Effects of cognitive and mental health factors on the outcomes following carpal tunnel release: A systematic review and meta-analysis

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Effects of cognitive and mental health factors on the outcomes following carpal tunnel release: A systematic review and meta-analysis

Running head: Psychosocial factors in carpal tunnel release

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Abstract

Objective: To determine the effects of the cognitive and mental health factors on the outcomes following carpal tunnel release (CTR).

Data sources: Embase, Pubmed/MEDLINE, Web of Science, CINAHL and Cochrane Central Register of Controlled Trials (CENTRAL) databases from inception to August 14, 2021.

Study selection: Randomized controlled trials and observational studies of patients with CTR were included. The included studies aimed to determine the effect of the

cognitive (catastrophic thinking, kinesiophobia and self-efficacy) or mental health factors (symptoms of anxiety and depression) on the outcomes at least three months post-CTR.

Data extraction: Two independent reviewers performed data extraction and assessed the risk of bias. Data were extracted using a standardized protocol and reporting forms. The risk of bias of the included studies was assessed using the Quality in Prognosis Studies risk-of-bias tool. Random-effects models were used for meta-analysis.

Data synthesis: A total of fifteen studies involving 2599 patients were included in this systematic review. The majority of studies indicate a significant association between the cognitive or mental health factors and outcomes following CTR. Quantitative analysis showed a moderate association of symptoms of depression on symptom severity (n = 531, r = 0.347, 95% CI = 0.205 to 0.475, p = <0.0001), function (n = 386, r = 0.307, 95% CI = 0.132 to 0.464, p = 0.0008), and pain (n = 344, r = 0.431, 95% CI = 0.286 to 0.558, p = <0.0001). In general, the risk of bias in the included studies was low.

Conclusions: This systematic review and meta-analysis showed that symptoms of depression have a moderate association with symptom severity, function and pain after CTR. Symptoms of anxiety, catastrophic thinking, and self-efficacy are also important indicators of poor post-surgery outcomes. Physicians, physical therapists, and occupational therapists should consider evaluating these variables in patients undergoing CTR.

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Keywords: Carpal Tunnel Syndrome; Psychosocial factors; Disability; Patient Reported Outcome Measures; Postoperative pain.

Abbreviations

BCTQ-S: Boston Carpal Tunnel Questionnaire score-symptoms

BCTQ-F: Boston Carpal Tunnel Questionnaire score-function

BDI-II: Beck Depression Inventory

BMI: Body mass index

CES-D: Center of Epidemiologic Studies-Depression scale

CTS: Carpal tunnel syndrome

CTS-6: 6-item shortened Boston Carpal Tunnel Questionnaire

CTR: Carpal tunnel release

DASH: Disabilities of the Arm, Shoulder, and Hand

HADS: Hospital anxiety and depression scale

MHI-5: 5-item mental health index

PASS: Pain Anxiety Symptoms Scale

PCS: Pain Catastrophizing Scale

PHQ4: Patient Health Questionnaire-4

PEM: Patient evaluation measure

RCT: Randomized controlled trial

Introduction

Carpal tunnel syndrome (CTS) is the most prevalent compression neuropathy of the upper limb,[1] characterized by pain, paresthesia, and a tingling sensation in the region of the median nerve.[2] These symptoms cause significant functional impairment,[3] affecting the quality of life of the patient.[4] The prevalence of CTS ranges between 6.3% to 11.7%,[5] being more frequent in women than in men.[6] It is estimated that 65% of people diagnosed with CTS eventually require surgery, and the incidence of carpal tunnel release (CTR) per 100,000 person-years is 151 in women and 65 in men.[7]

CTR is one of the most common surgeries performed on the upper limb with a lifetime prevalence of 3.1%,[8] representing a considerable expense for healthcare systems.[9] CTR is indicated primarily in patients who do not respond to conservative treatment, in acute cases (e.g., trauma), and in severe cases with persistent hypoesthesia of the median nerve region and motor impairment.[10] While most patients improve after surgery,[11] approximately 5% of patients report persistent symptoms and require revision CTR within the first postoperative year.[12] The unfavorable outcome after CTR may also be due to pain related to the surgical scar, which may be affected by depressive symptoms.[13,14]

In musculoskeletal diseases, identified cognitive (catastrophic thinking, kinesiophobia, self-efficacy, and fear avoidance) and mental health factors (symptoms of anxiety and depression) have been reported to be relevant to optimizing the postsurgical outcomes. For instance, the patient's cognitions and emotions may affect the recovery and response to treatment in patients with chronic musculoskeletal pain.[15,16] In this context, the fear avoidance model proposes that patients with catastrophic cognitions about pain tend to interpret certain experiences as a threat, avoiding select activities and developing disuse, disability and depression.[17]

We can find a heterogeneous set of predictors related to emotions, cognitions, and coping strategies within the cognitive and mental health factors. Among them, catastrophizing, self-efficacy, fear related to pain, depression, and anxiety have taken on greater relevance in the last few decades due to their strong relationship with post-surgical pain and function.[18,19] Previous systematic reviews have shown that these factors are associated with poorer postoperative outcomes in shoulder surgery,[18,20] spine surgery,[19,21,22,] and knee replacements.[19,23,24] However, the relevance of cognitive and mental health factors as prognostic indicators of recovery to CTR is controversial.[25]

There is a growing literature supporting the role of modifiable cognitive and mental health factors in CTR,[14,26–31]. However, the assessment of these factors has not been taken into account in the recent clinical practice guidelines for patients with CTS[32] when most of the patients may end up needing surgery.[7] A better understanding of the association between cognitive and mental health factors and the surgery results could also help to provide more specialized interventions,

including the expertise of psychologists, physical therapists, occupational therapists, and physicians in the perioperative and postoperative period. In addition, the economic costs associated with mental health disorders and postoperative pain reinforce the need to examine these risk factors closely with a rigorous narrative approach and a quantitative synthesis of the available evidence. This systematic review and meta-analysis aims to determine the effects of the chosen cognitive and mental health factors on the outcomes following CTR, three months after surgery and beyond.

Methods

Protocols and registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[33] The meta-analysis was conducted according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE).[34] The protocol was previously registered on the International Prospective Register of Systematic Reviews PROSPERO (CRD42020181709) in July 2020.

