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Research Paper

The Interval Changes of Pain and Depression in Chronic Back Pain Patients After a Short-Term Pain Management: An Observational Study

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Introduction: Major depressive disorder (MDD) and chronic pain are two highly comorbid conditions and share common biological processes, underlying mechanisms, and pharmacological concepts. We conducted an observational survey to discern the clinical progression of both conditions in the chronic pain patients after short-term pain management.
Methods: This was a longitudinal, questionnaire-based survey involving patients with chronic back pain. Patients received individualized conservative and interventional therapies within 60 days. Based on the Structured Mini-International Neuropsychiatric Interview (MINI) conducted at enrollment, participants were allocated into the MDD and non-MDD groups. Pain intensity, depression, and functional outcomes were assessed at pre- and post-therapies by using the Numeric Rating Scale (NRS), MINI, Oswestry Disability Index, Chalder Fatigue Scale, Neurotoxicity Rating Scale, Hamilton Depression Rating Scale (HAM-D), and Beck Depression Inventory for comparison.
Results: Of the 198 enrolled participants, 95 completed this 60-day study. In the beginning, 29.3% (58/198) were diagnosed with MDD. Across all measures, the MDD group reported significantly worse outcomes than the non-MDD group ($P < 0.01$) at both baseline and 2 months later. After treatment, HAM-D scores improved significantly in both groups ($P < 0.05$), while NRS improved significantly only in the non-MDD group ($P < 0.01$).
Conclusion: MDD is prevalent among chronic pain patients. A combination of conservative and interventional pain management strategies resulted in a significant reduction in depressive symptoms and pain intensity. However, patients with MDD exhibited fewer therapeutic responses compared to those without MDD over the 60-day pain treatment.

Keywords: *Beck Depression Inventory (BDI), back pain and depression comorbidity, Hamilton Depression Rating Scale (HAM-D), major depressive disorder (MDD), Numeric Rating Scale (NRS), Oswestry Disability Index (ODI)*

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Introduction

Major depressive disorder (MDD) is one of the most common chronic psychiatric disorders with global lifetime prevalence ranging from 2.1% to 21.0% [1,2]. Several clinical and epidemiological studies have well documented the association between depression and chronic pain syndrome [3-5]. Chronic pain and major depression often co-occur (30%–50%) with overlapping symptomology [6-8], share biological pathways [9-11], and show commonalities in the treatment concept and responses [12,13]. Further, these two frequently comorbidities lead to devastating consequences in personal lives and enormous economic burden on society in terms of both medical care and lost productivity [2,14-17]. Although the comorbidity of pain and depression has been scrutinized extensively, the causal interlinks in response to treatment were debated and have not been fully elucidated [3].

Chronic pain generally results from a multifaceted interaction among biological, psychological, socio-economic, and psychiatric factors [18,19]. Chronic pain is a rampant clinical problem with about 20% to 60% of all people within a population [20-23]. Nearly 45% of patients see primary care providers, and 12% see pain medicine specialists [23]. Among the chronic pain syndromes, musculoskeletal pain is common, affecting between 13.5% and 47.0% of the general population at some period of life [24]. Especially, lower back pain, which is composed of a large part of musculoskeletal pain, some degenerative spine, and nerve compression or entrapment, occurs in adolescents with a high prevalence varying from 30% to 70% [25-27]. Studies on primary care patients with persistent pain found that a change in pain level was a strong predictor of depression severity and vice versa, strongly supporting their bidirectional relationship [28,29].

In recent years, there has been a growing interest in pharmacological [30,31] and non-pharmacological [32,33] approaches to control chronic pain. Beyond a single dimension of pain intensity, pain is a complex multidimensional construct influenced by individual cognition and attention, socio-cultural interactions, and psychological variables. Therefore, comprehensive pain measurements incorporating delicate techniques and tools to survey the whole picture in chronic pain patients are essential [34]. These refined measurements facilitate targeting multi-facet pain diagnosis, obtaining effective clinical care, and designing precise clinical research [35]. In a clinical setting, pain measurement commonly includes intensity by verbal and numeric self-rating scales, behavioral observation scales, and physiologic responses [34]. Interestingly, though they share many common mechanisms, pain is scarcely or not highlighted in standard measures of depression severity with different rating scales [36]. Therefore, for chronic refractory pain subjects at high risk of depression, careful screening of depression should be ever more crucial in enhancing effective treatment [37].

