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Anxiety and depression in patients with osteoarthritis: impact and management challenges

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Background: Anxiety and depression are common psychological comorbidities that impact the quality of life (QoL) of patients. In this systematic review, we 1) determined the impact of anxiety and depression on outcomes in patients with osteoarthritis (OA) and 2) summarized unique challenges these comorbidities present to current OA management.

Patients and methods: A systematic literature search was performed using the OVID Medline and EMBASE databases until April 2016. Full-text research articles published in English from the year 2000 onward with a sample size of >100 were included in this review. Eligible research articles were reviewed and the following data were extracted: study author(s), year of publication, study design, and key findings.

Results: A total of 38 studies were included in the present review. The present study found that both anxiety and/or depression were highly prevalent among patients with OA. Patients with OA diagnosed with these comorbidities experienced more pain, had frequent hospital visits, took more medication, and reported less optimal outcomes. Management strategies in the form of self-care, telephone support, audio/video education programs, and new pharmacotherapies were reported with favorable results.

Conclusion: Anxiety and depression adversely impact the QoL of patients with OA. Physicians/caregivers are highly recommended to consider these comorbidities in patients with OA. Ultimately, a holistic individualized management approach is necessary to improve patient outcomes.

Keywords: osteoarthritis, anxiety, depression, impact, management

Introduction

Osteoarthritis (OA) is the most common musculoskeletal disease worldwide.¹ It is characterized by degeneration of the articular cartilage, osteophyte formation, and asymmetric joint space narrowing.² These changes often lead to significant pain and disability and create a substantial individual, societal, and economic burden.^{3,4} Since the incidence and prevalence of OA increase with age, longer life expectancy will only increase these measures in the future.⁵ Current management largely emphasizes on alleviating symptoms and improving function, but for many these interventions do not provide adequate symptom relief. This variability in symptoms and outcomes among individuals with OA cannot be explained by the disease pathology alone.

Several factors are being investigated to explain differences in patient-reported symptoms and outcomes, of which anxiety and depression have begun to emerge as strong candidates.^{6,7} Anxiety is defined as the presence of “fear or nervousness about what might happen”.⁸ When this fear produces behavioral and physiological changes, the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V)*

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denotes this as anxiety disorder.⁹ Depression, on the other hand, is defined as the presence of sad, empty, or irritable mood. Both anxiety and depression are accompanied by somatic and cognitive changes that can significantly affect an individual's capacity to function.⁹ Outside of OA, studies have consistently reported that anxiety and depression have significant impacts on cardiovascular diseases, chronic respiratory disorders, and gastrointestinal conditions.^{10–12} Patients suffering from chronic painful disabling conditions frequently report anxiety and depression as comorbidities.¹³ This may predispose patients to experience pain more often, as recent evidence suggests that anxiety and depression can alter pain threshold levels.¹⁴ Since chronic pain in itself can cause or aggravate anxiety and depression,¹⁵ a vicious cycle begins, which can significantly impact the course and management of these chronic diseases.

Several studies have evaluated the concordance between OA, anxiety, and depression. Although substantial work has been conducted to elucidate the role of anxiety and depression in patients with OA, this study seeks to provide a comprehensive understanding regarding the impact these comorbidities have on OA symptoms, patient outcomes, and challenges they present towards disease management.

Patients and methods

Eligibility criteria

Original studies of 1) human subjects that 2) assessed anxiety or depression during any time point of the 3) OA disease course 4) regarding its impact on patient-reported symptoms and outcomes along with 5) different interventions employed to manage these comorbidities were included for this review. We limited eligibility to studies that were only in English language. Review articles, letters to the editor, published abstracts, book series, short

surveys, notes, editorials, and case series were excluded. It has been reported that even with statistically significant results, studies with low sample sizes are less likely to reflect a true effect;^{16,17} therefore, reports concerning <100 patients were excluded. Additionally, only articles with full-text versions published from the year 2000 onward were eligible for this review to focus on recent updates in OA, anxiety, and depression.

Search strategy and criteria

A manual electronic search of the OVID Medline (from 1996) and EMBASE (from 1974) databases was performed in duplicate by two authors (AS and PK) to identify studies published until April 2016 that assessed the impact or management of anxiety or depression in patients with OA. The following search string was used: “(osteoarthritis) and (anxiety or depression) and (impact or management)”. One thousand and sixty-seven records were identified after excluding non-English results. After performing automated deduplication using the OVID search interface, 866 studies remained.