Criteria for considering studies in this review

Randomized controlled trials (RCTs) and observational studies (cross-sectional, longitudinal, case control and cohort) of patients with CTR (open or endoscopic surgery) were included. The included studies aimed to determine the effect of the chosen cognitive or mental health factors on the outcomes at least three months post-CTR. The cognitive factors related to pain (i.e. catastrophic thinking, kinesiophobia, self-efficacy and fear avoidance) and mental health factors (i.e.

symptoms of anxiety and depression) should have been assessed using an objective measure. Therefore, we included studies with at least one of the following prognostic factors: I) Catastrophic thinking, measured by the Pain Catastrophizing Scale (PCS)[35]; II) Kinesiophobia, measured by the Tampa Scale of Kinesiophobia (TSK)[36]; III) Self-efficacy, measured by Self-Efficacy Scale.[37]IV) Fear Avoidance, measured by Fear Avoidance and Beliefs Questionnaire (FABQ)[38]; V) Symptoms of anxiety, measured by the Hospital Anxiety and Depression Scale (HADS)[39] or the Pain Anxiety Symptoms Scale (PASS)[40]; VI) Symptoms of depression, measured by the Hospital Anxiety and Depression Scale (HADS)[39] or Center for Epidemiologic Studies Depression Scale (CES-D),[41] Beck Depression Inventory (BDI-II),[42] 5-item mental health index (MHI-5)[43] or Patient Health Questionnaire-4 (PHQ-4).[44]

On the other hand, studies with at least one of the following outcomes after surgery were included: I) Functional limitations and symptoms, measured by a patient-reported scoring systems such as the Boston Carpal Tunnel Questionnaire (BCTQ)[45] or similar, 6-item shortened Boston Carpal Tunnel Questionnaire (CTS-6),[46] Disabilities of the Arm, Shoulder, and Hand (DASH),[47] Quick-DASH,[48] and the Michigan Hand Questionnaire[49]; II) Pain intensity, measured by a visual analogue scale (VAS), numerical rating scale (NRS), or another numerical ordinal rating scale; III) Patient satisfaction, measured by a satisfaction score (Likert scale or by categorical grading); IV) Work participation, measured as return to work, absenteeism, or time on benefits; V) Physical measures of recovery included grip and pinch strengths and range of motion. We included studies in any language published between January 1950 and August 2021. All editorials, letters to the editor, review articles, systematic review, and meta-analysis, in vivo and in vitro studies were excluded.

Search strategy

A systematic review of the literature was conducted to identify the studies that investigate the effect of the chosen cognitive and mental health factors on the outcomes following carpal tunnel release. We reviewed the Embase, Pubmed/MEDLINE, Web of Science, CINAHL and Cochrane Central Register of Controlled Trials (CENTRAL) databases, from inception to August 14, 2021. Manual searches with the followings terms were performed: I) For population: carpal tunnel release OR carpal tunnel decompression OR ((carpal tunnel syndrome OR median neuropathy) AND (surgery OR postoperative OR post-operative OR postsurgical OR post-surgical)); II) For exposition: psychological OR anxiety OR fear OR avoidance OR depression OR depress* OR mood OR catastrophizing OR catastrophic thinking OR self-efficacy OR kinesiophobia OR emotional OR coping; III) For condition: association* OR predict* OR "risk factor*" OR determinant* OR prognos*; IV) For main outcome: symptom severity OR disability OR pain OR patient reported outcome measures OR recovery of function OR range of motion, articular OR hand strength OR hand grip OR patient satisfaction OR return to work. The terms selected were combined using Boolean logical operators (OR, AND, NOT). We supplemented our search with the reference lists of all included studies to identify potentially relevant articles from other sources. All references were analyzed using the Rayyan web software.[50]

Reviewing procedure and data extraction

First, the titles and abstracts of all identified studies were reviewed by two investigators (RNC, CCM). The irrelevant references were removed. Any disagreements were solved by consensus. Second, the full text versions of the

articles selected in the first stage were read and checked against the eligibility criteria (RNC, CCM). Any disagreements were solved by a third reviewer (RTC). Then, two investigators (RNC, CT) extracted the data independently using a standardized protocol and reporting forms. The following information was extracted from each included study: design, population characteristics, type of surgery, follow-up time, prognostic factor, postoperative outcomes, results of univariate analysis and results of multivariate analysis. The authors were contacted to obtain the information if some relevant data were not included in the study.

Methodological quality assessment

The risk of bias in the included studies was assessed using the Quality in Prognosis Studies (QUIPS) risk-of-bias tool.[51] We classified the studies as high, moderate or low risk in relation to the domains of study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. The low risk of bias was assigned only if the majority (75% or more) of the prompting items were satisfied; moderate risk of bias if 50% to 74% of the prompting items were satisfied; and a high risk of bias if 50% or less of the prompting items were satisfied. Two authors carried out this evaluation independently (RNC-RTC), and discrepancies were resolved by consensus. The concordance was calculated using Cohen's kappa coefficient. The Robvis tool[52] was used to create risk of bias assessment plots.

Quantitative synthesis

The meta-analyses were performed in R v. 4.0.2[53] For the quantitative synthesis, the prognostic factors that were evaluated by 3 or more studies were considered to avoid performing low-power analyses. Studies that operationalized the risk factor in a

markedly different way than most other studies were excluded from the estimate. The quantitative synthesis was carried out in the following steps: I) The original data (e.g., correlations, regression coefficients, and odds ratios) were converted to Pearson's r using standard formulas.[54] To maintain consistency, the associations were recalculated so that they were in the same direction; II) The data were converted into Fisher's z using the escalc() function from the 'metafor' v. 3.0-2 R package[55]; III) 4 different random-effects models were fitted to synthesize the quantitative results of the published studies for each one the effect sizes under study (i.e., correlational data on prognostic factors and postoperative results). This kind of model was preferred as it accounts for study heterogeneity and does not assume that all studies come from a single common population and that were tested under identical or quite similar conditions.[56] These models were computed using the rma() function from the same package (i.e. 'metafor' v. 3.0-2) ; IV) The result of each meta-analysis was transformed back into Pearson's r for final interpretation. The effect size magnitude of r can be interpreted as follows: r=0.1, small, r=0.3, moderate; r=0.5, large.[57] Statistical heterogeneity was assessed using I^2 and classified as might not be important (I^2 = 0-40%), moderate (I^2 = 30–60%), substantial (I^2 = 50–90%) or considerable (I^2 = 75-100%).[58] Forest plots were generated as a way to visualize the effect sizes and CIs from the considered studies, along with the computed summary effect size. These plots were produced using the forest() function also available as part of the 'metafor' v. 3.0-2 R package.

Results

The initial search identified 247 potential studies through electronic databases. In addition, 466 potential studies were identified by reference screening. In total, 251

duplicate studies were eliminated, and 429 were excluded in the screening stage by their title and abstract. Thirty-three studies were assessed as full texts. Of these, ten studies were excluded for having the wrong study design, three for being the wrong publication type, two for involving the wrong population, and three for having the wrong outcome. Finally, fifteen studies were included in this review (Figure 1).[13,14,26–31,59–65] We observed a very high concordance between the reviewers when selecting the studies (kappa = 0.942, $p < 0.001$).

