Scandinavian Journal of Pain 15 (2017) 44–52

Contents lists available at ScienceDirect

Scandinavian Journal of Pain

journal homepage: www.ScandinavianJournalPain.com

Systematic review

Are preoperative experimental pain assessments correlated with clinical pain outcomes after surgery? A systematic review

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HIGHLIGHTS

- Most studies included in this review showed moderate to high risk of bias.
- Most QST variables showed no consistent correlations with pain after surgery.
- Responses to pain above the pain threshold showed more consistent correlations.

ARTICLE INFO

Article history:
Received 2 November 2016
Received in revised form
30 November 2016
Accepted 4 December 2016
Available online 19 December 2016

Keywords:
QST
Experimental pain testing
Postoperative pain
Pain after surgery
Systematic review

ABSTRACT

Background: Pain after surgery is not uncommon with 30% of patients reporting moderate to severe postoperative pain. Early identification of patients prone to postoperative pain may be a step forward towards individualized pain medicine providing a basis for improved clinical management through treatment strategies targeting relevant pain mechanisms in each patient. Assessment of pain processing by quantitative sensory testing (QST) prior to surgery has been proposed as a method to identify patients at risk for postoperative pain, although results have been conflicting. Since the last systematic review, several studies investigating the association between postoperative pain and more dynamic measures of pain processing like temporal summation of pain and conditioned pain modulation have been conducted.
Objectives: According to the PRISMA guidelines, the aim of this systematic review was to evaluate whether assessment of experimental pain processing including measures of central pain mechanisms prior to surgery was associated with pain intensity after surgery.
Methods: Systematic database searches in PubMed and EMBASE with the following search components: QST, association, and postoperative pain, for studies that assessed the association between QST and pain after surgery were performed. Two authors independently reviewed all titles and abstracts to assess their relevance for inclusion. Studies were included if (1) QST was performed prior to surgery, (2) pain was assessed after surgery, and (3) the association between QST and pain after surgery was investigated. Forty-four unique studies were identified, with 30 studies on 2738 subjects meeting inclusion criteria. The methodological quality of the include studies was assessed and data extraction included study population, type of surgery, QST variables, clinical pain outcome measure and main result.
Results: Most studies showed moderate to high risk of bias. Type of surgery investigated include 7 studies on total knee replacement, 5 studies on caesarean section, 4 studies on thoracic surgery, 2 studies on herniotomy, 2 studies on hysterectomy/myomectomy, 1 study on tubal ligation, 1 study on gynecologic laparoscopy, 1 study on arthroscopic knee surgery, 1 study on shoulder surgery, 1 study on disc herniation surgery, 1 study on cholecystectomy, 1 study on percutaneous nephrolithotomy, 1 study on molar surgery, 1 study on abdominal surgery, and 1 study on total knee replacement and total hip replacement. The majority of the preoperative QST variables showed no consistent association with pain intensity after surgery. Thermal heat pain above the pain threshold and temporal summation of pressure pain were the QST variables, which showed the most consistent association with acute or chronic pain after surgery.

DOI of refers to article: http://dx.doi.org/10.1016/j.sjpain.2017.01.012.
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http://dx.doi.org/10.1016/j.sjpain.2016.12.002
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Conclusions: QST before surgery does not consistently predict pain after surgery. High quality studies investigating the presence of different QST variables in combination or along with other pain-related psychosocial factors are warranted to confirm the clinical relevance of QST prior to surgery.
Implications: Although preoperative QST does not show consistent results, future studies in this area should include assessment of central pain mechanisms like temporal summation of pressure pain, conditioned pain modulation, and responses to pain above the pain threshold since these variables show promising associations to pain after surgery.
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Contents

1. Introduction

Pain after surgery is not uncommon and 30% of patients experience moderate to severe postoperative pain [1,2]. High postoperative pain intensity has consistently been associated with an increasing risk of chronic pain [3–5], and 10–50% of patients with acute postoperative pain develop chronic pain [6]. Early identification of patients prone to severe postoperative pain may be a step forward towards individualized pain medicine providing a basis for improved clinical management of postoperative pain through improved preemptive analgesia strategies targeting relevant pain mechanisms in each patient or by reducing the number of surgeries causing more pain than relief.

Assessment of pain processing by quantitative sensory testing (QST) prior to surgery has been proposed as a method to identify patients at risk [7–10]. QST is a psychophysical method using standardized mechanical, electrical, and thermal stimuli to assess sensory and pain perception [11]. Several different aspects of perception can be assessed for each modality including detection threshold, pain threshold, pain intensity, and pain tolerance. Moreover, central pain processing in humans can reliably be assessed by measures of temporal summation of pain (TSP) [12] and conditioned pain modulation (CPM) [13].