Given the sophisticated nature of pain and depression, individual symptom changes and progression patterns of the intertwining complex after treatment are largely unclear [7]. Our first objective was to clarify the percentage of chronic pain patients who simultaneously suffered from MDD with multiple questionnaire approaches. The second objective was to evaluate whether aggressive pain treatments alter pain and depression phenotypes at a short-term follow-up. Through conducting this longitudinal and descriptive survey, our aim was to elucidate the nuanced and complex relationship between chronic pain and MDD, especially in the Taiwanese population.

Methods

This study was designed to be a longitudinal, descriptive survey using multiple questionnaires and clinical interviews. The study protocol was reviewed and approved by the ethics committee of the China Medical University Hospital, Taichung, Taiwan. All participants were enrolled at their first one or two visit of our clinics if eligible. Because our tertiary pain center is specialized for image-guided interventional therapies, most patients came for possible aggressive interventional pain management. All study procedures and data collection were carried out at the outpatient department of the pain division by a trained nurse practitioner.

Study Procedures

The participants were recruited at the outpatient department and screened by a study physician for eligibility according to the study criteria as below. Each eligible participant received conservative or combined interventional pain therapies based on the physician's discernment. All patients acknowledged their willingness to participate and understood the signed informed consent.

Study Criteria

Inclusion criteria were Taiwanese subjects of both sexes between 20 and 90 years old presenting with a diagnosis of spine-related back pain for at least 3 months and having a pain level greater than four points in the Numeric Rating Scale (NRS) [38]. Assessment and recording of the baseline demographic data were separately performed by the physician and the study nurse. Exclusion criteria were association with neurological problems in the central nervous system, multi-location pain, cancer-related pain, drug or substance abuse record within 1 year, other severe organic-related depression, pregnancy, or concomitant pain medication, physical therapy, or chiropractic treatment at different sites. Besides, for those cases that received more than one interventional treatment in a row, they had to complete their follow-ups for pain progression with the 60-day study course. These interventional treatments include various procedures such as ultrasound- or fluoroscopic-guided spinal steroid injections, ablation or pulsed radiofrequency, prolotherapy, disc procedures, epidural adhesiolysis, or others.

Assessment

Participants were evaluated their baseline status of chronic pain and MDD by the following 7 questionnaires: (1) 21-item Hamilton Depression Rating Scale (HAMD-21) [39]; (2) Beck Depression Inventory (BDI) [40]; (3) Neurotoxicity Rating Scale [41]; (4) Structured Mini-International Neuropsychiatric Interview (MINI) [42]; (5) Oswestry Disability Index (ODI) [43]; (6) Chalder Fatigue Scale (CFS) [44], all in Chinese version.

At baseline, we assessed pain by NRS, a valid, self-reported pain intensity scale scoring from zero to ten, indicating no pain and the maximum severity, respectively. If the NRS was higher than four, patients would be asked to complete the rest six questionnaires (MINI, ODI, CFS, Neurotoxicity Scale [NTRS], HAM-D, and BDI). Among them, MINI is a short but accurate structured psychiatric interview to assess psychiatric diagnoses of the patients according to DSM-IV and ICD-10 criteria [45]. Then, we divided the participants into two groups by the MINI result: the MDD group and the non-MDD group. Two months later, another assessment of the abovementioned questionnaires was performed as the end data of the study for comparison.

Data Analysis

Data management and statistical analysis were performed by SPSS version 22.0 statistical software (Armonk, NY, USA, USA). To compare between-groups, an independent sample t-test was used for continuous variables, and a chi-square test was used for categorical variables. A paired sample t-test was used for within-group comparison at baseline and follow-up. Pearson's correlation was used to determine the correlation between each questionnaire. The threshold of statistical significance was P-value < 0.05, and all reported P values reflect the two-sided significance test.

Results

Of 280 patients, 82 declined to participate, and 198 patients were enrolled eventually. Based on MINI, 58 patients (29.3%) were diagnosed as MDD. The follow-up rate was 60% in total (76% with the MDD group and 53% with the non-MDD group) at the 60-day study period. We excluded 23 subjects (12 in the MDD group and 11 in the non-MDD group) whose treatment duration exceeded 60 days (Figure 1).

