



Gender differences in outcomes of a multimodal pain management program

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ABSTRACT

Although gender differences in pain and analgesia are well known, it still remains unclear whether men and women vary in response to multimodal pain treatment. This study was conducted to investigate whether men and women exhibited different outcomes after an intensive multimodal pain treatment program. The daily outpatient program consisted of individual treatment as well as group therapy, with a total amount of therapy of 117.5 h per patient. Overall, 496 patients (254 women) completed the multimodal program. Pretreatment parameters for pain, disability due to pain, pain duration, and pain chronicity stage, as well as age or psychiatric comorbidities, did not differ between genders. The average pain, measured with a Numeric Rating Scale, decreased after treatment of $-1.54 (\pm 1.96)$ with a large effect size (ES) of .911 for the total sample. However, there were considerable differences in the benefit for women (-1.83 ± 2.12 ; ES 1.045) compared with men (-1.23 ± 1.74 ; ES .758). Consistently, women (ES .694) improved more in pain-related disabilities in daily life than men (ES .436). These distinctions are not due to differences in pain duration, received medication, psychiatric comorbidities, pain chronicity stage, or application for a disability pension. Therefore, gender differences not only refer to chronic pain prevalence, pain perception, or experimental pain measurement, but also seem to have a clinically relevant impact on the response to pain therapy.

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1. Introduction

Gender differences in pain perception are well described in the literature. Studies with representative samples showed a higher prevalence of women suffering from chronic pain compared with men [9]. Furthermore, women report more intense and frequent pain than men [34] and appear more likely to experience pain in multiple body regions [3].

Meanwhile, a great number of studies analyzed gender differences in experimental pain. To date, there is strong evidence that female subjects are more sensitive to pressure, heat, and cold pain stimuli [9]. This coincides with data showing more efficient diffuse noxious inhibitory controls for male than female subjects [30].

Concerning the response to opioid and nonopioid medication, numerous experimental studies provided no consistent evidence

for gender differences [9]. A recent review and meta-analysis revealed a greater morphine-induced analgesia for women in both experimental pain studies and clinical patient-controlled analgesia studies [28]. Data from the investigation of nonpharmacological pain intervention and gender distinctions are rather rare. A study showed a greater benefit in men receiving conventional physical therapy [16], whereas women seem to profit more from cognitive behavioral therapy [23].

Although outcomes of interdisciplinary pain management have been thoroughly studied [10], reliable data on gender differences are still lacking. Krogstad et al. showed a persistent reduction in orofacial pain only for women 2 years after treatment [26]. Accordingly, Jensen et al. found gender differences in quality of life after a rehabilitation program for chronic spinal pain [23]. Another study found a similar reduction in pain intensity in both sexes after interdisciplinary pain management, with only men remaining stable in the outcome after 3 months, whereas women worsened to pretreatment scores [25]. Fibromyalgia patients showed a better outcome in some scales of the Short Form Health Survey (SF-36) for men compared with women in a study by Hooten et al. [18].

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Although it is likely that men and women benefit unequally from pain management, evidence for specific gender differences is still weak. Consequently, the Sex, Gender and Pain Special Interest Group of the International Association for the Study of Pain (IASP) stated as a main goal for future research the determination of gender differences in outcome when similar treatments (pharmacological, interventional, and behavioral) are applied [15]. Within this consensus report, the investigators gave recommendations for studying sex and gender differences in pain and analgesia [15]. Considering these recommendations, the current study was conducted to analyze the impact of gender on the outcome of a multimodal pain management program.

2. Methods

2.1. Participants

Data from all patients who completed a pain management program from 2006 to 2010 at the pain clinic in Weiden, Germany, were analyzed retrospectively. An outpatient visit for clinical diagnostics preceded the program. This visit consisted of a diagnostic evaluation by a physician, a nurse, a specialist for psychosomatic medicine, and a physical therapist, all with special knowledge in pain therapy. Inclusion criteria were defined as follows: (1) patients agreed to be admitted and to participate in all treatment units; (2) chronic nonmalignant pain that existed for over 6 months (independent of type or region of pain); (3) appropriate linguistic understanding; (4) a clear level of suffering and a manifest or imminent reduction of quality of life; (5) failure of a previous unimodal pain therapy or surgery because of pain; (6) no other pain treatment (for example inpatient or psychiatric treatment) that appeared to be more sufficient.