The association between postoperative pain and pain processing assessed before surgery has previously been investigated by 3 systematic reviews [14–16] with the latest systematic review including 15 studies published in 2011 [14]. Although some QST variables showed some consistency with postoperative pain, the authors concluded that more research including other QST variables was required to establish whether a correlation between preoperative pain processing and postoperative pain truly does exist. Since the last systematic review, a series of studies investigating the association between postoperative pain and pain processing have been published and several studies have demonstrated an association between postoperative pain and measures of more central pain processing [9,17,18]. Preoperative assessment of temporal summation predicted postoperative chronic pain after total knee replacement surgery [9], and less efficient CPM assessed before surgery predicted chronic pain in patients after thoracotomy [7] and abdominal surgery [19].

Thus the primary aim of this systematic review was to investigate the association between postoperative pain and preoperative assessment of experimental pain processing including measures of central pain mechanisms. The findings and the implications for use of QST to identify patients at-risk for postoperative pain as well as the implications for future research in this area will be discussed.

2. Methods

According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [20], this systematic review investigated the association between preoperative pain processing and pain intensity after surgery.

2.1. Search strategy

In October 2016, we searched PubMed and EMBASE for original articles investigating the association between preoperative pain

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Table 1
Search strategy.

Components	Synonyms
QST	Quantitative sensory testing, heat pain sensitivity, heat detection threshold, heat pain threshold, heat pain tolerance, cold pain sensitivity, cold detection threshold, cold pain threshold, cold pain tolerance, pressure pain sensitivity, pressure pain threshold, pressure pain tolerance, electrical pain sensitivity, electrical pain threshold, electrical pain tolerance, CPM, conditioned pain modulation, temporal summation of pain, windup
Association	Associated, correlation, predictor, predict, predictive
Postoperative Pain	Pain after surgery, postsurgical pain, surgery [MeSH], pain after operation

processing and pain after surgery. A collaborate search strategy with the following search components: QST, association, and postoperative pain were used to increase the search sensitivity (Table 1). Moreover, reference lists from included studies and previous systematic reviews were screened by hand and experts within the field were consulted.

2.2. Inclusion and selection criteria

Two authors (A.S and C.S) independently reviewed all titles and abstracts to assess their relevance for inclusion. Studies were included if (1) QST was performed prior to surgery, (2) pain was assessed after surgery, and (3) the association between QST and pain after surgery was investigated. The full text articles were retrieved for studies fulfilling all 3 criteria, and duplicates were removed. The 2 authors then assessed all full texts for final inclusion. Disagreement was resolved by consensus or by consulting the third investigator (H.B.V).

2.3. Data extraction, assessment and analysis

From the included studies, bibliographic data such as authors, year of publication and journal were registered and the following data was extracted independently by 2 reviewers (A.S and C.S): study population, QST variables and assessment sites, time of QST, type of surgery, method and time for assessment of pain intensity, statistical methods, main findings, and effect sizes (Table 2). For estimation of effect sizes, the correlation coefficient was converted to the Fisher's z scale and Cohen's d was calculated [21]. Effects sizes were evaluated as small ($d = 0.20$), medium ($d = 0.50$), and large ($d = 0.80$). After individual data extraction, discussion and agreement was made. If disagreement still existed between the 2 reviewers, the third investigator (H.B.V) was consulted. The methodological quality of the included studies was assessed independently by 2 reviewers (A.S and C.S) using the criteria by Hayden et al., which assesses bias in studies of prognostic factors [22]. A checklist for each prognostic criteria was made, and the risk of bias were graded as low, moderate or high (Table 3). Given the substantial clinical heterogeneity in the individual studies, we decided that a meta-analysis would be inappropriate and instead focused on the narrative interpretation of the results.

3. Results

3.1. Studies included

The literature search identified 436 hits of which 30 studies on a total of 2738 subjects (1377 women and 1351 men) were included in this systematic review (Fig. 1 and Table 2). As illustrated in Table 2 the following surgeries were performed: 7 studies on total knee replacement, 5 studies on caesarean section, 4 studies on thoracic surgery, 2 studies on herniotomy, 2 studies on hysterectomy/myomectomy, 1 study on tubal ligation, 1 study on gynecologic laparoscopy, 1 study on arthroscopic knee surgery, 1 study on shoulder surgery, 1 study on disc herniation surgery, 1 study on cholecystectomy, 1 study on percutaneous nephrolithotomy, 1 study on molar surgery, 1 study on abdominal surgery, and 1 study on total knee replacement and total hip replacement. The timing of the preoperative sensory testing varied widely among the studies. Sensory testing was done on the day of surgery [19,23,24], 1–3 days before surgery [7,8,10,17–19,25–33], and 4 days to 4 weeks before surgery [34–39]. Time of preoperative QST was not mentioned in 7 studies [9,40–45]. Pain intensity after surgery was assessed with Visual Analogue Scale (VAS) or Numerical Rating Scale (NRS). Acute postoperative pain was assessed in 23 studies with an interval of assessment from immediately after surgery up to 30 days after surgery. Chronic postoperative pain was assessed in 11 studies with an interval of assessment from 3 to 18 months after surgery. Four studies assessed both acute and chronic pain.