[FIGURE 1 ABOUT HERE]

Study characteristics

The studies were conducted in the USA (six studies),[60–65] South Korea (three),[13,26,27] the United Kingdom (two),[29,59] the Netherlands (two),[14,31] Spain (one)[28] and Denmark (one).[30] All of the included studies were written in English. Seven studies (47%) were published less than five years ago (after 2016).[14,26–31] The designs of the studies included one RCT,[28] twelve prospectives[13,14,27,29–31,59,61–65] and two retrospectives.[26,60] The sample sizes varied between 60[26–28] and 455 participants.[29] A total of 2599 patients were included, with a mean age that varied between 46 ± 9 and 62 ± 12 years respectively. The eight studies included open CTR[13,14,26,27,31,60–62] and five studies included open and endoscopic CTR,[28,30,63–65] while two studies did not report the type of surgery.[29,59] The total time of the follow-up ranged from three months[13,26,27] after CTR to two years.[60] Table 1 is the descriptive summary of the included studies.

[TABLE 1 ABOUT HERE]

Methodological quality assessment

We assessed the risk of bias across six domains using the QUIPS tool for the included studies (Figure 2). A very high concordance between the reviewers in the quality assessment was observed (kappa = 0.875, $p < 0.05$). In general, the risk of bias in the included studies was low. We assessed thirteen studies (87%) as having a low overall risk of bias.[13,14,26–30,60–65] Figure 3 shows the summary of each 'Risk of bias' domain.

[FIGURE 2 ABOUT HERE]

[FIGURE 3 ABOUT HERE]

Narrative synthesis

Estimates of the association between prognostic factors and outcomes after CTR are shown in Table 1. Most of the predictors were associated with the symptom severity, function, pain, satisfaction or return to work after CTR, both in the bivariate and multivariate analysis.

Regarding the severity of symptoms, symptoms of depression were associated with higher severity of symptoms in 71% of the studies that considered this prognostic factor, followed by symptoms of anxiety (66%). Regarding the function, pain catastrophizing was associated with higher functional impairment in 100% of the studies that considered this prognostic factor, followed by symptoms of depression (57%) and symptoms of anxiety (0%). Regarding pain, symptoms of depression were associated with higher pain intensity in 100% of the studies that considered this prognostic factor, followed by symptoms of anxiety (0%). Regarding patient satisfaction, symptoms of depression were associated with higher satisfaction in 60% of the studies that considered this prognostic factor, followed by pain

catastrophizing (33%) and symptoms of anxiety (25%). Regarding return to work, lower pain catastrophizing was associated with early return to work in 100% of the studies that considered this prognostic factor, followed by symptoms of anxiety (100%) and symptoms of depression (33%). Table 2 summarizes the results and conclusions of the included studies.

[TABLE 2 ABOUT HERE]

Quantitative synthesis (Meta-analyses)

The meta-analyses included estimates of the predictive role of symptoms of depression on symptom severity, function, pain, and satisfaction. We decided not to pool data from studies evaluating symptoms of anxiety, self-efficacy, and pain catastrophizing. In all these variables, there were not enough articles to analyze their operationalizations separately.

Symptoms of depression and symptom severity

Four studies reported estimates of the depressive symptoms on symptom severity (n = 531). The overall result of the random effects model was r = 0.347 (95% CI = 0.205 to 0.475, p = <0.0001) (Figure 4). Heterogeneity between studies was substantial (I^2= 63.13%).

Symptoms of depression and function

Four studies reported estimates of the depressive symptoms on function (n = 386). The overall result of the random effects model was r = 0.307 (95% CI = 0.132 to 0.464, p = 0.0008) (Figure 5). Heterogeneity between studies was substantial (I^2= 65.51%).

Symptoms of depression and pain

Three studies reported estimates of the depressive symptoms on pain intensity (n = 344). The overall result of the random effects model was r = 0.431 (95% CI = 0.286 to 0.558, p = <0.0001) (Figure 6). Heterogeneity between studies was moderate (I^2= 51.29%).

Symptoms of depression and satisfaction

Three studies reported estimates of the depressive symptoms on satisfaction (n = 330). The overall result of the random effects model was r = 0.202 (95% CI = 0.096 to 0.305, p = 0.0002) (Figure 7). Heterogeneity between studies was extremely low (I^2= 0.01%).

[FIGURE 4 ABOUT HERE]

[FIGURE 5 ABOUT HERE]

[FIGURE 6 ABOUT HERE]

[FIGURE 7 ABOUT HERE]

Discussion

This systematic review and meta-analysis provides updated evidence on the association between cognitive and mental health factors with self-reported outcomes in patients with CTS who undergo surgery. The majority of studies indicate a significant association between the cognitive or mental health factors and the

outcomes following CTR. In general, the risk of bias in the included studies was low. Despite the heterogeneity of the available evidence, the results were consistent in the quantitative analysis regarding the impact of the symptoms of depression on symptom severity, function and pain following CTR, three months after surgery and beyond.

This evidence agrees with the other systematic reviews that emphasize the potential impact of the cognitive and mental health factors on post-surgical outcomes in individuals with chronic musculoskeletal pain.[66,67] For example, symptoms of depression and anxiety and pain catastrophizing can predict poor outcomes in patients undergoing shoulder surgery,[18,20] spine surgery,[21,22] and knee replacement.[23,24] Therefore, physicians, physical therapists, and occupational therapists should consider evaluating the cognitive and mental health factors in patients undergoing hand surgery.

An interesting finding is that most of the studies found that the level of the symptoms of depression was associated more with the severity of the symptoms and postoperative pain than with functional impairment. This seems relevant since the severity of the symptoms is the most important reason for the patients undergoing surgery.[68] Postoperative pain control is an essential goal in rehabilitation due to the possibility of reducing the costs associated with the use of opioids.[9] On the other hand, although a quantitative analysis was not possible, the symptoms of depression with self-efficacy showed a significant association with a late return to work. The early identification of patients at a greater risk of a delayed return-to-work could prevent a prolonged absence from work or sub-optimal performance at work.[69]

Strengths and limitations

This systematic review has several strengths. We used the current guidelines to develop the systematic review.[33,34] We conducted a comprehensive search of five databases and additional sources to identify the relevant studies. Rigorous narrative approaches and a meta-analysis were considered to synthesize the available evidence. Most of the included studies were of high methodological quality and carried out a long-term follow-up (3 to 24 months). In contrast, a limitation of this review was the lack of measurement of the cognitive and mental health factors that may influence the CTR outcomes beyond those identified in the available studies. This limited the possibility of performing a quantitative synthesis of the data (meta-analysis) for all of the prognostic factors considered (i.e., symptoms of anxiety, catastrophic thinking, and self-efficacy). In addition, we did not find any studies that evaluated some of the psychosocial factors that we included in our search strategy (i.e., fear avoidance or kinesiophobia). Although kinesiophobia, for example, has been shown to be an important predictor of upper-extremity-specific disability in patients with CTS,[70] its prognostic value in postoperative outcomes has not yet been considered, therefore future studies should evaluate this aspect. Another limitation was that we focused on evaluating the cognitive and mental health factors while we know that many variables can modulate the symptoms in patients with CTS. For example, education level, intrinsic risk factors such as obesity, age and gender, and occupational risk factors such as exposure to higher manual forces play a part.[32,71] In addition, peripheral nerve injury triggers changes in the central nervous system. These changes include central sensitization and changes in the cortical representation.[72] A comprehensive assessment that considers all of these aspects will allow clinicians to make more appropriate decisions and deliver greater benefits to their patients.

