In women with non-cyclical pain, all correlation coefficients between size of painful area and each summary pain measure were significant ($p < 0.05$). None of these relationships were significant in the women with cyclical pain. It appears that the size of the painful area has little explanatory value in women with cyclical pain, but is significantly related to pain descriptors in women with non-cyclical pain.

Principal components factor analysis was used to examine the relationship between overall measures of pain and ancillary descriptors in cyclical and non-cyclical breast pain groupings, see Figure 4. In the cyclic group, age, size of breast in pain, and brief or periodic descriptors all clustered around zero on both factors, implying minimal contribution; while the use of medications, presence of other pains clustered together and with duration of pain were related to the quality of life measure along factor 2. Non-cyclical breast pain had also clustering of use of medications and presence of other pains (again related along factor 2 with quality of life measure), as well as a clustering of steadiness of pain with the size of breast in pain. The results of the principal components analysis closely agree with the regression analysis and the correlation analysis.

Sites of other pain

A total of 110 women reported pain at other sites, which could be organized into five main categories: abdominal/pelvic pain, back pain, headache, fibromyalgia, and arthritic pain. Back pain was the most frequent, being reported by 42 women (38%), followed by abdominal/pelvic pain (33%), headache (12%), arthritic pain (9%), and fibromyalgia (8%). There was no obvious difference in the report of pain at other sites between cyclical and non-cyclical pain.

Proportion of women with severe pain

We next examined the distribution of the summary pain measures to see what proportion of women suffer from severe pain which compromises their quality of life. The quartile distributions of these measures are shown in Table 3. Relatively few women (about 2%) suffer the extremes of the sensory and affective components of mastalgia. However, 4–28% of women suffer from moderate or severe mastalgia, and fall in the upper half of the distribution of scores for %Qtotal, %VAS, and %QOL. With regard to total breast pain