Demographics

As shown in Table 1, there were no significant baseline differences between the two groups in demographics (age, gender, education, body mass index, and marital status). The mean age was 58 years, and 107 patients (54.0%) were women (Table 1). In terms of primary psychiatric diagnosis, 58 patients (29%) had MDD, and 140 patients (71%) had no MDD at the inclusion time point; neither of the groups had a significant correlation with family history of depression. Regarding to history of previous spine-related surgery, we observed that significantly more patients in the MDD group experienced previous surgeries than those in the non-MDD groups (72% vs. 40%, $P < 0.01$). In addition, there was no difference between groups in comparing their pain sources from the 6 most possible diagnoses.

Treatment Outcomes

Data from the multiple questionnaires between the MDD and the non-MDD groups at baseline and follow-up were analyzed (Figure 2 and Table 2). The performance with the MDD group showed a significantly worse trend in comparison with the non-MDD group in all aspects at the beginning and the end of

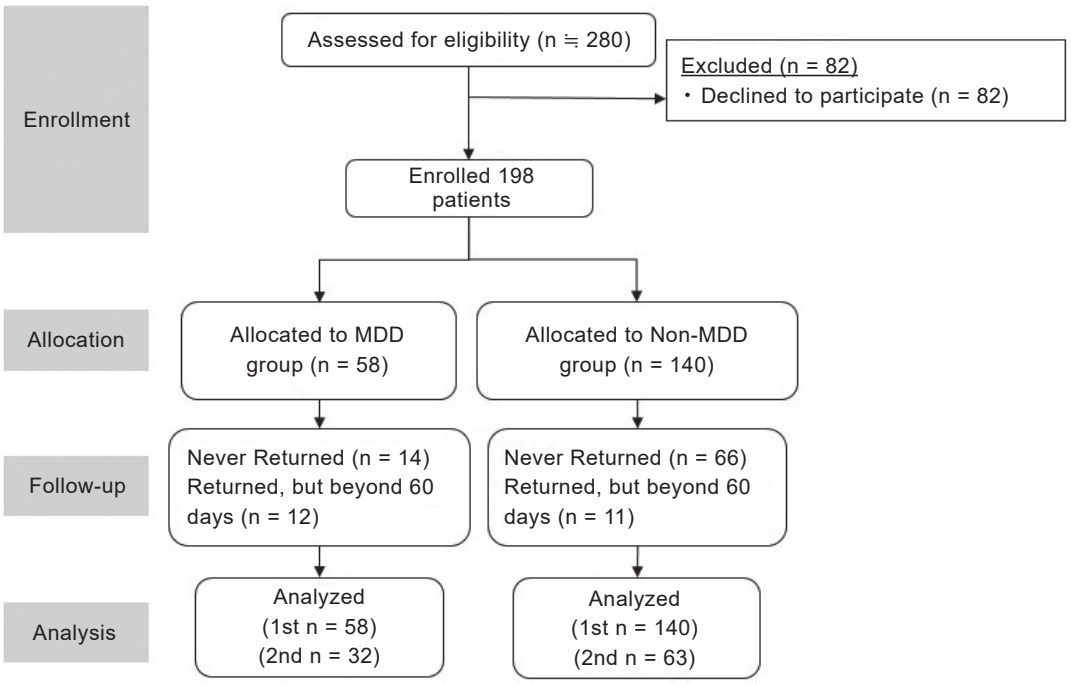

Figure 1. Flow Chart

Abbreviation: MDD, major depressive disorder.