Directions for future studies

While some patients may experience an improvement in their depressive symptoms after CTR,[14,27] the effect of treating the depressive symptoms before surgery has been little studied. In other musculoskeletal pain conditions, it has been observed that depressed patients who received preoperative psychotherapy (e.g., cognitive-behavioral therapy) had fewer medical complications and resource utilization compared with those who did not receive psychotherapy.[73] In addition, perioperative psychotherapy has been shown to be effective at reducing the level of postoperative pain and functional impairment in orthopedic surgery patients.[74] Future studies should therefore evaluate the efficacy of similar interventions in patients with CTS undergoing surgery, incorporating the approach to other aspects that negatively influence depressive symptoms, such as sleep quality.[75]

On the other hand, it is not just about identifying those at risk of a poor outcome but also providing evidence to support that having more positive emotional and cognitive responses can benefit the patient and their outcomes. For example, expectations and resilience measures (e.g., optimism) have been shown to be strong predictors of postoperative functionality.[76] Therefore, implementing strategies early on that reinforce these more positive beliefs, attitudes, and behaviors could positively influence their current and future pain experience (e.g., educational program).[77] In addition, educating patients on the expectations and beliefs that they hold before surgery may help them to increase their participation in the shared decision-making process while setting realistic expectations regarding the postoperative outcomes.[31] Similarly, the efficacy of treatments following CTR should focus on more favorable outcomes such as quality of life.[78] Future studies should consider this point to reframe the conversation about how more positive cognitive and emotional

responses can lead to better rehabilitation outcomes. For this reason, addressing the patient's emotional state and coping strategies could be an essential treatment opportunity that results in the improvement of the health of patients undergoing CTR.

Conclusions

This systematic review and meta-analysis showed that symptoms of depression have a moderate association with symptom severity, function and pain after CTR. Symptoms of anxiety, catastrophic thinking, and self-efficacy are also important indicators of poor post-surgery outcomes and should be considered. Therefore, a preoperative evaluation of this variable could help to identify patients at risk for unfavorable surgical outcomes and provide timely treatment. As more is learned about the role of the cognitive and mental health factors and their potential impact on CTR, clinicians will be able to use these findings to approach patients more effectively.

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Legends

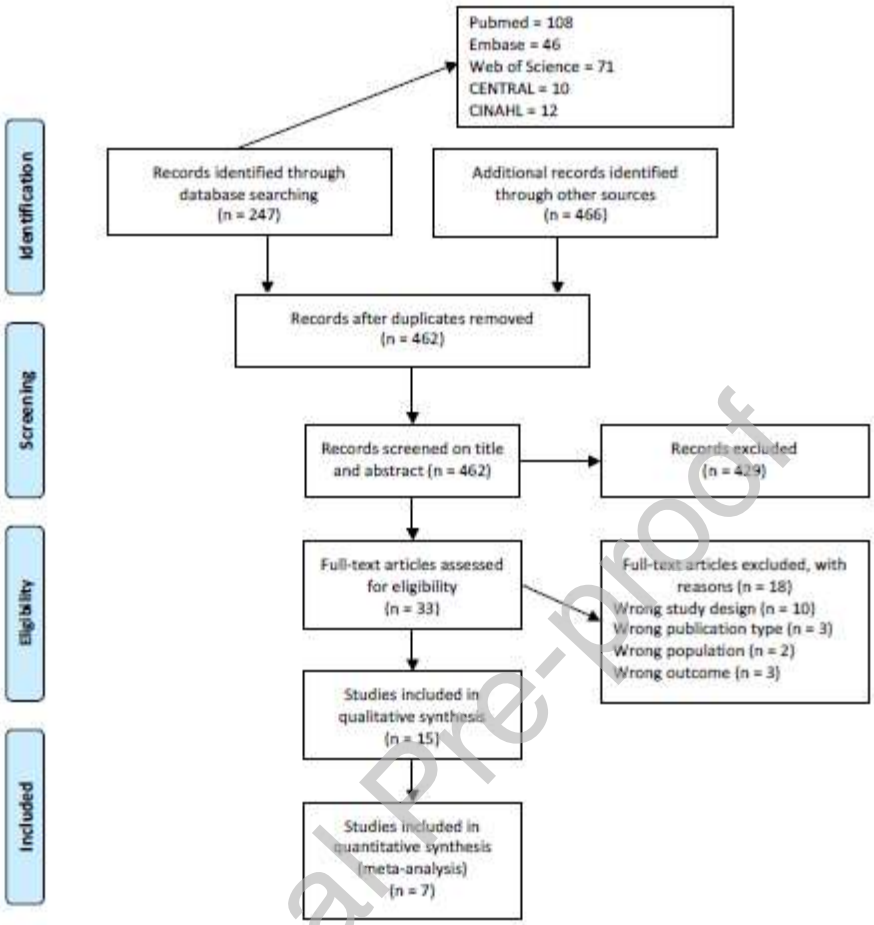

Figure 1. Study selection process.