Study selection

Citation records were extracted to Excel spreadsheet software (Microsoft Corp, Redmond, WA, USA) and sorted by publication-type metadata. No specialized systematic review software packages were used. Publication types not meeting inclusion criteria were removed (Figure 1). These records were manually screened for eligibility by two authors (AS and PK), and any doubt regarding inclusion/exclusion of a particular study was addressed by discussion between the two authors. Unresolved conflicts were managed by discussion with two additional authors (QS and RG). Four hundred and thirty-five records were excluded as 233 were review

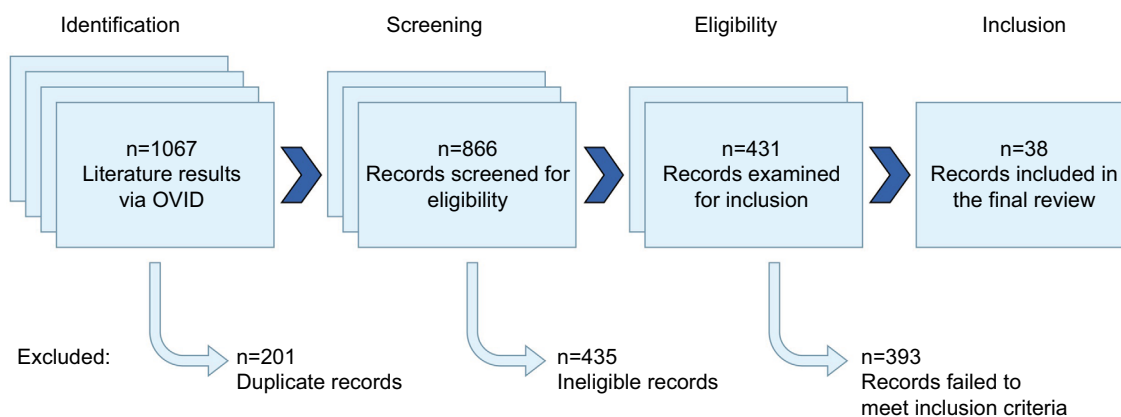


Figure 1 Flow diagram summarizing the literature search, screening, and review.

articles, 174 were published abstracts, seven were conference papers, seven were notes, six were editorials, three were short surveys, two were letters, two were meta-analysis, and one was a book series. After excluding further 356 records based on title and abstract information, 21 records with a sample size of <100, and 16 records based on year of publication,

38 records were included in the final review.^{18–55} No systematic search of article bibliographies or conference proceedings was performed in an attempt to identify any additional unpublished or otherwise unidentified data. Full-length articles of the remaining 38 records were obtained and included in our final synthesis (Table 1).

Table 1 Final studies with authors, year of publication, design, and key findings

Authors	Year	Design	Key findings
Axford et al ⁵⁵	2008	n=170 patients completed trial of PEP to determine what may hinder its efficacy in knee OA.	Greater pain was associated with reduced coping, increased depression, and reduced physical ability.
Ayral et al ⁵⁴	2002	Prospective randomized study of n=112 (56/group) to access impact of video information on pre-operative anxiety of patients scheduled to undergo joint lavage for knee OA.	Pre-operative anxiety was lowered by half for patients who had viewed the video. Tolerability of knee lavage was also significantly better in the video group.
Blagestad et al ⁵³	2016	Cross-sectional study of n=39,688 participants undergoing THA from 2005 to 2011 to investigate redeemed medications.	Surgery reduced prescriptions of analgesics, hypnotics, and anxiolytics, but not anti-depressants.
Buszewicz et al ⁵²	2006	Randomized controlled trial, n=812 patients aged >50 hip and/or knee OA and pain and/or disability randomized to six sessions of self-management and education booklet (intervention group) or education booklet alone (control group).	The two groups showed significant differences at 12 months on the anxiety sub-score of HADS. No significant difference was seen in number of visits to the GP at 12 months.
Collantes-Esteve and Fernandez-Perez ⁵¹	2003	Open-label multi-center study with n=2,228 investigated the effect of a switch from celecoxib to rofecoxib among patients with OA.	The switch to rofecoxib from celecoxib favorably influenced proportions of patients with self-reported depression.
Croft et al ⁵⁰	2005	Mailed patient survey of n=8,995 individuals aged >50 years. Patients completed the SF-36, HADS, and WOMAC.	Severity of knee pain and related disability are worse in the presence of pain elsewhere.
Dailiana et al ⁴⁹	2015	Investigate and compare the impact of primary THA (n=174) and TKA (n=204) on QoL, patients' satisfaction and detect the effect of patients' demographic and clinical characteristics on outcome. WOMAC and CES-D10 pre- and post-operative.	WOMAC and CES-D10 improved significantly 1 year post-operatively.
Dieppe et al ⁴⁸	2000	Prospective study, n=500 patients, study of natural history of peripheral joint OA and its impact over 8 years. Patients reviewed at 3 and 8 years. HAQ and HADS.	The mean HAQ and HADS scores at 8 years were high, especially in those with knee disease, indicating significant disability as a result of the disease.
Ellis et al ⁴⁷	2012	Effect of psychopathology on the rate of improvement following TKA (n=154).	Subjects in the psychopathology group showed significantly lower SF-36 mental component summary scores both at baseline and 1 year post-operatively.
Gerrits et al ⁴⁶	2014	Prospective analysis of impact of chronic diseases and pain characteristics in n=1,122 individuals with remitted depressive or anxiety disorder.	Pain, not chronic disease, increases the likelihood of depression recurrence, largely through its association with aggravated sub-threshold depressive symptoms.
Gignac et al ⁴⁵	2013	Middle- and older-age adults with OA, n=177 or no chronic disabling conditions, n=193, aged >40 years completed a telephone interview and self-administered questionnaire assessing demographics, SRPQ, and psychological variables.	Middle-aged adults with OA reported significantly greater role limitations and more health care utilization than all other groups. Middle-aged adults and those with OA also reported greater depression, stress, role conflict, and behavioral coping efforts than older adults or healthy controls.
Hanusch et al ⁴⁴	2014	n=100, influence of psychological factors, including perception of illness, anxiety, and depression, on recovery and functional outcome after TKA. Function was assessed pre-operative, 6 weeks, and 1 year after using OKS and ROM.	Pre-operative function had the biggest impact on post-operative outcome for ROM and OKS. Depression and anxiety associated with a higher (worse) knee score at 1 year.