2.2. Treatment

The 5-week multimodal pain program was comprised of physicians, psychologists, physical therapists, a nutritionist, a social worker, and relaxation therapists. The medical staff consisted of an anesthetist, a neurologist, and a specialist for psychosomatic medicine and psychotherapy. An average of 8 patients was included in each group. The daily outpatient program lasted from Monday to Friday (8 am to 4 pm) and consisted of individual treatment as well as standardized group therapy. The main modules of the CBT-orientated group program are (1) acceptance, (2) development of resources, (3) resolving conflicts and strengthening social competency, (4) stabilization, and (5) implementation in daily life. The entire amount of therapy per patient was 23.5 h per week and 117.5 h per program, respectively.

2.2.1. Individual treatment

- *Doctor's appointment*: 0.5 h twice per week.
- *Physical therapy*: 0.5 h twice per week.
- *Psychotherapy*: 1 h/week.

2.2.2. Group treatment

- *Relaxation techniques (e.g., progressive muscle relaxation according to Jacobson or autogenics)*: 3.5 h/week.
- *Physical therapy*: 8 h/week
- *Cognitive behavioral therapy*: 6 h/week.
- *Pain education*: 2 h/week.
- *Nutrition advice and social counseling*: 1 h/week.

2.3. Pain chronicity stage

The validated Mainz Pain Staging System (MPSS) [11,13] was used to determine pain chronicity stage at the beginning of the treatment (time 1). The MPSS distinguishes 3 pain stages (from 1 to 3), considering temporal and spatial dimensions of pain, medication usage, and lifetime utilization of the health care system [14].

2.4. Pain measurement

At the beginning (time 1) and end (time 2) of the pain program, the following self-rating instruments were assessed to measure pain and resulting disabilities:

Numeric Rating Scale (NRS): An 11-point numeric scale, scored 0 (no pain) through 10 (worst possible pain) to rate minimum, average, and maximum pain within the past 4 weeks [7,23]. The NRS is a valid and reliable method of measuring pain [22] that is recommended for use in patients with chronic pain [20,24].

Pain Disability Index (PDI) in the validated German version [4]: This is a self-rating instrument to assess pain-related disabilities. The respondent rates the degree to which pain interferes with functioning from 0 (no disability) to 10 (total disability) in 7 broad areas: family/home, responsibilities, recreation, social activity, occupation, sexual behavior, self-care, and life-support activity [33].

2.5. Additional investigated parameters

Because disability pension is thought to influence the therapy outcome [1], the patient's statement regarding whether he or she had applied for such assistance was documented. Possible psychiatric comorbidities (according to the International Classification of Diseases, 10th Revision) were evaluated by a specialist in psychosomatic medicine and psychotherapy. The diagnosis was made by a standardized semistructured psychiatric interview according to the International Classification of Diseases, 10th Revision, symptom checklist for mental disorders.

The following tests were completed by only a fraction of the patients in the study and were included to contribute to the clinical impression of the results: (1) the German version of the Center for Epidemiological Studies Depression Scale [27], the Allgemeine Depressionskala (ADS) [17] (N = 447), and (2) the SF-36 [35] (N = 111).

2.6. Pain medication

Individual medication was adjusted at the doctor's appointment according to the recommendations of the World Health Organization analgesic ladder for cancer pain [38]. The medication was recorded without a further specification for substance or doses for (1) opiates, (2) nonopioid analgesics, and (3) coanalgesics (such as muscle relaxants, antidepressants or anticonvulsants).

2.7. Statistics

For the statistical analysis, we used SPSS version 18.0 (SPSS Inc., Chicago, Illinois, USA). Two-tailed significance level was set at .05. All variables were tested for normal distribution with a Kolmogorov-Smirnov test. Mean values and standard deviations were counted with a descriptive statistic, and cross tables were used for frequencies in case of ordinal variables. For comparison before and after treatment, we performed a paired *t* test and a Wilcoxon

test based on the distribution. To investigate gender differences at baseline parameters, we performed a *t* test (in case of normal distribution) or a Mann-Whitney *U* test. Therapy outcome was defined as the baseline minus the final values. Gender differences according to therapy outcome were analyzed with a Mann-Whitney *U* test or *t* test and the results were controlled by an analysis of variance. For multiple testing adjustments, we utilized a Bonferroni correction. The effect size (Cohen's *d*) was determined as mean difference scores divided by the pretreatment standard deviation. Differences in ordinal variables were counted with a χ^2 test.