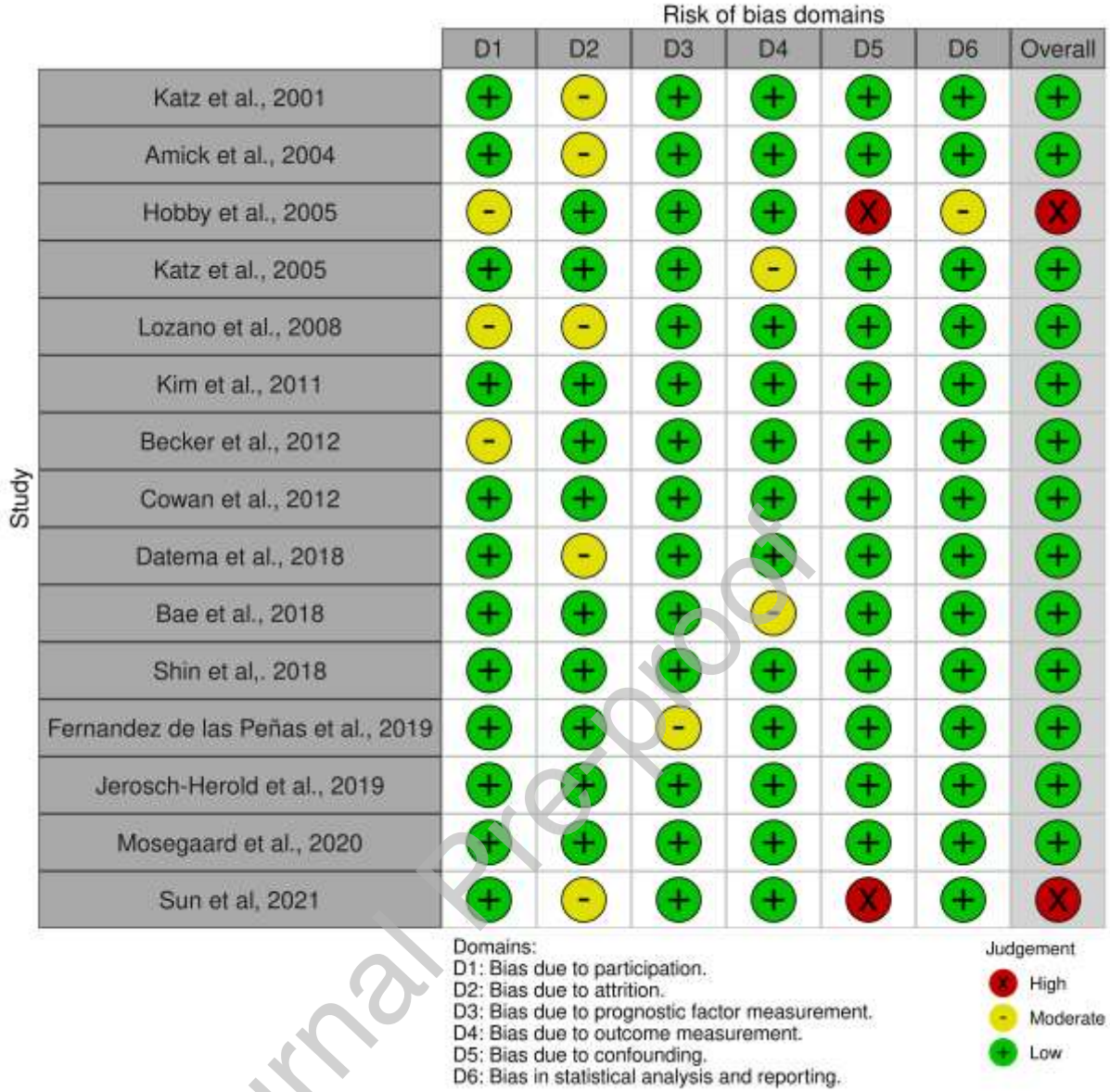

Figure 2. Summary of the risk of bias assessment using the QUIPS tool.

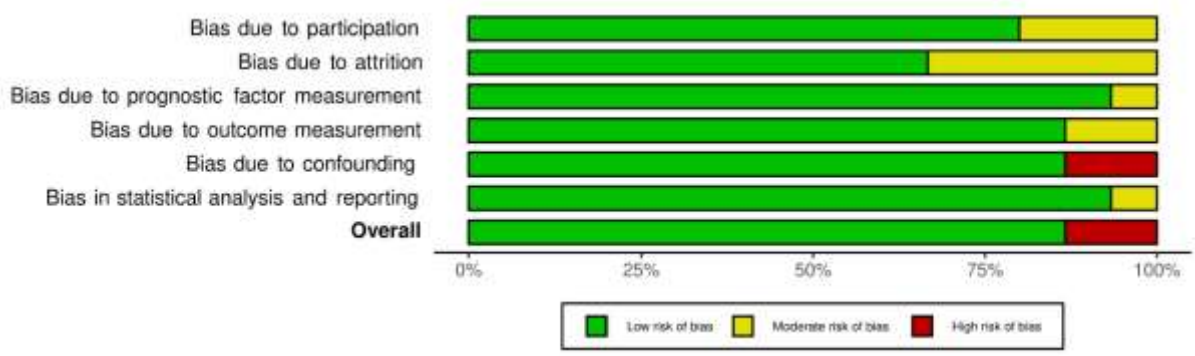

Figure 3. The proportion of included studies with low, high, or unclear risk of bias using the QUIPS tool.

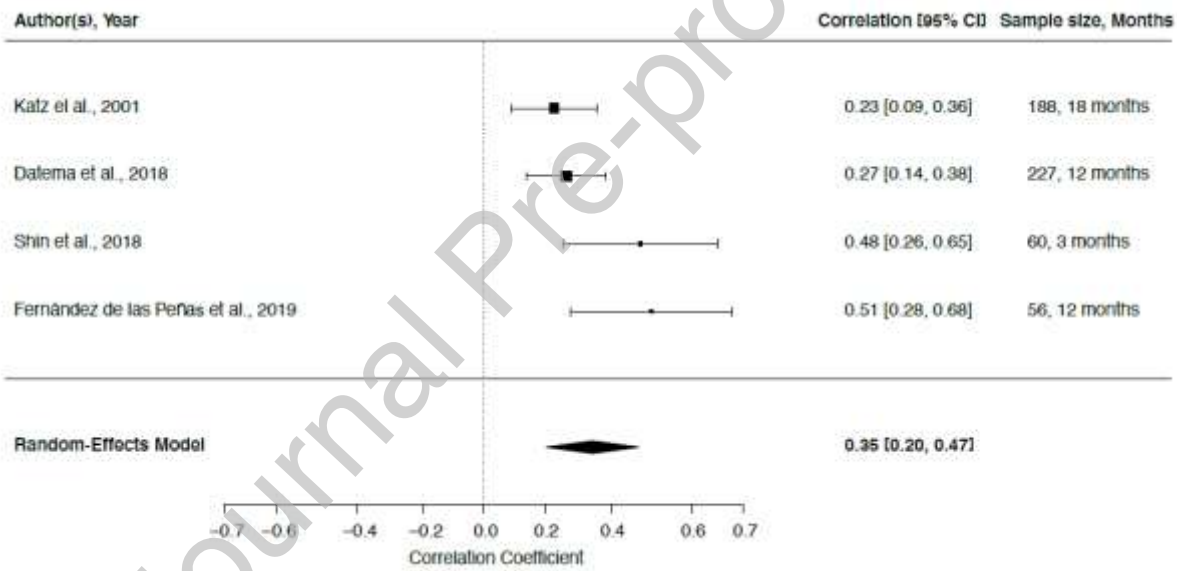

Figure 4. Forest plot of the relationship between symptoms of depression and symptom severity. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size as compared to other studies.