3.2. QST variables

3.2.1. Thermal sensory testing

3.2.1.1. Warm detection threshold (WDT). Warm detection threshold was assessed in 3 studies (Table 2). None of the studies (tubal ligation [42], herniotomy [37], and molar surgery [24]) demonstrated a significant association with acute pain intensity after surgery.

3.2.1.2. Heat pain threshold (HPT). Heat pain threshold was assessed in 13 studies (Table 2). HPT was negatively associated with acute pain intensity after thoracic surgery [8], and caesarean section [34] suggesting that a lower threshold to heat pain prior to surgery was associated with higher acute pain intensity after surgery. Eleven studies (caesarean section [10,28], hysterectomy/myomectomy [41], tubal ligation [42], total knee replacement [29], knee arthroscopy [36], herniotomy [37], shoulder surgery [18], and molar surgery [24]) demonstrated no significant association between HPT and acute or chronic pain intensity.

3.2.1.3. Suprathreshold heat pain intensity (STHPI). Suprathreshold heat pain intensity was assessed in 12 studies (Table 2). STHPI was positively associated with acute pain intensity after thoracic surgery [8], caesarean section [10,28], total knee replacement [35], herniotomy [37], and molar surgery [24] indicating that a higher pain intensity to a supra-threshold heat stimuli prior to surgery was associated with higher acute pain intensity after surgery. Five studies (thoracic surgery [7], caesarean section [34], tubal ligation [42], total knee replacement [29], and shoulder surgery [18]) demonstrated no significant associations between STHPI and acute or chronic pain intensity.

3.2.1.4. Cold detection threshold (CDT). Cold detection threshold was assessed in 1 study prior to hysterectomy/myomectomy [41]. The study did not demonstrate a significant association between CDT and acute pain intensity.

3.2.1.5. Cold pain threshold (CPT). Cold pain threshold was assessed in 3 studies (Table 2). None of the studies (thoracic surgery [25], hysterectomy/myomectomy [41], and total knee replacement [29])

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Table 2
Correlations between QST and pain intensity after surgery. Age of the study population is presented as mean ± standard deviation or median (range). CDT, cold detection threshold; CPT, cold pain threshold; CPTol, cold pain tolerance; CPM, conditioned pain modulation; EDT, electrical detection threshold; EPT, electrical pain threshold; EPTol, electrical pain tolerance; HPT, heat pain threshold; PPT, pressure pain threshold; PPTol, pressure pain tolerance; STCPI, suprathreshold cold pain intensity; STHPI, suprathreshold heat pain intensity; STPPI, suprathreshold pressure pain intensity; TSP, temporal summation of pain; WDT, warm detection threshold; NA, data not presented in study; (U), univariate analysis; (M), multivariate analysis.