(Continued)

Table 1 (Continued)

Authors	Year	Design	Key findings
Hawker et al ⁴³	2011	Community cohort, n=529 participants with hip/knee OA. Telephone interviews assessed OA pain and disability using three time points over 2 years.	Current OA pain strongly predicted future fatigue and disability; fatigue and disability in turn predicted future depressed mood; depressed mood and fatigue were interrelated such that depressed mood exacerbated fatigue and vice versa, and that fatigue and disability, but not depressed mood, led to worsening of OA pain.
Kingsbury and Conaghan ⁴²	2012	Random online survey on assessment and treatment of OA, n=1,006 GPs randomly selected and invited to participate in, on factors influencing their management, burden on their practice, and on the need for improving care.	Achieving adequate pain control and lack of time were the most frequently cited challenges, whereas more time with patients, collaboration with specialist colleagues, and improved communication tools were the most common needs identified to improve OA management.
Kirkness et al ⁴¹	2012	Pre- and post-operative measures of pain, physical function using LEFS, and QoL of n=168 patients were evaluated.	Most common comorbidities in these patients were osteoarthritis, hypertension, and major depressive disorders.
Lin et al ⁴⁰	2003	Randomized controlled trial, n=1,801, depressed older adults with coexisting arthritis, performed at 18 primary care clinics to evaluate whether care for depression changes pain and outcome.	Benefits of improved depression care extended beyond reduced depressive symptoms and included decreased pain as well as improved functional status and QoL.
Lin et al ³⁹	2006	Multi-site randomized-controlled trial n=1,001 participants with depression and arthritis. Baseline and 12-month interviews assessed arthritis pain severity and activity interference, depression, analgesic use, and overall functional impairment.	Systematic depression management was more effective than usual care in decreasing pain severity among arthritis patients with lower initial pain severity.
Liu et al ³⁸	2016	Patients with primary hand OA, n=247, consulting secondary care, underwent physical examination for the number of joints with bony joint enlargements, soft tissue swelling and deformities, and radiographs.	Hand OA patients report esthetic dissatisfaction with their hands regularly. This dissatisfaction has a negative impact in a small group of patients who also reported more depression and negative illness perceptions.
Lopez-Olivo et al ³⁷	2011	Evaluation of n=241 patients undergoing TKA, before and 6 months after surgery. Multiple regression models evaluated associations of baseline demographic and psychosocial variables.	Perioperative psychosocial evaluation and intervention are crucial in enhancing TKA outcomes.
Marks ³⁶	2007	Cross-sectional analyses, n=100, unilateral and bilateral radiographic and symptomatic knee OA patients underwent standard assessment using several validated questionnaires and a series of walking tests on level ground.	Efforts to heighten self-efficacy for pain and other symptoms management may influence the affective status, function, and effort-related perceptions of people with knee OA quite significantly.
Marks ³⁵	2009	n=1,000 hip OA surgical candidates examined for any historical/concurrent evidence of depression/anxiety.	Those with depression and anxiety histories were more impaired before surgery and tended to recover more slowly than those with no such history.
Montin et al ³⁴	2007	Longitudinal follow-up study, n=100 participants. State Trait Anxiety Inventory was used to measure patients' level of anxiety before surgery and at 1 month, 3 months, and 6 months post-operatively.	Patients' pre-operative trait anxiety impaired HRQoL both before and after surgery.
Nour et al ³³	2006	Older adult women (n=102) and men (n=11) with OA or RA were randomly assigned to experimental (n=68) or wait list control (n=45) groups. CES-D at baseline, pre-intervention, and post-intervention.	Self-management intervention can successfully improve involvement in exercise and relaxation among housebound older adults with arthritis.
Ozcakir et al ³²	2011	n=100 knee OA patients; investigate relationship between radiological severity and clinical/psychological factors. KL, WOMAC, 15 m walk, 10-step climb.	Depression was significantly higher in late-stage knee OA group. Radiological severity is an important indicative factor for pain, disability, depression, and social isolation.
Perruccio et al ³¹	2012	Prospective study of n=494 participants who completed patient-reported outcome pre- and 12 months post-TKA. WOMAC, POMS, and HADS scoring methods used.	As symptomatic joint count increase, so does anxiety and depression both pre- and post-operatively. A comprehensive approach to OA management/care is warranted.
Pinto et al ³⁰	2013	n=124 patients assessed 24 hours before (T1) and 48 hours after (T2) surgery. Demographic, clinical, and psychological factors were assessed at T1 and several post-surgical pain issues, anxiety, and analgesic consumption were evaluated at T2.	Positive correlation between post-surgical anxiety and acute pain was reported.