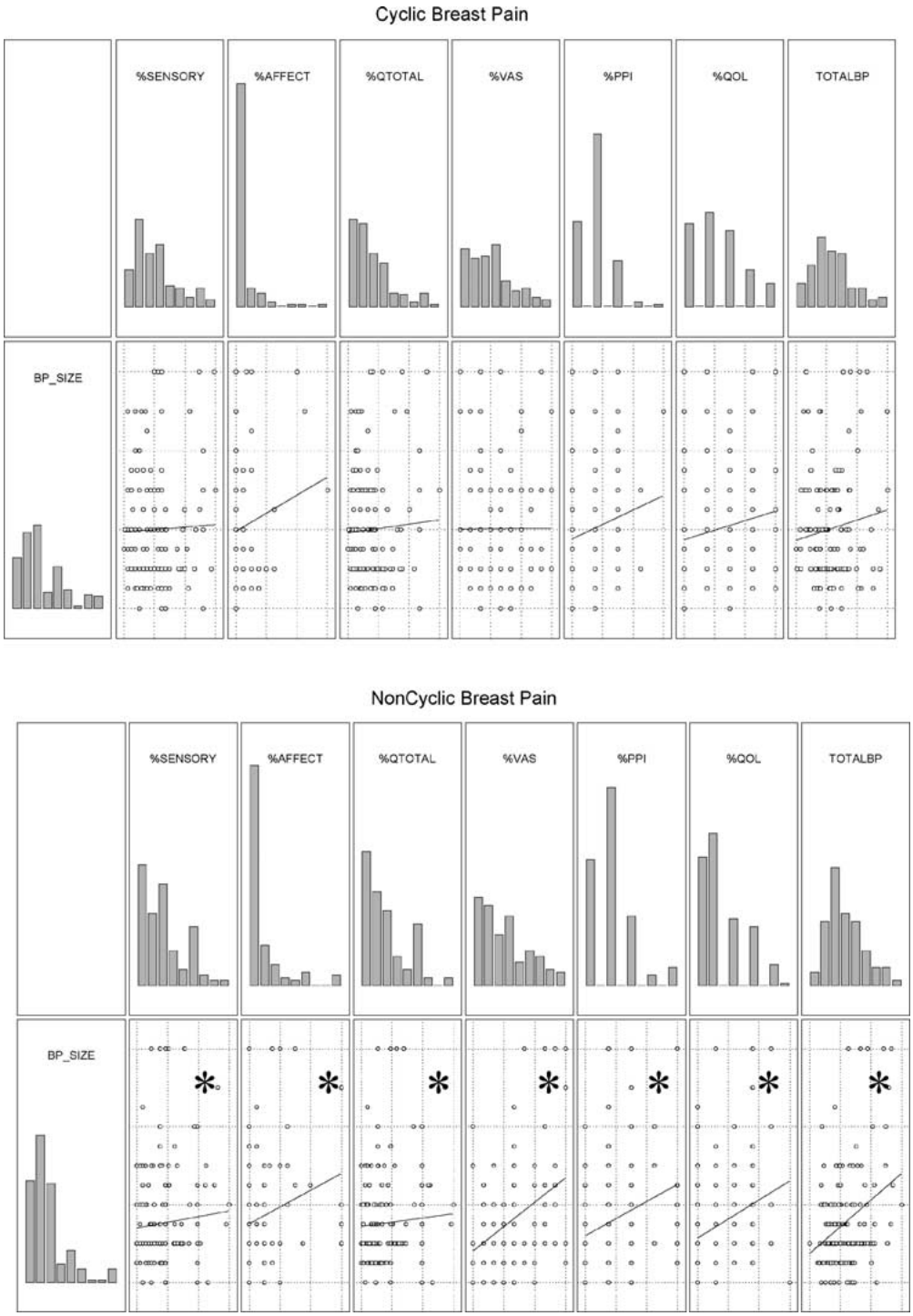

Figure 3. Frequency histograms of the summary pain measures are related to the size of the painful area: for non-cyclical pain, all summary pain measures are significantly and positively related to the size of the painful area. In contrast, in cyclical mastalgia the size of the painful area is not significantly related to any of the measures. *Asterisks denote significant relationships, $p < .05$.