Reference	Study population Number (F/M) Age	Type of surgery	QST parameter	Clinical pain outcome (type and timing)	Statistical methods	Main findings (QST parameter associated with pain after surgery)	Effect size (Cohen's *d*)
Grosen et al. [17]	42 (0/42) 19 (17–23)	Thoracic surgery	PPT, CPM	NRS (acute and chronic)	Univariate analysis Multivariate regression model	No significant associations	–
Weissman-Fogel et al. [8]	84 (35/49) 62 ± 13	Thoracic surgery	HPT, STHPI, TSP (heat), PPT, STPPI, TSP (pressure)	NRS (acute)	Univariate analysis Multivariate regression model	HPT ($r = -0.24$) (U) STHPI ($r = 0.23$) (U) STPPI ($r = 0.25$) (M) TSP (pressure) ($r = 0.23$) (M)	0.50 0.48 0.53 0.48
Lautenbacher et al. [25]	54 (0/54) 19 ± 4	Thoracic surgery	CPT, HPT, TSP (heat), PPT	NRS (acute)	Multivariate regression model	No significant associations	–
Yarnitsky et al. [7]	62 (24/38) 62 ± 14	Thoracic surgery	HPT, STHPI, CPM	NRS (acute and chronic)	Univariate analysis Multivariate regression model	CPM and chronic pain ($r = -0.37$) (U)	0.84
Buhagiar et al. [26]	65 (65/0) 30 ± 5	Caesarean section	EPT, PPT, PPTol	NRS (acute)	Univariate analysis Multivariate regression model	EPT ($r = -0.26$) (U) PPTol ($r = -0.21$) (U)	0.55 0.44
Pan et al. [34]	34 (34/0) NA	Caesarean section	WDT, HPT, HPI	VAS (acute)	Univariate analysis Multivariate regression model	HPT ($r = -0.44$) (M)	1.07
Nielsen et al. [27]	39 (39/0) 35 (32–37)	Caesarean section	EDT, EPT	VAS (acute)	Univariate analysis	EPT ($r = -0.65$) (U)	2.46
Strulov et al. [28]	47 (47/0) 33 ± 5	Caesarean section	HPT, STHPI	VAS (acute)	Univariate analysis Multivariate regression model	STHPI ($r = 0.41$) (M)	0.97
Granot et al. [10]	58 (58/0) NA	Caesarean section	HPT, STHPI	VAS (acute)	Univariate analysis	STHPI ($r = 0.53$) (U)	1.46
Hsu et al. [23]	40 (40/0) 41 ± 6	Hysterectomy/ myomectomy	PPT, PPTol	VAS (acute)	Univariate analysis Multivariate regression model	PPTol ($r = -0.52$) (M)	1.41
Ahmad et al. [41]	120 (120/0) 42 (38–48)	Hysterectomy/ myomectomy	CDT, CPT, WDT, HPT	NRS (acute)	Univariate analysis	No significant associations	–
Rudin et al. [42]	59 (59/0) 38 (35–41)	Tubal ligation	WDT, HPT, STHPI	VAS (acute)	Univariate analysis Multivariate regression model	No significant associations	–
Jarrell et al. [43]	61 (61/0) 33 ± 5	Gynecologic laparoscopy	PPT, allodynia	NRS (chronic)	Multivariate regression model	Allodynia ($r = -0.32$) (M)	0.70
Martinez et al. [29]	20 (19/1) 69 ± 2	Total knee replacement	CPT, STCPI, HPT, STHPI, PPT	VAS (acute and chronic)	Univariate analysis	No significant associations	–
Petersen et al. [9]	78 (46/32) (47–86)	Total knee replacement	PPT, TSP (pressure), CPM	VAS (chronic)	Univariate analysis Multivariate regression model	TSP (pressure) ($r = 0.24$) (U)	0.50
Lunn et al. [35]	97 (50/47) 66 (60–73)	Total knee replacement	STHPI	VAS (acute)	Univariate analysis Multivariate regression model	STHPI ($r = 0.25$) (U)	0.53
Wylde et al. [40]	TKR: 239 (125/114) 69 ± 8 THR: 254 (149/105) 67 ± 10	Total knee replacement Total hip replacement	PPT	VAS (chronic)	Univariate analysis Multivariate regression model Univariate analysis Multivariate regression model	PPT ($r = -0.11$) (M)	0.22
Vaegter et al. [39]	14 (7/7) 66 ± 6	Total knee replacement	CPM	NRS (chronic)	Univariate analysis	CPM ($r = -0.57$) (U)	1.70
Thomazeau et al. [33]	109 (78/31) 69 ± 9	Total knee replacement	EPT	NRS (acute)	Univariate analysis Multivariate regression model	No significant association	–
Petersen et al. [45]	103 (66/27) 69 ± 2	Total knee replacement	PPT, PPTol, CPM, TSP (pressure)	VAS (chronic)	Univariate analysis Multivariate regression model	PPT ($r = -0.22$) (M) Patients with a combination of impaired CPM and facilitated TSP had less pain relief	0.46

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Table 2 (*Continued*)