Authors	Year	Design	Key findings
Rosemann et al ²⁹	2007	Survey of n=1,021 participants to assess the prevalence, severity, and predictors of depression in a large sample of patients with OA.	There is high prevalence of depression among patients with OA and perceived pain and few social contacts were strongest predictors.
Rosemann et al ²⁸	2007	Patient questionnaires, n=1,021 to assess the impact of concomitant depression on QoL and health service utilization of patients with OA.	Appropriate treatment of depression would appear not only to increase QoL but also to lower costs by decreasing health service utilization.
Rosemann et al ²⁷	2007	Cross-sectional survey, n=1,250 OA patients to assess factors associated with visits to GPs, orthopedists, and non-physician practitioners.	Psychological factors contribute to the increased use of health care providers.
Rosemann et al ²⁶	2007	Determined factors associated with functional disability in n=1,021 patients with OA via questionnaires.	Main factors associated with functional disability were depression, pain, and few social contacts.
Rosemann et al ²⁵	2008	Cross-sectional survey of n=1,021 OA patients to determine factors associated with pain intensity in primary care.	Severity of depression showed the strongest association with pain intensity.
Sale et al ²⁴	2008	Prospective cohort study, n=1,227 individuals ≥62 years with hip/knee OA completed CES-D, WOMAC, and other questionnaire.	Prevalence of depressive symptoms was high in adults with OA. Higher depressed mood was independently and significantly associated with female gender, greater pain and fatigue, stressful life events, more coping behaviors, and receiving treatment for depression/mental illness.
Stamm et al ²³	2014	Health interview survey including n=3,097 subjects aged >65 years with OA, back pain, or osteoporosis to explore health care utilization compared to controls.	Patients with OA, back pain, or osteoporosis visited GPs and were hospitalized more often than controls. Problems in the ADLs, pain intensity, and anxiety/depression influenced GP consultations.
Steigerwald et al ²²	2012	Open-label, Phase 3b study of n=195 patients to evaluate the effectiveness and tolerability of tapentadol for severe, chronic OA knee pain.	Tapentadol significantly improved pain intensity, HRQoL, and function in patients with inadequately managed, severe, chronic OA knee pain.
Theiler et al ²¹	2002	3-week prospective open-label multi-center study with rofecoxib 25 mg daily in n=134 (mean 69 years, SD=8) outpatients with painful OA flares of the knee or the hip.	Rofecoxib significantly SF-12 and WOMAC scores, in OA patients.
Wylde et al ²⁰	2012	Patients listed for a primary TKA were recruited from pre-operative assessment clinics. Pre-surgical evaluation included WOMAC, PSES, HAD, and SACQ questionnaires and questions about other painful joints. Patients then completed the WOMAC Pain and Function Scales at one year post-operatively.	Significant predictors of post-operative pain were greater anxiety and higher pain severity. Other significant predictors of post-operative disability were greater anxiety, worse functional disability, and a greater number of painful joints elsewhere.
Yilmaz et al ¹⁹	2015	Patients with RA (n=142), FMS (n=136), knee OA (n=139) and healthy women controls (n=152) were analyzed using VAS, BDI, FIQ, TPC, DAS-28, HAQ, and WOMAC.	Positive correlation was determined between BDI, VAS, and WOMAC scores in the knee OA group. However, level of depression was only related to disease severity in women with FMS.
Zullig et al ¹⁸	2015	Data were from patients (n=300) enrolled in a randomized control trial examined the association of comorbidities with baseline-OA PROs: pain, physical function, depressive symptoms, fatigue, and insomnia.	Depression was associated with worse pain, fatigue, and insomnia. Evidence that comorbidity burden is associated with worse OA-related PROs.