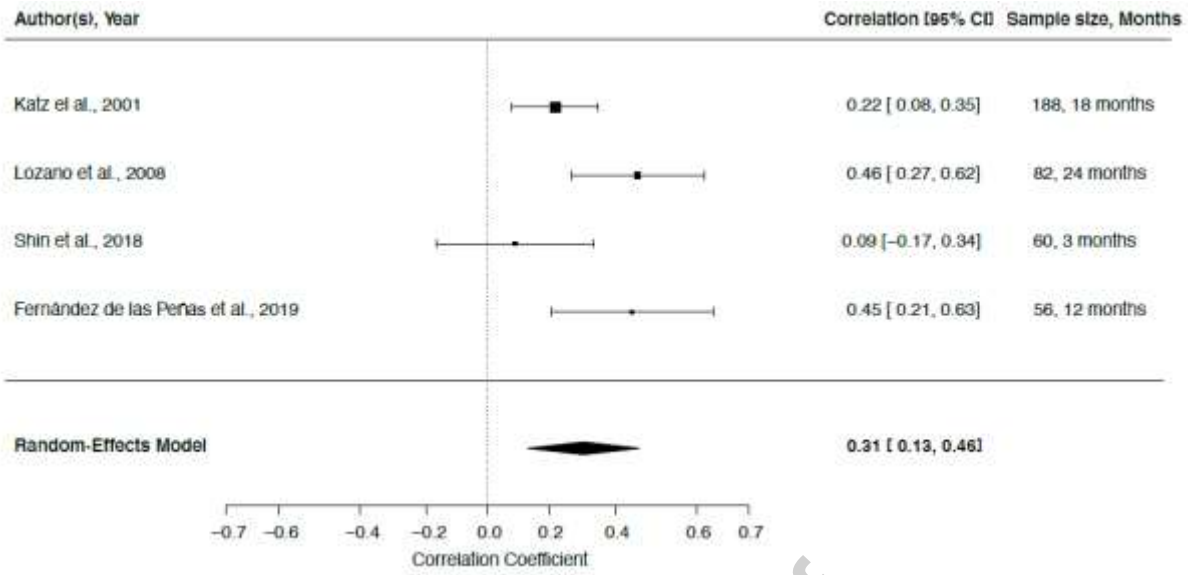

Figure 5. Forest plot of the relationship between symptoms of depression and function. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size as compared to other studies.

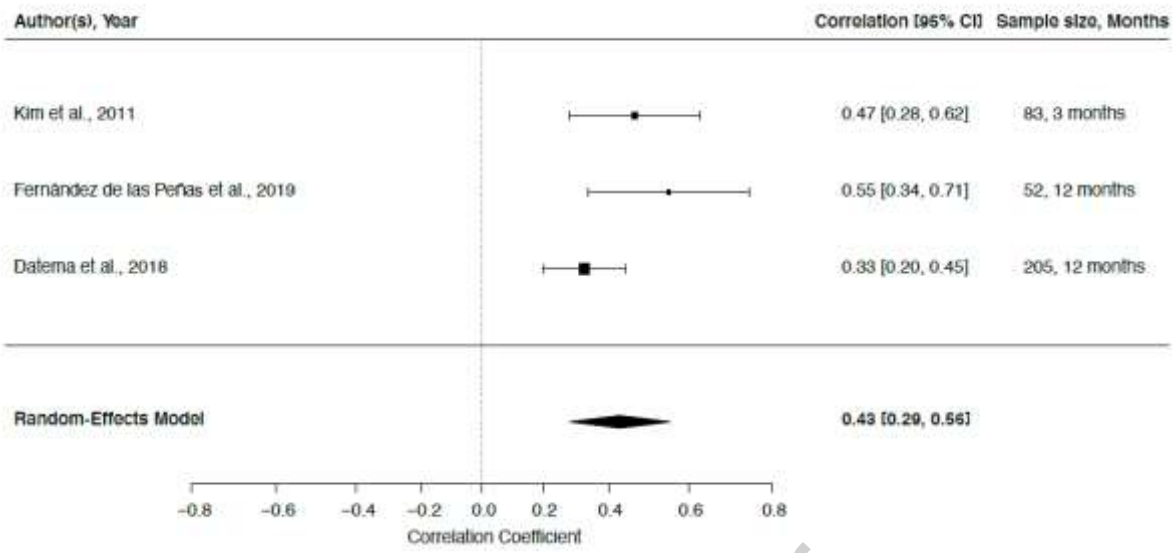

Figure 6. Forest plot of the relationship between symptoms of depression and pain. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size as compared to other studies.

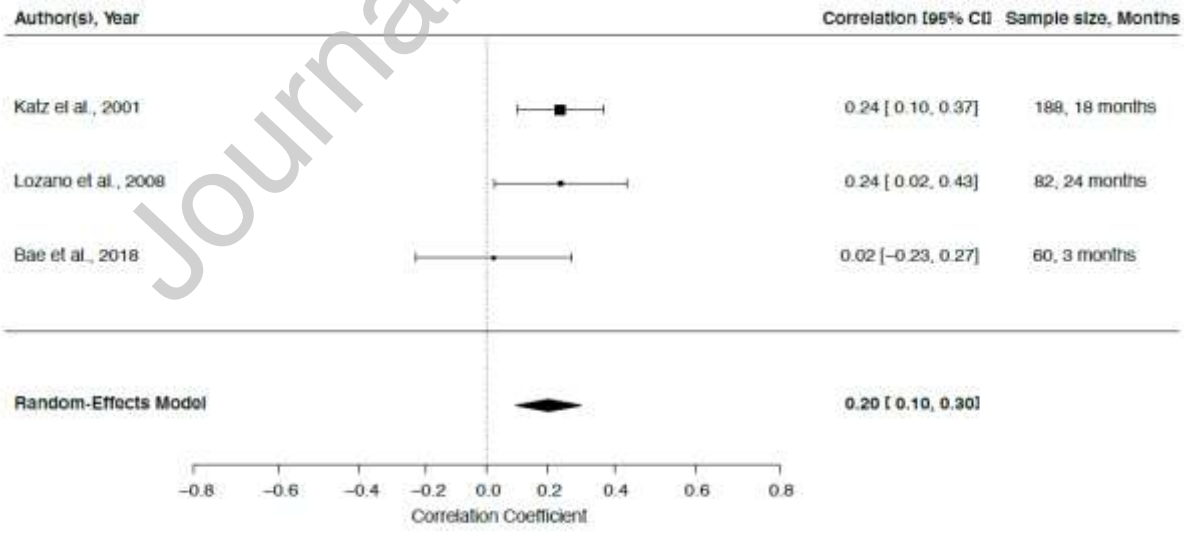

Figure 7. Forest plot of the relationship between symptoms of depression and dissatisfaction. Each study considered in the meta-analysis corresponds to a point estimate, which is bounded by a 95% CI. The polygon at the bottom of the plot

corresponds to the summary effect, and its width represents its 95% CI. Studies with larger squares have contributed more to the summary effect size as compared to other studies.