Reference	Study population Number (F/M) Age	Type of surgery	QST parameter	Clinical pain outcome (type and timing)	Statistical methods	Main findings (QST parameter associated with pain after surgery)	Effect size (Cohen's *d*)
Lundblad et al. [30]	69 (35/34) 68 (40–80)	Total knee replacement	EDT, EPT	VAS (chronic)	Multivariate regression model	EDT ($r = -0.46$) (M) EPT ($r = -0.52$) (M)	1.15 1.41
Werner et al. [36]	20 (6/14)	Knee arthroscopy	HPT, PPT, STPPI	VAS (acute)	Univariate analysis	No significant associations	–
Aasvang et al. [38]	162 (0/162) 59 (21–85)	Herniotomy	EDT, EPT	NRS (acute)	Univariate analysis	No significant associations	–
Aasvang et al. [37]	442 (0/442) 55 ± 13	Herniotomy	WDT, HPT, STHPI	NRS (acute)	Univariate analysis	STHPI ($r = 0.26$) (U)	0.55
Valencia et al. [18]	73 (20/53) 45 ± 19	Shoulder surgery	HPT, STHPI, CPM	NRS (chronic)	Univariate analysis Multivariate regression model	No significant associations	–
Wilder-Smith et al. [44]	41 (10/31) (21–64)	Disc herniation surgery	EDT, EPT, EPTol	NRS (acute)	Univariate analysis	No significant associations	–
Bisgaard et al. [31]	150 (129/21) 41 (20–79)	Cholecystectomy	CPTol	VAS (acute)	Univariate analysis Multivariate regression model	CPTol ($r = -0.30$) (U)	0.65
Pedersen et al. [32]	44 (19/25) 56 (48–66)	Percutaneous nephrolitho-tomy	EPT, TSP (electrical), PPTol	NRS (acute)	Univariate analysis	No significant associations	–
Rudin et al. [24]	38 (23/15) 30 (25–38)	Molar surgery	WDT, HPT, STHPI	VAS (acute)	Multivariate regression model	STHPI ($r = 0.36$) (M)	0.81
Wilder-Smith et al. [19]	20 (13/7) 53 (47–59)	Abdominal surgery	EPTol, PPTol, CPM	VAS (acute and chronic)	Univariate analysis	CPM ($r = -0.68$) (U)	2.97

Table 3
Risk of bias assessment of the 30 studies included in this systematic review. The 6 factors assessed for bias were: Study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis [21].

Reference	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis
Grosen et al. [17]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk
Weissman-Fogel et al. [8]	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Lautenbacher et al. [25]	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk
Yarnitsky et al. [7]	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Buhagiar et al. [26]	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk	Low risk
Pan et al. [34]	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk	Low risk
Nielsen et al. [27]	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk	Low risk
Strulov et al. [28]	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Granot et al. [10]	High risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Hsu et al. [23]	Moderate risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ahmad et al. [41]	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk	Low risk
Rudin et al. [42]	Moderate risk	High risk	Moderate risk	Moderate risk	Moderate risk	Moderate risk
Jarrell et al. [43]	High risk	Moderate risk	Moderate risk	Moderate risk	High risk	Low risk
Martinez et al. [29]	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Petersen et al. [9]	Moderate risk	Low risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Lunn et al. [35]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk
Wylde et al. [40]	Low risk	Moderate risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Vaegter et al. [39]	Low risk	Low risk	Moderate risk	Low risk	Moderate risk	Low risk
Thomazeau et al. [33]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Petersen et al. [45]	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk	Low risk
Lundblad et al. [30]	Moderate risk	Moderate risk	Low risk	Moderate risk	Moderate risk	Low risk
Werner et al. [36]	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Aasvang et al. [38]	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk
Aasvang et al. [37]	Moderate risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk
Valencia et al. [18]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk
Wilder-Smith et al. [44]	Moderate risk	Moderate risk	Low risk	Low risk	Moderate risk	Low risk
Bisgaard et al. [31]	Moderate risk	Moderate risk	Low risk	Low risk	Moderate risk	Low risk
Pedersen et al. [32]	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk
Rudin et al. [24]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Wilder-Smith et al. [19]	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk

demonstrated significant associations between CPT and acute or chronic pain intensity.

3.2.1.6. Suprathreshold cold pain intensity (STCPI). Suprathreshold cold pain intensity was assessed in 1 study prior to total knee replacement surgery [29]. No significant association between STCPI and acute or chronic pain intensity were found.

3.2.1.7. Cold pain tolerance (CPTol). Cold pain tolerance was assessed in 1 study prior to cholecystectomy [31]. A significant negative association with acute pain intensity was found, indicating