2.8. Source of funding and ethical considerations

This study was planned and conducted in accordance with the Declaration of Helsinki and ethical laws pertaining to the medical professions. All participants signed a consensus declaration and agreed to the analysis of their anonymous data. This study was conducted independent of any institutional influence and was not funded externally.

3. Results

Overall, 496 patients (254 women) completed the pain program from 2006 to 2010 at the pain clinic in Weiden, Germany. Overall, 13 patients (6 women) abandoned the treatment because of severe medical complications. Characteristics of the study sample are presented in Table 1.

The pretreatment values for pain duration or chronicity stage and age, educational background, psychiatric comorbidities, analgesic release medication, or application for a pension (χ^2 1.51, *df* 1, *P* value .219) did not differ between men and women (Table 1). Furthermore, baseline values did not vary between genders (PDI: *T* = 1.32, *df* = 488, *P* = .188; NRS minimum: *U* = 28946, *Z* = −.596, *P* = .551; NRS average: *U* = 27315, *Z* = −1.811, *P* = .07; NRS maximum: *U* = 30113, *Z* = −.001, *P* = .999). Baseline and end values for pain measurement (minimum, average, and maximum NRS, PDI) for the total sample and separated by sex are presented in Table 2.

Improvement due to therapy was defined as the difference between baseline and end values. Mean differences in all investigated parameters demonstrated an improvement (after the appropriate corrections were applied) for the total sample as well as for each sex (Table 3). The changes relate to the average pain perception measured by NRS (*T* = 3.330; *df* = 494; *P* = .001) and disabilities because of pain measured by PDI (*U* = 2.5873; *Z* = −3.083; *P* = .002) (Table 3). The effect sizes depend on the outcome parameters and range between .410 and .911 (Table 3). To evaluate gender differences in reached improvement, we performed a *t* test or a Mann-Whitney *U* test. The effect sizes (concerning the therapy improvement) differ between men and women in both investigated main parameters (PDI and NRS average) (Table 3). To recheck the results, we performed an analysis of variance for both of the main parameters (PDI and NRS average). The intersubject effects for time and gender confirmed the results of the conducted analysis for the PDI (*F* = 8.677; *df* = 1/442; *P* = .003) and NRS average (*F* = 9.978; *df* = 1/453; *P* = .002). Gender differences also appear in the NRS minimum and maximum scores, but do not reach the significance level after the appropriate corrections have been applied (Table 3).

The ADS (*N* = 447) gave no indication of gender differences in the pretreatment scores (time 1) of women (*M* ± *SD*: 27.60 ± 11.4) and men (*M* ± *SD*: 27.73 ± 10.5) (*T* = .132; *df* = 490; *P* = .895). Posttreatment ADS scores (time 2) differed between women (*M* ± *SD*: 18.80 ± 11.2) and men (*M* ± *SD*: 22.17 ± 11.0) (*T* = 3.164; *df* = 446; *P* = .002). The SF-36 (*N* = 111) indicated that although pretreatment scores did not differ between men and women, women (*M* ± *SD*: 12.89 ± 14.5) improved significantly more in the summary item “mental component summary” than did men (*M* ± *SD*: 6.52 ± 12.9) (*T* = −2.451; *df* = 109; *P* = .016).

4. Discussion

Although no gender differences were observed at baseline (Table 2), there was a distinct and clinically relevant discrepancy between men and women in terms of the benefit derived from the

Table 1
Study sample.

	Total sample	Men	Women	<i>t</i>	<i>df</i>	<i>P</i>
<i>Age (years)</i>						
<i>M (±SD)</i>	48.47 (±10.05)	48.01 (±9.78)	48.91 (±10.31)	−.992	493	.322
<i>Pain duration (months)</i>				<i>U</i>	<i>Z</i>	<i>P</i>
<i>M (±SD)</i>	85.94 (±79.17)	81.34 (±77.60)	90.55 (±80.65)	15599	−1.134	.257
<i>Pain chronicity stage (MPSS)</i>				χ^2	<i>df</i>	<i>P</i>
1	12	3	9	3.989	2	.136
2	144	66	78			
3	338	173	165			
Overall	494	242	252			
<i>Psychiatric comorbidities</i>						
Somatoform disorder	98	42	56	1.721	1	.190
Affective disorder	299	145	154	.026	1	.871
Further psychiatric comorbidity	86	45	41	.492	1	.483
<i>Education</i>						
<9 years	13	3	10	4.541	3	.209
9–10 years	331	170	161			
11–13 years	17	7	10			
>13 years	10	5	5			
Overall	371	185	186			
Unknown	115	57	68			
<i>Analgesic medication</i>						
Opiates	266	137	129	1.69	1	.194
Nonopioid analgesics	129	58	71	1.023	1	.312
Coanalgesics	225	114	111	.580	1	.446

MPSS = Mainz Pain Staging System; *U* = Mann-Whitney *U* test; *Z* = *z* statistic; *T* = paired *t* test; *df* = degrees of freedom; *M* = mean; *SD* = standard deviation; *P* = *P* value (2-tailed).