Table 1. Description of included articles.

Author, Year	Country	Design	N (M/F)	Age (years)	Type of surgery	Follow-up (N)	Prognostic Factor	Postoperative Outcomes	Significat Result of Univariate analysis	Significan Result of Multivariate analysis	Overall Risk of Bias (QUIPS)
Katz et al., 2001	USA	Prospective	241 (82/159)	44.6 ± 11.5	Open or endoscopic CTR	18 months (188)	MHI-5	BCTQ-S BCTQ-F Satisfaction	yes yes yes	yes yes yes	Low
Amick et al., 2004	USA	Prospective	197 (NR)	NR	Open or endoscopic CTR	6 months (122)	MHI-5 Self efficacy (4-item scale)	Return to work Return to work	yes yes	yes yes	Low
Hobby et al., 2005	UK	Prospective	97 (22/75)	53.4 (21 - 85)	NR	6 months (86)	HADS (depression) HADS (anxiety)	PEM BCTQ-S BCTQ-F Satisfaction PEM BCTQ-S BCTQ-F Satisfaction	no no no no no no no yes		High
Katz et al., 2005	USA	Prospective	181 (76/105)	45.7 ± 9.4	Open or endoscopic CTR	6 and12 months (158, 157)	MHI-5 Self efficacy (4-item scale)	Work status Work status	no, no yes. yes	no yes	Low
Lozano et al., 2008	USA	Retrospective	82 (29/53)	61 ± 12.8	Open CTR	2 years (82)	CES-D PASS PCS	DASH Satisfaction DASH Satisfaction DASH Satisfaction	yes yes no no yes yes	yes yes no no yes no	Low
Kim et al., 2011	South Korea	Prospective	83 (10/73)	54 ± 10.4	Open CTR	3 months (83)	CES-D PASS	Scar pain (ordinal scale) Scar pain (ordinal scale)	yes no	yes no	Low
Becker et al., 2012	USA	Prospective	66 (17/49)	50 ± 11	Open CTR.	6 ± 5 months (66)	CES-D PASS	DASH Satisfaction DASH	no no no	no no no	Low

							PCS	Satisfaction DASH Satisfaction	no no no	no yes no	
Cowan et al., 2012	USA	Prospective	66 (17/49)	49.7 ± 11.3	Open CTR	2 to 4 months (66)	CES-D PASS PCS	Return to work Return to work Return to work	no yes yes	no yes yes	Low
Datema et al., 2018	Netherlands	Prospective	227 (60/167)	58 (49-73)	Open CTR	12 months (227)	CES-D	BCTQ Palmar pain scale (0-9)	yes yes	no yes	Low
Bae et al., 2018	South Korea	Retrospective	60 (7/53)	55 (36-80)	Open CTR	3 months (60)	CES-D PASS	Satisfaction Satisfaction	yes no	yes no	Low
Shin et al., 2018	Republic of Korea	Prospective	60 (7/53)	55 (36-80)	Open CTR	3 months (60)	CES-D PASS	BCTQ-S BCTQ-F BCTQ-S BCTQ-F	yes no yes no	yes no yes no	Low
Fernandez de las Peñaz et al., 2019 Spain	Spain	RCT	60 (0/60)	46 ± 9	Open or endoscopic CTR	6 and 12 months (60,56)	BDI-II	Pain (0-10) BCTQ-S BCTQ-F		yes, yes yes, yes yes, yes	Low
Jerosch-Herold et al., 2019	UK	Prospective	455 (293/162)	62 ± 12	NR	18 months (455)	HADS (depression) HADS (anxiety)	CTS-6 GROC CTS-6 GROC	yes yes	no yes yes yes	Low
Mosegaard et al., 2020	Denmark	Prospective	417 (148/269)	58 (18–92)	Open or endoscopic CTR	12 months (417)	PCS	Satisfaction	yes	yes	Low
Sun et al., 2021	Netherlands	Prospective	307 (91/216)	56	Open CTR	6 months (307)	PHQ-4 PCS	BCTQ BCTQ	no yes	yes yes	High

Data are shown as Mean ± SD, Median (Inter-quartile range), n (%)

BCTQ-S(F): Boston Carpal Tunnel Questionnaire score-symptoms (function), **BDI-II:** Beck Depression Inventory, **BMI**: Body mass index, **CES-D:** Center of Epidemiologic Studies-Depression scale, **CI:** confidence interval, **CTS:** Carpal tunnel syndrome, **CTS-6:** 6-item shortened Boston Carpal Tunnel Questionnaire, **CTR**: carpal tunnel release, **DASH**: Disabilities of the Arm, Shoulder, and Hand, **F:** Female, **GROC**: global rating of change, **HADS**: Hospital anxiety and depression scale, **M**: Male, **MHI-5:** 5-item mental health index, **NR:** Not reported, **PASS**: Pain Anxiety Symptoms Scale, **PCS:** Pain Catastrophizing Scale, **PHQ4**: Patient Health Questionnaire-4, **PEM**: Patient evaluation measure, **RCT**: Randomized controlled trial.