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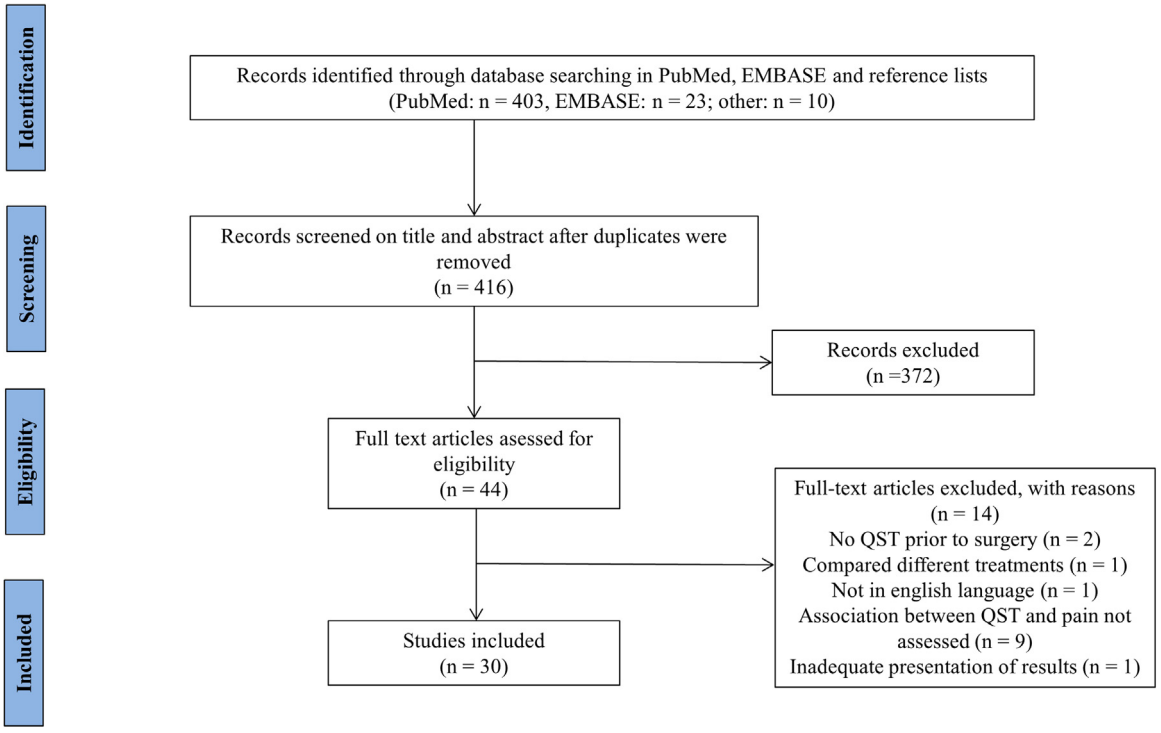

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) flow diagram.

that a lower pain tolerance to cold stimuli prior to surgery was associated with higher acute pain intensity after surgery.

3.2.2. Electrical sensory testing

3.2.2.1. Electrical detection threshold (EDT). Electrical detection threshold was assessed in 4 studies (Table 2). EDT was negatively associated with chronic pain intensity after total knee replacement [30], indicating that a lower electrical detection threshold prior to surgery was associated with higher chronic pain intensity. Studies on caesarean section [27], herniotomy [38] and disc herniation surgery [44] demonstrated no significant associations between EDT and acute pain intensity.

3.2.2.2. Electrical pain threshold (EPT). Electrical pain threshold was assessed in 7 studies (Table 2). Two studies on caesarean section [26,27], and 1 study on total knee replacement [30] demonstrated significant negative associations with acute pain intensity and chronic pain intensity respectively, indicating that a lower pain threshold to electrical stimuli prior to surgery was associated with higher pain intensity after surgery. Four studies (herniotomy [38], disc herniation surgery [44], total knee replacement [33], and percutaneous nephrolithotomy [32]) demonstrated no significant associations between EPT and acute pain intensity.

3.2.2.3. Electrical pain tolerance (EPTol). Electrical pain tolerance was assessed in 2 studies (Table 2). No significant associations were found between EPTol and acute or chronic pain intensity after disc herniation surgery [44] or abdominal surgery [19].

3.2.3. Mechanical sensory testing

3.2.3.1. Pressure pain threshold (PPT). Pressure pain threshold was assessed in 11 studies (Table 2). Significant negative associations between PPT and acute pain intensity after total knee and total hip replacement surgery [40], and between PPT assessed with cuff algometry and pain relief 12 months after total knee replacement surgery [45] were found indicating that a lower pain threshold to pressure prior to surgery was associated with higher acute pain intensity after surgery and less pain relief 12 months after. Nine studies (thoracic surgery [17], caesarean section [26], hysterectomy [23], gynecologic laparoscopy [43], arthroscopic knee surgery [36], and total knee replacement [29]) demonstrated no associations between PPT and acute or chronic pain intensity.

3.2.3.2. Suprathreshold pressure pain intensity (STPPI). Suprathreshold pressure pain intensity was assessed in 2 studies (Table 2). No significant associations were found between STPPI and acute pain intensity after knee arthroscopy [36] or thoracic surgery [8].

3.2.3.3. Pressure pain tolerance (PPTol). Pressure pain tolerance was assessed in 5 studies (Table 2). Significant negative associations with acute pain intensity after caesarean section [26] and hysterectomy/myomectomy surgery [41] were demonstrated suggesting that a lower pain tolerance to pressure prior to surgery was associated with higher pain intensity after surgery. Three studies (percutaneous nephrolithotomy [32], total knee replacement [45], and abdominal surgery [19]) demonstrated no significant associations between PPTol and acute or chronic pain intensity.