Table 2
Baseline and end values for the total sample and separated by gender.

	Baseline value (time 1) M ± SD (n)	End value (time 2) M ± SD (n)	T	df	P
<i>PDI</i>					
Total sample	39.62 ± 13.42 (490)	31.97 ± 14.96 (485)	13.511	443	<.001
Men	40.44 ± 12.81 (240)	34.86 ± 14.26 (238)	8.250	212	<.001
Women	38.84 ± 13.97 (250)	29.29 ± 15.13 (247)	10.848	230	<.001
<i>NRS minimum</i>					
Total sample	4.46 ± 2.34 (489)	3.51 ± 2.10 (470)		Z	P
Men	4.37 ± 2.09 (238)	3.62 ± 2.03 (232)		−9.180	<.001
Women	4.55 ± 2.55 (251)	3.40 ± 2.16 (248)		−5.601	<.001
<i>NRS average</i>					
Total sample	7.03 ± 1.69 (491)	5.49 ± 1.90 (483)		−13.399	<.001
Men	6.88 ± 1.61 (240)	5.66 ± 1.83 (239)		−8.680	<.001
Women	7.17 ± 1.76 (251)	5.33 ± 1.96 (246)		−10.196	<.001
<i>NRS maximum</i>					
Total sample	8.74 ± 1.34 (491)	7.88 ± 1.69 (479)		−9.692	<.001
Men	8.75 ± 1.33 (240)	8.02 ± 1.63 (234)		−6.421	<.001
Women	8.74 ± 1.35 (251)	7.74 ± 1.73 (245)		−7.270	<.001

NRS = Numeric Rating Scale; PDI = Pain Disability Index; Z = z statistic; T = paired *t* test; df = degrees of freedom; M = mean; SD = standard deviation; P = *P* value (2-tailed); n = amount of values.

Table 3
Benefit from the pain management for the total sample and for each sex.

	Benefit	SD	d	T	df	P
<i>PDI</i>						
Total sample	−7.64	11.58	.570			
Men	−5.89	10.30	.436	3.330	494	.001
Women	−9.32	12.48	.684			
<i>NRS minimum</i>						
Total sample	−.95	2.09	.410	U	Z	P
Men	−.76	1.83	.359	27,027	−2.348	.019
Women	−1.14	2.30	.451			
<i>NRS average</i>						
Total sample	−1.54	1.96	.911			
Men	−1.23	1.74	.758	25,873	−3.083	.002
Women	−1.83	2.12	1.045			
<i>NRS maximum</i>						
Total sample	−.87	1.73	.642			
Men	−.74	1.55	.549	28,421	−1.475	.140
Women	−.99	1.87	.741			

NRS = Numeric Rating Scale; PDI = Pain Disability Index; U = Mann-Whitney *U* test; Z = z statistic; T = paired *t* test; df = degrees of freedom; M = mean; SD = standard deviation; n = set of numbers; P = *P* value (2-tailed); d = Cohen *d*.

pain management program (Table 3). The improvement in the main outcome parameter (average pain during the past 4 weeks measured with an NRS) was measured to be −1.83 (ES 1.045) for women, as compared with −1.23 (ES .758) for men. Consistently, pain-related disabilities in daily life (measured with the PDI) decreased more in women (−9.32; ES .694) than men (−5.89; ES .436). However, nonsignificant differences were seen for the reduction of the minimum and maximum pain (NRS) after the appropriate corrections were made (Table 3). Regarding the Cohen conventional criteria, the size of the distinctions between men and women in response to the treatment (average NRS and PDI) revealed a small effect [2].

Similar to previous findings regarding the efficacy of multimodal pain programs [10], medium to large effect sizes were found for the total sample, depending on the parameters used (Table 3). Average pain (measured with NRS) decreased with an effect size of .911; pain-related disabilities (measured with the PDI) decreased with an effect size of .570. Gender differences not only applied to pain parameters, but also were seen in the reduction of depressive symptoms as well as in the improvement of the quality of life. Overall, women benefit significantly more than men from

multimodal pain management. These distinctions are not due to differences in pain duration, pain medication, psychiatric comorbidities, pain chronicity stage, or application for a disability pension.