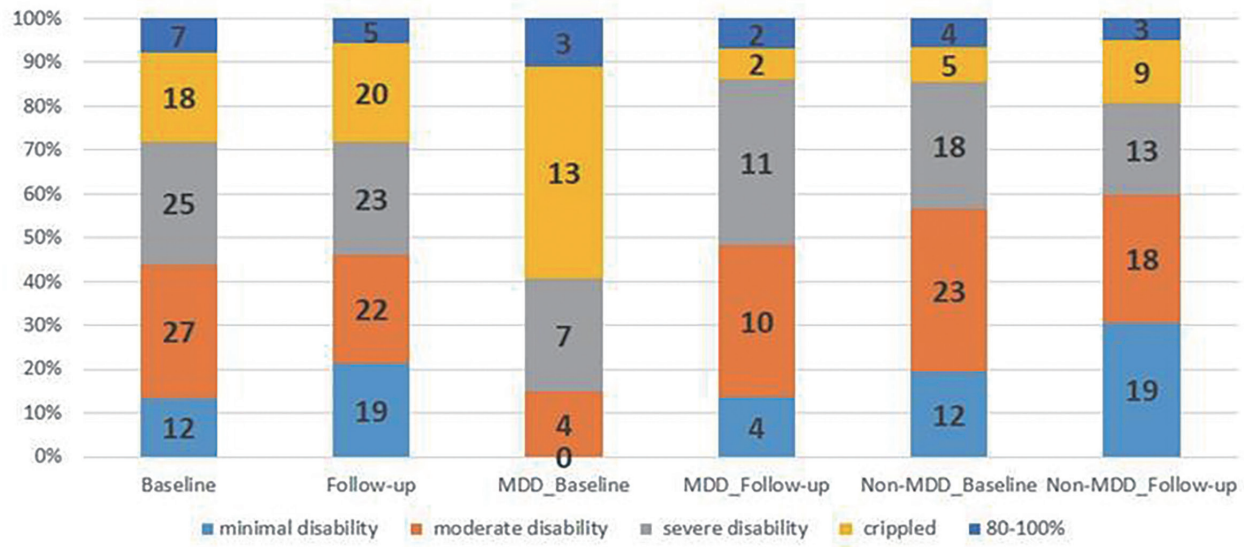

Figure 2. Scoring of the Oswestry Disability Index (ODI) Before and After Pain Treatment in the Major Depressive Disorder (MDD) and the Non-MDD Group

In ODI measures, all patients were classified based on their scores into either 81%–100%, crippled disability (score 61%–80%), severe disability (score 41%–60%), moderate disability (score 21%–40%), or minimal disability (score 0%–20%). $^{*}P < 0.05$ between the cripple class before and after treatment in the MDD group.

the study (Table 3). Although we were able to observe improvement in both groups after pain treatment when comparing the scores between baseline and at the follow-up time point, especially that scores of HAM-D in both groups and NRS in the non-MDD group were reduced significantly ($P < 0.05$). According to the detailed analysis of the case numbers in the individual ODI classification, the number of crippled

Table 1. Demographic Baseline Data of Refractory Chronic Spinal Pain Patients With or Without Major Depression[a]

Variable	Total (N = 198)	MDD (n = 58, 29%)	Non-MDD (n = 140, 71%)	*P*
Age (years), mean ± SD	58 ± 16	56 ± 15	59 ± 16	0.116
Gender, female, n (%)	107 (54)	36 (62)	71 (51)	0.145
Education (years), mean ± SD	11 ± 4	10 ± 4	11 ± 5	0.200
BMI (kg/m^2), mean ± SD	24 ± 4	25 ± 5	24 ± 4	0.377
Marital status				0.190
Married, n (%)	148 (75)	47 (81)	101 (72)	
Smoker, n (%)[b]	37 (19)	11 (19)	26 (19)	0.966
Alcohol use, n (%)[b]	18 (9)	4 (7)	14 (10)	0.481
Family history of psychiatric disorders				0.344
None, n (%)	172 (87)	49 (84)	123 (88)	
1st-degree relatives, n (%)	22 (11)	7 (12)	15 (11)	
2nd-degree relatives, n (%)	3 (2)	2 (3)	1 (1)	
History of previous spine surgery				< 0.001
With, n (%)	98 (49.5)	42 (72)	56 (40)	
Without, n (%)	100 (50.5)	16 (28)	84 (60)	
Diagnosis category				0.126
Spondylosis	48 (24)	6 (10)	42 (30)	
MFPS	18 (9)	2 (3)	16 (12)	
HIVD or radicular pain	53 (27)	15 (26)	38 (27)	
FBSS/FNSS	73 (37)	35 (60)	38 (27)	
Lumbar/cervical stenosis	1 (1)	0 (0)	1 (1)	
(Subacute) compression fracture	4 (2)	0 (0)	4 (3)	

Abbreviations: BMI, body mass index; FBSS, failed back surgery syndrome; FNSS, failed neck surgery syndrome; HIVD, herniated intervertebral disc; MDD, major depressive disorder; MFPS, myofascial pain syndrome; SD, standard deviation.
[a]Most values have been rounded off.
[b]Smokers and alcohol use were self-reported by the interviewee, who thought they took cigarettes or alcohol as a daily life habit.