3.2.4. Temporal summation of pain (TSP)

Temporal summation of pain was assessed in 5 studies (Table 2). Three studies assessed temporal summation of pressure pain (procedure: NRS scores during 10 repeated Von Frey Filaments 225.1-g stimulations, between stimulation intervals unknown) [8], (procedure: NRS scores during 10 repeated Von Frey Filaments 25.6 g, 1 s between stimulation intervals) [9], (procedure: Electronic VAS scores during 10 repeated computer controlled cuff stimulations with an intensity at the average of the cuff pressure pain threshold and tolerance, 1 s stimulations and 1 s between stimulation intervals) [45], 1 study assessed temporal summation to electrical pain (procedure: NRS scores during 5 repeated stimuli (each stimulus was a train of 5 pulses at 200 Hz) at 2 Hz) [32], and 1 study assessed

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temporal summation to heat pain (procedure: NRS scores during 15 repeated heat stimuli at pain-60 level, 0.7 s stimulations and 2 s between stimulation intervals) [8]. Temporal summation of pressure pain was negatively associated with acute and chronic pain intensity after thoracic surgery [8], and chronic pain after total knee replacement [9] respectively, indicating that higher degree of temporal summation of mechanical pain prior to surgery is associated with higher pain intensity after surgery. Temporal summation to electrical [32] and heat pain [8] respectively, were not associated with acute pain intensity after percutaneous nephrolithotomy and thoracic surgery.

3.2.5. Conditioned pain modulation (CPM)

Conditioned pain modulation was assessed in 7 studies (Table 2). Five studies used the cold pressor test (procedure: PPT at the knee assessed before and after hand immersion in 2 °C water, maximum duration 2 min) [9], (procedure: PPT at the thigh assessed before and after hand immersion in 1 °C water, maximum duration 2 min) [17], (procedure: suprathreshold heat pain intensity at the thenar eminence assessed before and 1 min after hand immersion in 8 °C water, maximum duration 1 min) [18], (procedure: electrical pain threshold and tolerance at the leg assessed before and within 1 min after hand immersion in 1 °C water, maximum duration 3 min) [19], (procedure: PPT at the legs, arm and shoulder assessed before and during hand immersion (after 1 min) in 2 °C water) [39], 1 study used cuff algometry (procedure: cuff pressure pain threshold at the lower leg assessed before and during tonic painful cuff pressure on the opposite leg, intensity 30–60 kPa) [45], and 1 study used hot water (procedure: suprathreshold heat pain intensity at the forearm assessed before and during (after 30 s) hand immersion in 46.5 °C water) [7] as the conditioning stimulus. Significant negative associations between CPM and acute and chronic pain intensity after abdominal surgery [19], thoracic surgery [7], and total knee replacement [39] were demonstrated, suggesting that less efficient CPM preoperatively is associated with higher pain intensity after surgery. Four studies (total knee replacement [9,45], shoulder surgery [18], and thoracic surgery [17]) demonstrated no significant associations between CPM and acute or chronic pain intensity.

3.2.6. Cutaneous allodynia

Cutaneous allodynia was assessed in 1 study (Table 2). Allodynia (dynamic test with cotton-tipped applicator on the anterior abdominal wall) prior to gynecologic laparoscopy [43] was associated with higher pain intensity after surgery.

3.3. Quality assessment

Quality assessments of the included studies are presented in Table 3. The reviewers (A.S and C.S) initially agreed on 83% of the ratings. Consensus was reached on all items following discussion.

4. Discussion

This systematic review identified 15 new studies since the last systematic review conducted in 2011 [14]. Nineteen studies demonstrated an association between a preoperative QST variable and pain after surgery, however; no consistent association between any preoperative QST and postoperative pain intensity was found. An important finding in this systematic review was that the response to thermal pain above the pain thresholds as well as the QST variables related with central pain mechanisms like temporal summation of pain, and conditioned pain modulation more frequently demonstrated an association with pain intensity after surgery compared to the QST variables more related to the detection and pain thresholds. The association between the QST variables of central pain mechanisms and post-operative pain has not previously been included in systematic reviews across different surgeries. In agreement with previous systematic reviews [14,16,46], this systematic review indicates that detection thresholds for electrical and thermal stimuli as well as thermal pain thresholds are poor predictors of pain intensity after surgery.