Abbreviations: AIMS, Arthritis Impact Measurement Scale; ASMP, Arthritis Self-Management Program; BDI, Beck Depression Inventory; CES-D, Centre for Epidemiological Studies Depression Scale; DAS-28, Disease Activity Score-28; FIQ, Fibromyalgia Impact Questionnaire; FMS, fibromyalgia syndrome; GPs, general practitioners; HADS, Hospital Anxiety and Depression Scale; HAQ, Health assessment questionnaire; HSCL-20, Hopkins Symptom Checklist Depression Scale; IPQ-R, Illness Perceptions Questionnaire-Revised; KL, Kellgren-Lawrence grading; KSS, Knee Society Scale; LEFS, Lower Extremity Function; OA, osteoarthritis; OKS, Oxford Knee Score; PEP, Patient Education Program; PHQ-9, Patient Health Questionnaire; POMS, Profile of Mood States; PSES, Pain Self-Efficacy Scale; RA, rheumatoid arthritis; ROM, Goniometer-measured range of movement; SACQ, Self-Administered Co-morbidity Questionnaire; SF-36, SF-12, Short Form Health Survey; SRPQ, Social Role Participation Questionnaire; THA, total hip arthroplasty; TKA, total knee arthroplasty; TPC, tender point counts; WOMAC, Western Ontario & McMaster Universities Osteoarthritis Index; VAS, Visual Analog Scale; PROs, Patient-reported Outcomes; ADLs, Activities of Daily Living.

Data collection

Data extraction included the following elements: 1) authors, year of publication, 2) study design, and 3) key findings.

Study designs and study quality

Of all the final studies included in this review, six were randomized controlled trials,^{18,33,39,40,52,54} 14 were prospective cohort studies,^{20,21,30,31,34,37,41,44,46,48,49,51,55,56} 14 were

cross-sectional studies,^{19,25–29,32,36,38,43,45,47,53,57} one was a retrospective analysis,³⁵ and three were surveys.^{23,42,50}

Results

Sample and setting

Of the original 866 English articles, 38 articles fulfilled our aforementioned criteria and thus were included for analysis in this review.^{18–55} These 38 articles outline the impact of

anxiety and/or depression on patients living with OA and the challenges these comorbidities present in OA management, wherein some studies also examined approaches on how to address these challenges. The age of patients analyzed in most of these studies was consistent with the age at which OA and depression are commonly diagnosed. However, one study specified a younger cutoff age range in their inclusion criteria.⁴⁵ Gignac et al⁴⁵ reported that middle-aged patients with OA (mean age 50.8 years) reported more depression compared to elderly subjects (mean age 67.8 years) having similar OA severity. This difference was attributed to role limitation and dissatisfaction among middle-aged OA individuals. Most studies included both male and female participants. However, in one study, sex was an eligibility criterion, as this study focused solely on female participants.¹⁹ Studies were carried out in different settings viz university hospital, general practitioner (GP) clinics, and via telephone/mailed surveys. All studies published after year 2000 were analyzed (Table 1).

Anxiety and depression

All studies evaluated anxiety and/or depression either as a primary or a secondary objective. Various scoring methods were utilized, of which Centre for Epidemiological Studies Depression Scale (CES-D)⁵⁸ and Hospital Anxiety and Depression Scale (HADS) were most popular.⁵⁹ Both CES-D and HADS have been extensively used and studied, and are considered reliable and valid research tools.⁶⁰ Other scoring methods used were Composite International Diagnostic Interview,¹³ 36-Item or the 12-Item Short Form Health Survey (SF-12, SF-36),⁶¹ Hopkins Symptom Checklist Depression Scale,⁶² Patient Reported Outcome Measurement Information System,⁶³ Patient Health Questionnaire (PHQ),⁶⁴ visual analog scale, Arthritis Impact Measurement Scale,⁶⁵ Beck Depression Inventory,⁶⁶ and the Health Education Impact Questionnaire.⁶⁷ Apart from these scores, clinical diagnosis based on patient interviews was also utilized.