Table 2. Number and Frequency of Interventional Pain Management in the MDD and the Non-MDD Group[a]

Time	Total (N = 198)	Non-MDD (n = 140)	MDD (n = 58)	*P*
0	138 (70)	100 (71)	38 (66)	0.424
1	50 (25)	32 (23)	18 (31)	
2	8 (4)	7 (5)	1 (2)	
3	2 (1)	1 (1)	1 (2)	

Abbreviation: MDD, major depressive disorder.
[a]All values are expressed in numerical and percentage form.

MDD patients significantly reduced from 13 to 2, though the ODI score of all participants or the individual score of each group did not change before and after treatment. Besides, comparing the differences (delta, δ) between the baseline and follow-up within each group, no significant changes occurred except for the pain level by NRS measurement ($P = 0.018$). The correlation among NRS, HAM-D, BDI, CFS, NTRS, and ODI scores was statistically strong with coefficients ranging from 0.2 to 0.9.

Table 3. Comparison of Pain Score, Functionality, Psychiatric, and Quality of Life Measurements Between the MDD and Non-MDD Groups

Variable	Group	MDD (n = 32)	Non-MDD (n = 63)	*P*
NRS	Baseline	7.260 ± 2.016	6.250 ± 1.772	< 0.01**
	Follow up	6.810 ± 2.120	4.750 ± 2.304##	< 0.01**
	Difference	0 ± 2	–2 ± 2	< 0.05*
Ham-D	Baseline	24.500 ± 3.877	8.570 ± 5.360	< 0.01**
	Follow up	22.870 ± 5.339#	7.570 ± 5.232#	< 0.01**
	Difference	–2 ± 4	–1 ± 3	
BDI	Baseline	32.340 ± 11.201	7.680 ± 6.132	< 0.01**
	Follow up	30.220 ± 12.961	6.860 ± 6.311	< 0.01**
	Difference	–2 ± 11	–1 ± 5	
CFS	Baseline	22.780 ± 7.551	10.540 ± 6.770	< 0.01**
	Follow up	22.310 ± 7.394	9.780 ± 6.392	< 0.01**
	Difference	0 ± 6	–1 ± 5	
NTRS	Baseline	164.410 ± 57.488	54.560 ± 41.260	< 0.01**
	Follow up	159.190 ± 58.102	46.920 ± 34.256	< 0.01**
	Difference	–5 ± 43	–8 ± 31	
ODI	Baseline	30.670 ± 8.357	19.810 ± 10.569	< 0.01**
	Follow up	29.000 ± 7.621	18.730 ± 11.543	< 0.01**
	Difference	–2 ± 4	–1 ± 6	

Abbreviations: BDI, beck depression inventory; CFS, Chalder Fatigue Scale; Ham-D, Hamilton Depression Rating Scale; MDD, major depressive disorder; NRS, Numerical Rating Scale; NTRS, Neurotoxicity Scale; ODI, Oswestry Disability Index.

*$P < 0.05$, **$P < 0.01$

The *P*-value for within-group comparison between the baseline and follow-up; #$P < 0.05$ and ##$P < 0.01$.

Frequency of Intervention Procedure

We compared the frequency of interventional pain treatment between groups to inspect whether the MDD group could be subjected to more invasive treatment in terms of higher pain level at baseline. In Table 2, we found that more patients in the MDD group received interventional treatments regardless of the treatment times (35% vs. 29%, MDD vs. Non-MDD), but there was no statistical difference. Most cases experienced one time of injection procedure, whereas only 8 non-MDD cases and 2 MDD cases received more than one injection treatment.

Discussion

This study demonstrated a high prevalence of MDD among Taiwanese patients with chronic back pain, consistent with the global trends [7,46,47]. The incidence observed in our study is comparable to that reported in Hong Kong (31.5%) [48], but lower than that in the UK (72%) [49] and Brazil (47.3%) [50]. This discrepancy may reflect multiple contributing factors, about ethnicity, regional differences, genetic predispositions, and probably underreporting due to cultural or personal reluctance. Similarly, responses to pain treatment may vary by race or ethnicity [51]. Epidemiological studies also support that various socio-demographic factors are associated with chronic pain and depression [52-54]. In the present study, all participants were Taiwanese and recruited from a single outpatient clinic, suggesting a relatively homogeneous population. The homogeneity may minimize the impact of ethnic and socio-demographic variables on both symptom presentations and treatment outcomes. As a result, the observed changes in pain and depressive symptoms after a short-term treatment faithfully represent clinical distinctions between pain patients with or without depression.