4.1. Associations between QST variables and postoperative pain

Univariate analysis demonstrated a significant association between suprathreshold heat pain intensity (STHPI) and acute pain intensity after surgery; however, when multivariate analyses were performed most studies did not demonstrate significant associations [8,24,35] suggesting that when other potentially predictive factors are taken into consideration, no significant association between STHPI and pain intensity after surgery was demonstrated. A previous systematic review noted that the association between STHPI and pain after surgery were observed mainly in the studies on healthy female patients undergoing elective caesarean section or gynecologic procedures [14]. Since then 4 new studies with only males or mixed gender populations have been conducted on total knee replacement [35], herniotomy [37], shoulder surgery [18], and molar surgery [24]. Three of these studies demonstrated significant associations between STHPI and acute postoperative pain intensity, indicating that the association is also present in males. However, none of the recent published studies on mixed populations investigated whether potential associations were influenced by gender.

Pressure pain threshold (PPT) demonstrated significant negative associations between PPT and acute pain intensity in total knee replacement and between chronic pain intensity in total hip replacement when univariate analyses were performed, and for knee replacement when multivariate analyses were performed. Interestingly, a significant association between PPT and pain intensity after musculoskeletal surgery was found [40,45], but no significant associations were demonstrated for visceral surgeries [8,17,23,25,26,43] indicating that PPT may be valuable in predicting postoperative pain after surgery on the deeper musculoskeletal structures but not on the visceral structures.

Temporal summation of pain (TSP) was assessed in 5 studies. Univariate and multivariate analysis demonstrated significant associations between TSP and acute pain intensity [8], and chronic pain intensity [8,9]. All these studies used temporal summation to pressure pain suggesting that temporal summation to pressure pain may be a promising predictor of pain after surgery.

Conditioned pain modulation (CPM) demonstrated significant associations between CPM and acute and chronic pain intensity after thoracic surgery [7] and abdominal surgery [19], as well as between CPM and pain relief 6 months after total knee replacement [39]. However, no significant associations after shoulder surgery [18] or 12 months after total knee replacement [9,45] were found, suggesting that CPM is associated with the pain intensity after surgery on visceral structures, but not consistently after surgery on musculoskeletal structures. However, a recent study demonstrated that patients with knee osteoarthritis who demonstrated reduced CPM and facilitated temporal summation of pain prior to total knee replacement surgery had less pain relief 12 months after surgery [45] suggesting that different QST variables in combination may have relevance when determining which patients are at risk.

4.2. Quality assessment

Seven of the 30 included studies [17,18,23,24,32,33,35] showed low risk of bias. Among these, only 3 studies demonstrated significant association between QST and pain after surgery in univariate analyses [23,24,35], and only 1 after multivariate analysis [23],

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which indicate that studies with greater risk of bias tend to demonstrate significant associations, whereas studies with lower risk of bias do not. The 4 main areas for bias in the studies were study participation, study attrition, outcome measurement, and confounding measurement. In study participation inadequate description of the sampling frame, period, and place of recruitment were the main reasons for bias. Bias in study attrition was mainly due to the lack of description of patients lost at follow up. Uncertainty whether researcher was blinded to the results of preoperative testing, was another source of bias. Description of the possible confounding factors was not appropriately accounted for in most studies and multivariate analyses were not performed in the majority of the included studies.

4.3. Implications

The results from this systematic review do not consistently support the use of QST before surgery to identify patients at risk for acute of chronic pain after surgery. Although preoperative QST does not show consistent results, future studies in this area should include assessment of central pain mechanisms like temporal summation of pressure pain, conditioned pain modulation, and responses to pain above the pain threshold since these variables show promising associations to pain after surgery. In addition, 1 QST variable may not be adequate for identifying patients at risk, and a combination of different QST variables, e.g. patients with both facilitated temporal summation of pain and impaired conditioned pain modulation should be further investigated. Furthermore, multivariate analysis including other potential non-QST risk factors for pain after surgery, such as preoperative pain intensity, anxiety, age, and type of surgery should be included [16]. Finally, the body area for QST assessment needs further consideration as some studies assessed QST in painful body areas and others in non-painful body areas. Limitations to this systematic review include search strategies limited to 2 databases, and the lack of quantification of effects through meta-analysis.

5. Conclusion

This systematic review demonstrates that although the association between QST and pain after surgery has been studied extensively no consistent association between variables and pain after surgery exists. The response to thermal pain above the pain thresholds as well as the QST variables related with central pain mechanisms like temporal summation of pain, and conditioned pain modulation more frequently demonstrated an association with pain intensity after surgery compared to the QST variables more related to the detection and pain thresholds.

Ethical issues

Ethic Board approval was not required for this systematic review.

Conflict of interest

There are no actual or potential conflicts of interest for any of the authors.

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