OA pathology and disease severity

Most studies focused on lower extremity OA (hip and knee), with one study examining hand OA³⁸ patients. Diagnosis was based on clinical presentation or radiographs. Patients from the entire spectrum of disease severity were studied. The Kellgren and Lawrence (KL) radiographic grading system was most often used to report OA severity; however, some studies did not use any specific grading method. One study included patients with early (KL I, II) and late (KL III, IV) stage OA.³² Pain was a consistent feature across most studies and was assessed primarily using the Western Ontario &

McMaster Universities Osteoarthritis Index.⁶⁸ In addition to OA, two studies also assessed patients with rheumatoid arthritis.^{19,33}

Epidemiology of anxiety and depression in patients with OA

Three studies reported on the prevalence of anxiety and depression in patients with OA.^{24,29,41} Rosemann et al²⁹ conducted a cross-sectional survey in 1,021 patients with OA and reported that psychological factors (viz anxiety and depression) were highly prevalent among the patients (19.76% of male and 19.16% of female participants reported a PHQ-9 score of ≥ 15). Similar results were reported by Sale et al²⁴ in a cross-sectional study where 21.3% of 1,227 participants reported a CES-D score of ≥ 16 . Likewise, Kirkness et al⁴¹ reported that major depressive disorder was commonly prevalent in patients scheduled for total knee arthroplasty.

Impact

Impact of anxiety and depression on OA symptoms

Of the 38 studies included in our final analysis, 13 studies examined the impact of anxiety and depression on OA symptoms.^{18,19,26,31,32,38,43,45,46,48,50,55} There was a considerable overlap in reporting impact of these psychological conditions on patients with OA with pain being the key central element. Studies reported that the prevalence of anxiety and depression was interrelated to index joint pain,⁵⁵ pain at multiple sites,^{31,50} pain intensity,²⁵ and OA severity.³² Pain was in turn associated with depression and its recurrence.⁴⁶ Hawker et al⁴³ also reported that current OA pain predicted future fatigue, disability, and depressed mood. In addition to its impact on OA pain, concurrent depression was also interrelated to significant participation restriction and physical limitation.^{26,45}

Impact of anxiety and depression on OA outcomes

Nine studies examined the impact of anxiety and depression on the outcomes of patients with OA.^{20,27,30,34,35,37,44,52,53} Studies reported that anxiety and depression increased GP visits,⁵² health care utilization,²⁷ drug prescriptions,⁵³ adversely affected surgical outcomes,^{30,34,35,37,44} and increased post-surgical pain.²⁰

Impact of anxiety and depression on patients with OA: sex differences

Our results indicate that anxiety and depression differentially impact lives of male and female patients with OA.

Sale et al²⁴ reported that higher level of depressed mood was independently and significantly associated with the female sex.

Management challenges

Thirteen studies evaluated management challenges in patients with OA with comorbid anxiety and depression.^{21–23,28,33,36,39,40,42,47,49,51,54} The present study found that anxiety and depression posed unique challenges to physicians in 1) diagnosis, 2) structuring a proper management plan, and 3) effective pharmacotherapy.

Challenges in diagnosis of anxiety and depression

Primary care physicians or GPs infrequently considered or found it difficult to diagnose anxiety and/or depression in patients with OA.^{28,42}

Challenges in self-care, collaborative care, social/phone support

Management regimes advocating self-care, social/phone support, and educational engagements in patients with OA with comorbid anxiety and depression were reported. Lin et al³⁹ reported that systematic depression management (antidepressant pharmacotherapy and/or problem-solving treatment) was more effective than usual care in decreasing pain severity among patients with arthritis with lower initial pain severity, but not among patients with higher initial pain severity. On the contrary, Buszewicz et al⁵² reported that although self-management reduced anxiety, it had no significant effect on pain, physical functioning, or number of GP visits at 12 months.

Challenges in pharmacotherapy

Pharmacological challenges exist in managing patients with OA with comorbid anxiety and depression. These challenges juxtaposed with the demographics of this patient cohort (advanced age and presence of other medical comorbidities) make pharmacotherapy difficult. Therefore, it is vital to investigate new treatment modalities that could effectively manage these conditions with minimum adverse effects. The present study found that rofecoxib and tapentadol were reported to improve pain and depressive symptoms of patients with OA. Theiler et al²¹ assessed the effects of rofecoxib on quality of life (QoL) in elderly patients with painful OA flares who were not responsive to or had adverse reactions to previous NSAID therapy. The authors reported that rofecoxib significantly improved QoL, as measured by the SF-12. Similarly,

Collantes-Esteve and Fernandez-Perez⁵¹ found rofecoxib to favorably influence patients with OA with self-reported depression. In addition to rofecoxib, use of tapentadol (prolonged and immediate release) has also been reported in patients with chronic painful knee OA. Steigerwald et al²² evaluated effectiveness of tapentadol prolonged release in 195 patients with chronic OA knee pain and found significant improvement in pain intensity, QoL, SF-36, and HADS.