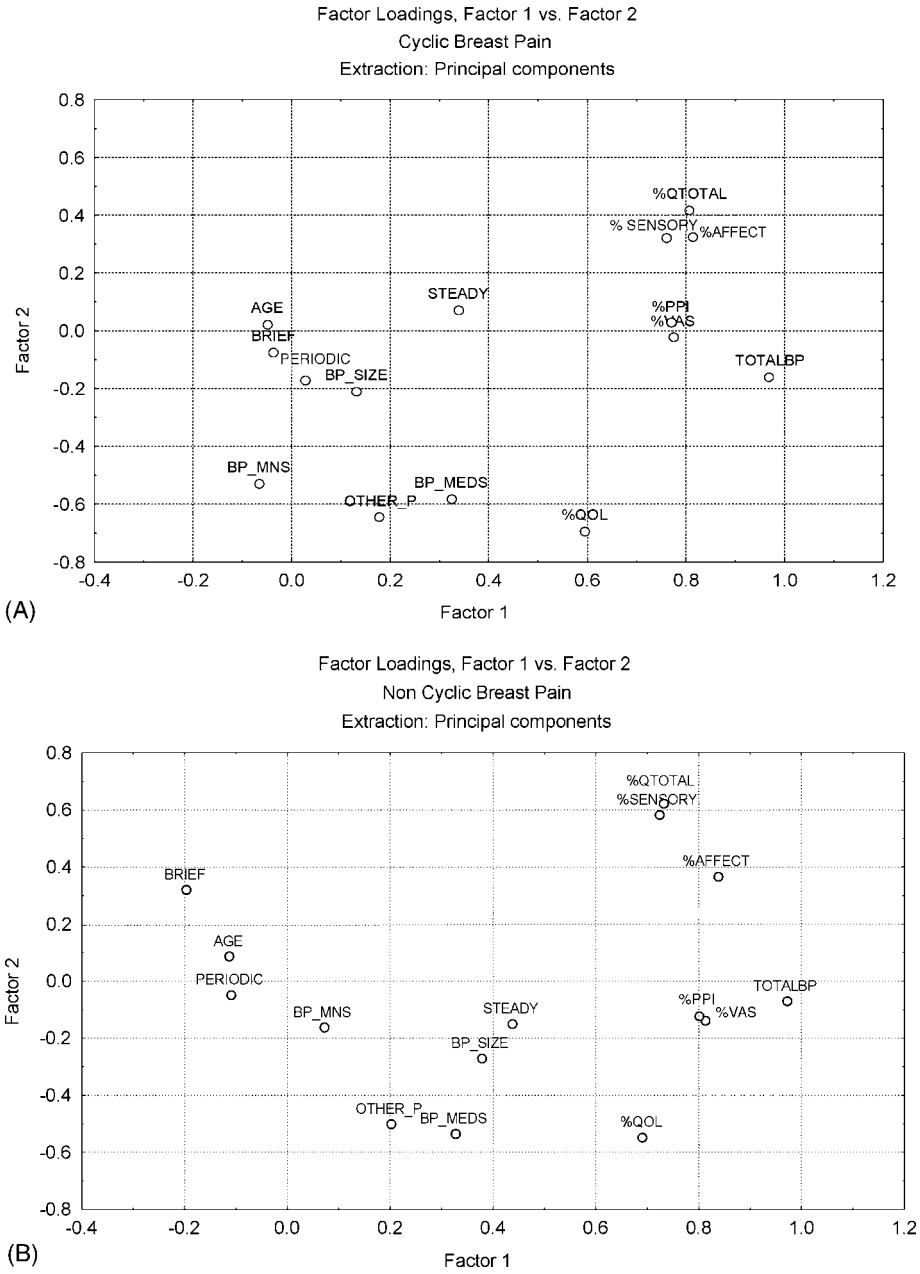

Figure 4. Principal components two-factor relationship between persistence of pain (i.e., steady, periodic or brief), chronicity of pain (i.e., duration in months), the size of the painful area, the use of medications for breast pain, and the presence of other pain with overall measures of pain. (A) Results are shown for women with cyclical pain; (B) results for women with non-cyclical pain.

score, 7% of women with any mastalgia report scores in the upper half of the distribution.

Best summary measures of total breast pain

In an attempt to identify the most efficient estimators of total breast pain, we then used stepwise backwards regression starting with %sensory, %affective, %VAS, %PPI, %QOL as explanatory variables. The two most parsimonious models included: (1) %VAS, %PPI, and % QOL ($F = 661$, adjusted $R^2 = 0.94$) and (2) %VAS, % QOL, and %sensory ($F = 1041$, adjusted $R^2 = 0.96$). These models suggest that there is little information gained by asking women to score

Table 3. Proportion of women in upper quartile of distribution of pain measures

Quartiles	Number (%) in upper quartile	Number (%) in upper half
Sensory	10 (1.4)	50 (13.5)
Affective	6 (2.3)	13 (3.8)
Qtotal	8 (1.3)	42 (14.2)
VAS	37 (13.7)	77 (28.4)
PPI	14 (4.7)	60 (20.2)
QOL	19 (7.0)	57 (21.0)
Total breast pain	20(2.8)	55 (7.1)

the sensory and affective components of their pain, and that questions which include a visual analog score, quality of life questions, and a present pain index, effectively captures total pain with equal efficiency, and can be used in prospective studies where repeated measurement of pain is required. This abbreviated measurement instrument may also be useful in large cohort studies investigating the relationship of breast pain with outcomes such as cancer, and where questionnaire space is at a premium.