Whereas gender differences are frequently described in pain perception and analgesia, the literature on the outcome of multimodal pain therapy is rather limited and remains inconsistent. Therefore, only a few comparable studies are available. Keogh et al. already predicted but could not prove that women would show greater improvements in pain, disabilities, and distress than men after interdisciplinary pain management [25]. The authors found significant posttreatment reduction for men as well as for women, but no differences between sexes [25]. Explanations for the diverse findings discovered by the recent study could include differences in sample size (98 versus 496 patients) and the treatment conducted (3- or 4-week residential program as well as a 3-week hospital-based format versus a standardized 5-week program in the present study). The authors already discussed a type 2 error due to the small sample size as one reason for their unexpected findings [25]. Moreover, George et al. found similar outcomes for men and women with regard to reduction in pain intensity and pain-related disorders in 165 patients with low back pain [12], whereby the sample (acute pain) as well as the assessed treatment (physical therapy intervention) varied in this study. Whereas the current results complemented previous findings showing a better outcome for women than men after pain management, Jensen et al. evaluated a behavioral medicine rehabilitation program and found gender differences in the outcome of quality of life [23]. Krogstad et al. found a reduction in sensory and emotional pain for women suffering from temporomandibular pain, but not for men [26]. As a limitation of this study, one must consider the small sample size of 53, with a clear gender mismatch and only 13 male subjects.

The current results confirm clinically relevant gender differences in pain outcome after multimodal pain management within a representative sample. The cause for distinctions between men and women in pain and analgesia is still not clear, but multiple explanations exist [29]. Some evidence suggests that endogenous and exogenous modulation of pain may vary in women versus men [9]. A recent review showed a greater morphine-induced analgesia for women in both experimental pain studies and clinical patient-controlled analgesia studies [28]. Women overall appear more sensitive to both dosage and type of analgesic medication

[29]. Additionally, it is described that female physicians prescribe higher doses of opioid pain medication for women than men [36]. In contrast, male physicians were more likely to recommend activity restrictions for female patients [32]. There is some evidence that both men and women consider women more sensitive to pain, less enduring of pain, and more willing to report pain compared with men [31,37]. Furthermore, pain coping strategies may vary between men and women [9]; few studies found higher levels of catastrophizing among women when examining both patients [21] and healthy controls [5]. As these results point to an interaction between patient gender and physician gender, it is necessary to consider that the majority of the health care team at the pain unit in Weiden was female.

In interpreting the data, the following limitations must be mentioned. Because of the retrospective and naturalistic design, all variables show a high standard deviation. Further, manifold types of pain disorders were mixed with no specification for type or location. Within the pain program, the group treatment was standardized, whereas the individual treatment focused on each individual's solitary impairment. Potential differences in substances and doses of the received medication were only studied for the major analgesic groups but were not in individual detail. Even if the exclusive intake of the prescribed analgesics was suggested and the handing out of medication was documented, a possible double prescription from another physician as well as the use of nonprescription analgesics cannot be excluded. This could bias the current results, as a higher use of prescription and nonprescription analgesics is described for women as compared with men [6,19]. A follow-up examination was offered but not standardized or implemented; hence, no statement regarding duration of treatment effects can be made. Finally, within the multimodal treatment group, numerous therapeutic strategies were interlinked and no conclusion regarding which part of the treatment is more effective for women is possible.

The strengths of the present study included its sample size, the standardized group program, and the covariables included. The findings indicate that women benefit more from multimodal pain therapy than men. These results complemented the increasing numbers of studies representing that men and women do not respond to pain and the treatment of pain in the same way [8]. Further research should distinguish whether this effect is due to the complete pain program or relates to one particular aspect. If the response to several parts of the treatment is dependent on gender, the question arises whether standardized pain therapy for men as well as for women is most effective for both sexes. Alternatively, if the response to special modules varies between men and women in multimodal pain therapy, an adaption based on gender could optimize the outcome.

In sum, the gender differences not only refer to pain prevalence, pain perception, and experimental pain measurement [9], but also seem to have a clinically relevant impact on the outcome of a multimodal pain management program.

Conflict of interest statement

None of the authors have a conflict of interest.

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