New management approaches: music, video, and yoga

In recent years, various new and innovative management methodologies have been investigated. Ayril et al⁵⁴ reported that advocating video education information on the planned procedure before surgery lowered perioperative anxiety. Music therapy and yoga have also been reported to help improve patient anxiety and depression; however, the sample sizes of their respective studies were small.^{69,70}

Discussion

Psychological comorbidities (anxiety and depression) are highly prevalent among patients with OA.^{24,29,41,49} These comorbidities are frequently associated with higher pain and physical limitation,^{18,19,26,31,32,38,43,45,46,48,50,55} poor outcomes to both conservative and surgical interventions,^{20,30,31,34,35,37,44,47,56} and increased pharmacotherapy and health care utilization.^{23,48} Our results indicate that standardized interventions to manage these comorbidities are lacking as a number of different self-care management programs, telephone support programs, video information support programs, and new drug treatments were reported in the literature with varied success.^{21–23,28,33,36,39,40,42,47,49,51,54} This variability in patient care highlights the complex relationship that exists between OA, anxiety, and depression (Table 2). Yet, these comorbidities are commonly overlooked by many primary care physicians and GPs who either solely focus on physical aspects of OA or simply fail to assess patients' psychological state altogether.⁷¹ It is imperative to recognize these comorbidities, as these can influence disease course and management, ultimately affecting functional outcomes.

Anxiety and depression are interrelated with pain and physical limitation, the two key OA symptoms. Studies in our review have revealed that anxiety and depression can significantly impair QoL of patients by altering pain perception and functional capacity.²⁴ Therefore, educating physicians about timely identification of psychosocial factors such as anxiety and depression that may pre-date OA pathology or result as a

Table 2 Summary of results

Impact	Summary	
Epidemiology	Psychological factors such as anxiety and depression are commonly prevalent in patients with OA.	
OA symptoms	Anxiety and depression contribute to index joint pain and its intensity. This pain can predict future fatigue, disability, and depressed mood.	
OA outcomes	Anxiety and depression increase GP visits, health care and drug utilization, post-surgical pain, and adverse outcomes.	
Sex differences	Anxiety and depression differentially impact lives of male and female patients with OA, with females showing higher levels of depressed mood.	
Management challenges	Summary	Suggestions
Challenges in diagnosis	Physicians found it difficult to diagnose anxiety and/or depression in patients with OA.	Adopt NICE guidelines toward holistic assessment of patients with OA.
Challenges in self-care, collaborative care, social/phone support	Anxiety and depression pose as a challenge to physicians in structuring a management plan. Studies have reported use of various management programs with variable success.	Use "à la carte" approach. Thorough timely patient assessment required following initiation of program to access for improvement.
Challenges in pharmacotherapy	Rofecoxib and tapentadol were reported to have favorable results.	Cocktail pharmacotherapy. Other drugs like duloxetine have been approved by FDA for use in this patient cohort.
New management approaches	Music, video, and yoga have been tried with favorable results.	Can be employed as adjuvants.

Abbreviations: FDA, US Food and Drug Administration; GP, general practitioner; NICE, National Institute for Health and Care Excellence; OA, osteoarthritis.

consequence of the disease can improve the QoL of patients living with these comorbidities. The National Institute for Health and Care Excellence (NICE) has outlined recommendations regarding holistic assessment of patients with OA (<https://www.nice.org.uk/guidance/cg177>), which serves as an excellent starting point and it is highly recommended that physicians consult this document. Thus, implementation of appropriate screening questionnaires can help identify these psychological comorbidities at an earlier stage, which could in effect provide adequate lead time to implement a management plan that could improve outcomes and lower future health care burden and costs.

OA is a progressive disease and a large portion of patients with OA will, at some point, undergo surgery. Patients awaiting surgery can experience anxiety; however, educating them about the procedure and advocating a self-care plan can change health-directed behaviors. While surgery does improve QoL of patients, patients with OA with comorbid anxiety and depression may not experience similar favorable clinical outcomes following joint replacement surgery as seen in patients with OA without these comorbidities,^{20,30,34,35,37,44,47,56} even after a structured rehabilitation program.⁷² Thus, surgical indications in patients with OA with comorbid anxiety and depression should be critically assessed as not all patients report similar benefits following surgery.