Discussion

The distinction between cyclical and non-cyclical mastalgia has been made by many authors, and is a standard part of the etiologic and clinical classification of breast pain [16, 19]. In this study, we describe the first use of a standard pain instrument for the measurement of breast pain. The MPQ is one of the most widely used tests for the measurement of pain [20, 21]. It is commonly used in diagnosis and research in various pain problems. The short-form of MPQ has a very high correlation with the long-form MPQ, and is an instrument that has been validated, tested for reproducibility, and shown to be sensitive to traditional clinical therapies. The SF-MPQ provides a standard method for characterizing pain on a multidimensional scale, and allows comparisons across different pain conditions. Our data on mastalgia, gathered using this extensively validated instrument, recapitulate some of the established clinical impressions about mastalgia, and provide added insights. Thus cyclical pain tends to be a diffuse, heavy ache, most prominent towards the end of the menstrual cycle, but we also find that a minority of women with the most severe pain also experience it during menstruation. Non-cyclical mastalgia is also characterized as heavy aching tenderness, but the affective components of fearful and punishing are more prominent than for cyclical pain, and there is a relationship of the overall severity with the size of the painful area. Thus our data using a standard pain instrument capture, in a quantitative fashion, the qualitative characteristics of cyclical mastalgia, which has been repeatedly described as a diffuse, heavy tenderness or aching in one, but more often both, breasts [7]. The overall magnitude of the pain, which has not been directly compared previously, is very similar for both types of mastalgia. And the mean pain-rating index for breast pain when compared to other chronic pain conditions, is similar to chronic cancer pain, and just below the mean pain ratings for rheumatoid arthritis [23]. Therefore, we conclude that breast pain is of sufficient magnitude to require serious therapies.

Our analyses of the ancillary descriptor components of mastalgia and their contribution to the summary pain measures (Table 2) show that there are really few other differences in cyclical and non-cyclical breast pain. Thus the steadiness of the breast pain, the presence of other (non-breast) pain, and the use of medications for breast pain are consistent independent predictors of the various measures of pain severity, in both cyclical and non-cyclical groups. A previously undescribed finding is that the presence of pain early in the cycle (i.e., through menstruation) correlates strongly with severity of pain, and these women, although a minority, report the highest overall pain scores. However, the majority of women who describe cyclical pain, point to the pre-menstrual phase as being the most painful time of the cycle, and as a group, they have lower overall pain scores than the women whose pain continues through menstruation. The significance of this in terms of the hormonal etiology of mastalgia is unclear, but it suggests that severe cyclical mastalgia can extend into the early cycle, and instruments designed to measure and classify breast pain should account for this subset.

One of the important issues in studies of mastalgia relates to the high prevalence of the condition, and raises the question of whether a minimum threshold for the magnitude of pain should be used in the definition of mastalgia. An earlier study of breast pain used an arbitrary threshold for inclusion (mean VAS of 3.5 over 7 days prior to onset of menstruation) [22]. However, the appropriate threshold remains to be defined, and further studies using a standardized measurement instrument need to be performed to

accomplish this. Our data also suggest that cyclical mastalgia may be most severe during menstruation, and therefore an emphasis on pre-menstrual pain would exclude the subjects with the highest magnitudes of breast pain. The results of our study show that VAS alone is a poor metric for examining breast pain. We have included all women who answered 'yes' to the question 'have you had breast pain in the past 3 months?'. This was a compromise to select patients with clear presence of pain at the time of data collection to minimize confounders related to recall bias [15].

The proposed etiology of mastalgia points to the involvement of several hormonal influences: progesterone deficiency [23], increased basal prolactin levels [3], increased prolactin response [24], and a possible role of gamma linoleic acid deficiency [2]. Although the hormonal hypothesis is reasonable given the temporal relationship to the menstrual cycle, the mechanism of why hormonal exposure or deficiency (both hypotheses have been advanced) should cause pain remains unexplained. The possibility of an association with increased or decreased risk of breast cancer makes it even more urgent that the biology of breast pain is studied rigorously, and prospective investigations of a link to cancer risk be carried out.

Our analyses of data from the McGill short form indicate that almost the entirety (96%) of the information collected with this instrument can be captured with a few short, focused questions which include a visual analog scale, a present pain index, and four quality of life indicators. These questions can provide the basis of the collection of pain data prospectively from large numbers of women in order to examine questions of etiology, dietary relationships, and link to cancer.

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