Most of the participants who visited our tertiary pain center had experienced limited responses to multiple treatments over an extended period and were referred by various specialists for more aggressive management. Notably, 37% of cases were related to failed back surgery syndrome or failed neck surgery syndrome, while only 9% involved myofascial pain syndrome (Table 1). Additionally, a higher proportion of cases in the MDD group had undergone previous spine surgery compared to the non-MDD group, implicating that spine surgery may contribute to both the severity of chronic back pain and susceptibility to developing psychological disorders.

However, the percentage of interventional pain procedures between groups did not differ. Across various assessment tools, baseline scores in the MDD group were consistently worse than those in the non-MDD group. After pain management using conservative or interventional treatments, NRS and HAM-D scores showed significant improvement, indicating that alleviation of depression may parallel improvement in pain. However, alterations of BDI did not change significantly post-treatment, suggesting that either HAM-D might be more sensitive in detecting mood improvement in chronic pain patients or that the two questionnaires capture different dimensions of the pain-depression relationship. The applicability of each tool should be meticulously judged in chronic pain patients [55,56]. Nevertheless, the correlation between the changes in HAM-D and BDI was strong, positive, and statistically significant, aligning with findings from previous studies [57,58]. Both HAM-D and BDI could not only indicate alterations of psychological components but also reflect other physical performances, functionalities, and quality of life [59].

Another noteworthy observation is the minimal or obscure improvement in overall functionality and quality of life after the aggressive pain management. As above-mentioned, the participants were treatment-refractory to both pharmacological and non-pharmacological approaches. For such complex cases, a longer treatment duration and multidisciplinary approaches—potentially including psychiatric support—may be necessary to achieve optimal and measurable clinical improvements. Besides, the relatively short-term observation in this study, particularly for cases requiring multiple interventional procedures, may have limited our ability to detect significant changes through these questionnaire-based measurements. To summarize, this study confirms the knowledge that chronic pain patients present a strong association with a high incidence of depression, and the severity of both pain and depression could develop in a positive linear manner with chronicity.

To the best of our knowledge, few studies have employed validated multiple questionnaires to evaluate the treatment outcomes of comorbid chronic pain and comorbid depression [60,61]. However, caution is warranted when interpreting the data, as variability in the pain etiologies, individualized treatment protocols, and differences in mood or expectations regarding therapy outcomes across groups may introduce a potential confounding factor, despite the use of similar evaluation tools. These factors, some of which are presented in the current study, may limit the reliability of outcome comparisons within a short study period.

The main limitation of this study was the high discrepancy in the follow-up rate between groups, which may introduce study bias. Specifically, the dropout rates were 47.14% in the non-MDD group and 24.13% in the MDD group. Herein, we presented the full data without correcting it with statistical analytic methods. It was because various objective factors influenced the return of participants between groups, which may not be distinguished by pure figure management, such as more patients in the non-MDD group improved much and were hesitant to return due to concern about COVID risks, leading to a significant loss of large non-MDD follow-up. Other factors included varying tracking durations across groups, short observation period, psychological dependence on interventional treatment and physician care among the MDD patients, and low inclusion case numbers could interfere with scientific results in the real-world observation. We would initiate another well-designed, well-prepared, and well-conducted study protocol with more tailored measurement instruments to eliminate the experiment bias, enhance the accuracy and validity of findings, and improve research quality.

In conclusion, this study aimed to explore the impact of depression on short-term pain management in chronic pain patients. Our key findings are as follows: first, the prevalence of MDD is high among chronic pain patients; second, the MDD patients exhibit higher pain severity, psychological burden, and functional impairment compared to those without MDD; and third, aggressive pain management, even without targeted psychiatric treatment, significantly alleviates depressive symptoms. These results suggest that MDD is a major challenge influencing clinical

outcomes in pain management. Early identification of depression and the integration of psychiatric support should be prioritized as part of a comprehensive pain management strategy.

Conflict of Interest

All authors have no conflicts of interest to declare.

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