As seen in our results, OA management strategies include self-care, collaborative care, social/phone support, pharmacotherapy, music, educational videos about OA procedures, and yoga. Self-care, collaborative care, and social/phone support should be integrated into OA management, as these strategies

have been shown to alter comorbid anxiety and depression, as well as resulting physical and emotional pain. Similarly, pharmacotherapy should also be appropriately integrated into OA management; however, this should be done carefully, as the treatment of OA, depression, anxiety, and pain through pharmacotherapy carries the danger of drug interactions and adverse side effects. From our study, we can suggest rofecoxib and tapentadol to improve QoL and pain of patient with OA and encourage the development of new treatment modalities that work in tandem to treat OA symptoms, as well as comorbidities. Additionally, there is evidence that anti-depressant medications such as duloxetine can improve pain in patients with OA,⁷³ suggesting a central mechanism that may connect OA pain and depression. Therefore, it would be appropriate to consider implementing anti-depressant/anti-anxiety therapy in tandem with non-steroidal anti-inflammatory drugs and/or analgesic drugs to address these different pain pathways concurrently. This multi-faceted pharmacological approach can greatly benefit patients in this cohort. Other newer modalities such as music, videos, and yoga are management methods that have recently gained more attention, as they have been shown to improve patient outcomes. Music has been shown to reduce levels of anxiety, depression, and pain. Likewise, videos educating patients on their planned surgical procedures have lowered pre-operative anxiety. These modalities can act as adjuvants to current management strategies.

To create individualized OA management strategies, it is essential to recognize that patients with early OA disease experience less anxiety and depression compared to patients with late-stage disease.³² Therefore, radiological severity of

OA can serve as an indicative factor for intensity of depression in patients with OA. This concept should be further investigated. Similarly, sex differences are prevalent independently in OA, anxiety, and depression.^{74,75} Studies have reported that female patients with OA report greater anxiety and depression^{24,76} and lower QoL³⁸ than males. Moreover, female patients with OA may have different expectations than their male counterparts and therefore may require a completely different management approach.

It is important to state that present literature fails to fully address the management strategies in dealing with psychological comorbidities seen in patients with OA. It is rather clear that one treatment does not fit all, as seen in the present review. On one end self-management interventions did not improve pain, QoL, or depression,⁷⁷ while on the other hand, self-management did produce improvement in exercise and relaxation activities in depressed patients although not as much as in patients without depression.³³ These conflicting results highlight the challenges present in the management of these comorbidities today. It should also be highlighted that recruiting and retaining patients in management programs is also challenging and should be further evaluated to increase patient compliance, as depressed patients tend to lack interest from the outset. Furthermore, another factor in need of consideration is age, and how reports of depression/anxiety can differ based on patients' age group. To garner an accurate understanding of how depression/anxiety interacts with OA, it is important to consider the possibility that different age groups experience varying degrees of depression/anxiety, based on a diverse set of factors, such as socioeconomic status and health complications. Recent trends in depression suggest its high prevalence among individuals aged 40–59 years, which may thus affect the presentation of OA to a greater degree in middle-aged cohorts than younger or elderly cohorts.⁷⁸ Therefore, examining the impact and management challenges of anxiety and depression in an age-stratified OA cohort should be further investigated.

Although our results provide a comprehensive summary of the current state of literature, a considerable lack of studies originating from outside of North America and Europe is noted. This could be attributed to the fact that outpatient visits and in-patient admissions for mental health diseases are higher in the US and Europe,⁷⁹ or it could simply underscore a general lack of research initiatives in the developing world, or that psychological conditions largely remain under-recognized and/or under-diagnosed. Thus, the inclusion of studies from developing nations may provide a more detailed picture of the relationship between anxiety, depression, and

OA. We also acknowledge that the exclusion of reports not published in English may have introduced institutional bias. Furthermore, in addition to the inherent weaknesses of the studies reviewed, our study may be skewed by publication bias, as there is a well-described prejudice toward the publication of positive findings. Nevertheless, we believe that the present review accurately presents the current state of evidence concerning the impact and management challenges of anxiety and depression encountered by patients with OA.

Conclusion

In summary, the majority of evidence regarding impact of anxiety and depression in patients with OA suggests reduced QoL and poor clinical outcomes. The current literature fails to lay a blueprint to tackle the management challenges seen. OA stage-specific stratification may help guide management. However, further studies are needed to formulate definitive management strategies to deal with OA-associated anxiety and depression and should focus on high-quality randomized controlled trials with patients stratified into non-operative, pre-operative/operative, and post-operative groups.

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Disclosure

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