Table 2. Summary findings

Author	Follow-up (N)	Results	Conclusion
Katz et al., 2001	18 months (188)	Worse mental health status (MHI-5) was significantly associated with more severe symptoms (r = -0.23, p <0.005), Functional limitation (r = -0.22, p <0.005) and lower satisfaction (r = -0.24, p <0.005).	Clinicians should carefully evaluate patients' functional status, mental health status, health habits, and attorney involvement prior to performing carpal tunnel release
Amick et al., 2004	6 months (122)	A greater likelihood of a transition to successful work role functioning was related to self efficacy improvement (X^2=26.24, P<0.001). Univariate Models (Self-efficacy): OR: 10.44, 95% CI: 4.17–26.17, p<0.001; Univariate Models (Depression): OR: 0.34, 95% CI: 0.17– 0.72, p=0.004. In logistic regression model, only improved self-efficacy postsurgery and a supportive work organization significantly predict successful work role functioning.	The significance of improved self-efficacy at 6 months and depression at 2 months postsurgery highlights the importance of psychosocial management of musculoskeletal disorders.
Hobby et al., 2005	6 months	There was no association between the pre-operative HADS and the mean score of PEM (depression: p = 0.2; anxiety: p = 0.58), BCTQ-S (depression: p = 0.9; anxiety: p = 0.79), and BCTQ-F (depression: p = 0.18; anxiety: p = 0.77). There was no difference in patient satisfaction between depressed and normal patients (1.93 vs 1.53, p = 0.63). Anxious patients were less satisfied than normal patients (2.05 vs 1.28, p = 0.005).	There was no significant difference in the outcome of CTR between normal and psychologically disturbed patients.
Katz et al., 2005	6 and12 months (158, 157)	Change in self-efficacy between baseline and 2 months was also strongly associated with work absence at 6 months (Same or better was 89% vs 11% in working vs not working respectively, p<0.001). In logistic regression model, having the same or worse self-efficacy was associated with work absence at 6 months (Adjusted OR: 4.4, 95% CI: 1.4 to 14).	The factors associated with work absence at 6 and 12 months after CTR included preoperative physical functional status, lower self-efficacy, workers' compensation, and less supportive organizational policies and practices.
Lozano et al., 2008	2 years (82)	Significant association between satisfaction and the CES-D score (r = -0.24, p < .05). Significant association between the DASH score and the CES-D (r = 0.46, p < .01) and PCS scores (r = 0.35, p < .01).	Dissatisfaction and perceived disability after CTR is predicted primarily by depression and ineffective coping skills and to a lesser degree by clinical or electrophysiologic evidence of advanced nerve damage.
Kim et al., 2011	3 months (83)	CES-D score (r = 0.47, p = .001) was significantly correlated with scar pain intensity. Stepwise multivariable linear regression analysis showed that CES-D score (β = 0.44; p < .001) and postoperative BCTQ-S (β = 0.38, p < .01) best predicted scar pain intensity.	Depression score and postoperative symptoms predicted scar pain intensity after open CTR. However, the most important contributor to scar pain intensity variance remains unidentified.
Becker et al., 2012	6 ± 5 months (66)	The PASS score was the only correlate of actual improvement of tingling after surgery (r = 0.33, p = .009). There was no significant association between the CES-D and PASS with satisfaction with surgery and DASH scores. The best regression model for lower postoperative DASH score included men, lower PCS and actual improvement of weakness (adjusted R2 0.32, P .001).	Actual relief of symptoms with CTR matched patients' expectations. Satisfaction with treatment correlated with relief of symptoms.
Cowan et al., 2012	2 to 4 months (66)	Earlier return to full work duty was associated with a lower PCS score (p = .028), and a lower PASS score (p = .005). CES-D was not associated with earlier return to full work duty (p = .380)	The most important determinant of return to full duty work CTR is job type, but psychological factors such as patient expectations, catastrophic thinking, and anxiety in response to pain also have a role.
Datema et	12 months	Patients with a depression had significantly less favorable	Depression is not an independent

al., 2018	(227)	outcomes compared to patients without depression: BCTQ: 1.1 (1.0-1.6) vs 1.4 (1.2-2.1), p < .05; and Palmar pain score = 0: 58.4% vs 27.3%, p < .05. Multivariable analyses showed that preoperative CES-D had a small but statistically significant influence on palmar pain (β = 0.075, p < .05), but not on postoperative BCTQ (β = 0.005, p =.44).	predictor of residual CTS symptoms 1 year after CTR. Patients with CTS and depression may expect a somewhat higher degree of palmar pain after CTR, the clinical relevance of which is small.
Bae et al., 2018	3 months (60)	Univariate analyses demonstrated significant correlations of patient satisfaction with preoperative CES-D: OR: 0.923, 95% CI:0.880–0.968, p = .001. Multivariate analyses showed that preoperative CES-D were significantly correlated with patient satisfaction. OR:0.938, 95% CI: 0.895–0.982, p = .007. Age adjusted: OR: 0.922, 95% CI: 0.877–0.969, p = .001	Age and depression level were preoperative predictors influencing satisfaction after CTR.
Shin et al., 2018	3 months (60)	Postoperative CES-D (r = 0.48; p < .05) and PASS (r = 0.27; p < .05) were significantly correlated with postoperative BCTQ-S. In a multivariable linear regression model, the CES-D (β = 6.679; 95% CI, 3.462-9.895; p < .05) and PASS (β = 6.300; 95% CI, 0.404-12.195; p < .05) were significantly associated with the postoperative BCTQ-S.	The depression level and pain anxiety of CTS patients are associated with the symptom severity of CTS in both the preoperative and the postoperative period.
Fernandez de las Peñaz et al., 2019 Spain	6 and 12 months (60,56)	Depressive symptoms (BDI-II) were significantly and negatively correlated with Pain Intensity, BCTQ-S and BCTQ-F at 6 and 12 months (all, p < .001). Higher depressive symptoms at baseline contributed to poorer outcomes post-intervention (from 5% to 15% of the variance).	Baseline localized pressure pain sensitivity and depression were predictive of long-term clinical outcomes in women with CTS following surgery,
Jerosch-Herold et al., 2019	18 months (455)	A general linear model identified that lower anxiety is associated with lower symptom severity in CTS-6 (β = −0.02, 95% CI: 0.01–0.04, p < .001).	Multivariable modeling identified, independent of symptom severity at outset, higher health utility, fewer comorbidities, and lower anxiety as significant predictors of better outcome from CTR.
Mosegaard et al., 2020	12 months (417)	The risk of low patient reported satisfaction for patients with preoperative PCS > 30 compared to patients with PCS ≤ 30 was: Unadjusted: OR = 2.24, 95% CI: 1.27–3.96, p = .005; Adjusted for demographics: OR = 2.56, 95% CI: 1.38–4.74, p = .003).	Higher preoperative PCS seems to have a negative effect on postoperative patient reported satisfaction after CTR.
Sun et al., 2021	6 months (307)	The association between BCTQ total score post surgery and baseline pain catastrophizing was statistically significant (B=0.008, 95% CI: 0–0.01). In Multivariable Linear Regression Model, only before adding illness perceptions and expectations to the model, pain catastrophizing was significantly associated with outcome.	The effects of pain catastrophizing on CTR outcome may be captured by the mindset about the efficacy of CTS and the mindset regarding CTS.

Data are shown as Mean±SD, Median (Inter-quartile range), n (%)
BCTQ-S(F): Boston Carpal Tunnel Questionnaire score-symptoms (function), **BDI-II:** Beck Depression Inventory, **BMI**: Body mass index, **CES-D:** Center of Epidemiologic Studies-Depression scale, **CI:** confidence interval, **CTS:** Carpal tunnel syndrome, **CTS-6:** 6-item shortened Boston Carpal Tunnel Questionnaire, **CTR**: carpal tunnel release, **DASH**: Disabilities of the Arm, Shoulder, and Hand, **F:** Female, **GROC**: global rating of change, **HADS**: Hospital anxiety and depression scale, **M**: Male, **NR:** Not reported, **PASS**: Pain Anxiety Symptoms Scale, **PCS:** Pain Catastrophizing Scale, **PEM**: Patient evaluation measure, **RCT**: Randomized controlled trial.