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10-1-2016

# Evaluation and Management of Sleep Disorders in the Hand Surgery Patient.

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Gaspar, Michael P.; Kane, Patrick M.; Jacoby, Sidney M.; Gaspar, Patrick S.; and Osterman, A. Lee, "Evaluation and Management of Sleep Disorders in the Hand Surgery Patient." (2016). *Department of Orthopaedic Surgery Faculty Papers*. Paper 93. https://jdc.jefferson.edu/orthofp/93

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1	Title:
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3	
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5	Sleep Disorders in Hand Surgery
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45	Key Words:
46	Insomnia; Sleep Disorders; Hand Surgery; Carpal tunnel syndrome; Obstructive Sleep Apnea
47	

#### 48 Abstract

- 49 Despite posing a significant public health threat, sleep disorders remain poorly understood
- 50 and often mismanaged. Though seemingly unrelated, hand surgeons should be particularly
- 51 mindful of sleep disorders, as numerous conditions of the upper extremity have known
- 52 associations with sleep disturbances which can adversely affect patient outcomes, function
- 53 and satisfaction. In addition, patients with sleep disorders are at significantly higher risk
- 54 for severe, even life-threatening medical co-morbidities, further supporting the important
- <sup>55</sup> role of hand surgeons in the recognition and management of sleep disorders that are most
- 56 common in hand surgery.

#### 58 Introduction

- 59 Sleep disorders are a major public health concern, affecting as many as 70 million adults in
- 60 the United States alone, while accounting for billions of dollars in financial costs, disability,
- and even death. [1-5] Sleep disorders are also associated with a myriad of medical
- 62 conditions including obesity, hypertension, diabetes heart disease, and overall higher
- 63 mortality risk. [6]
- 64
- 65 Unfortunately, despite these exorbitant socioeconomic and health costs, sleep disorders are
- often overlooked or improperly treated. [7,8] In hand surgery, numerous conditions have
- 67 known associations with sleep disorders, and sleep symptoms can directly affect patient
- outcomes, function and satisfaction. Thus, these disorders are important for hand surgeons
- 69 to recognize and manage. The purpose of this review is to provide an overview of sleep
- 70 disorders that are most common in hand surgery, with focus on the preoperative
- 71 evaluation, and perioperative management of these disorders.
- 72
- 73

## 74 Sleep Disorders in Hand Surgery

- 75 This discussion will focus primarily on two classes of disorders most relevant to hand
- surgery: (1) dyssomnias which are disorders that produce excessive sleepiness or difficulty
- in initiating or maintaining sleep and (2) sleep disorders associated with other medical
- disorders. [9] A more inclusive outline of general sleep disorders is presented in Figure 1.
- 79

### 80 Intrinsic Dyssomnias

- 81 Intrinsic dyssomnias either (a) originate or develop within the body, or (b) arise
- 82 from causes within the body. [9] This group includes psychological or medical disorders
- 83 that *produce* a primary sleep disorder.
- 84

## 85 Obstructive Sleep Apnea

- 86 Perhaps the most widely recognized intrinsic dyssomnia in surgical patients is obstructive
- 87 sleep apnea (OSA). Patients with OSA who are to undergo surgery require specialized
- 88 management, as these patients are at higher risk for adverse events in the intraoperative

89 and postoperative periods. In the perioperative setting, the primary concern is airway

- 90 management; due to OSA patients' decreased ability to protect their airway, procedures
- 91 that would otherwise be performed under sedation may require monitored anesthesia care
- 92 (MAC) or even general anesthesia for. [10,11] Ideally, open communication between the
- anesthesiologist and the hand surgeon allows these determinations to be made prior to the
- 94 day of surgery, so as to minimize delays or complications.
- 95

In addition to patients with a known diagnosis of OSA, surgeons are often tasked with 96 97 caring for patients who lack a formal diagnosis, despite exhibiting clinical risk factors for 98 OSA. [12] Chung et al reported an alarming 66% of patients lacking a preoperative OSA 99 diagnosis with difficult intubations were confirmed to have OSA upon further evaluation. 100 [13] Mutter et al found that those patients with undiagnosed OSA were at significantly 101 higher risk of postoperative cardiac arrest than confirmed OSA patients, and that both 102 groups faired worse than non-OSA patients, [14] These studies together point out the 103 importance for the hand surgeon to recognize and screen for OSA, which can be done 104 utilizing validated OSA screening methods, such as the STOP-Bang questionnaire (Table 1). 105 Surgeons should also have a low threshold for referring patients with positive findings on 106 OSA screening for further evaluation. [13,15] Postoperative management of OSA patients is 107 also critical in avoiding morbidity, and OSA patients should resume continuous- or bilevel 108 positive-airway-pressure (CPAP or BiPAP) treatment as soon as they are able. [15] 109 Postoperative pain control regimens in OSA patients also merit special attention, which will 110 be discussed shortly.

111

## 112 Extrinsic Dyssomnias

113 Extrinsic dyssomnias are those that originate or develop from causes outside of the body.

- 114 [9] External factors are necessary to produce these disorders, and their removal is often
- 115 therapeutic to the sleep disturbance. [9] In hand surgery, these most notably include both
- 116 drug-induced and drug-dependant sleep disorders.
- 117

#### 118 Opioid-Induced Sleep Disorders

119 A true understanding of the complex interplay of pain, opioid medication, and sleep

- 120 disturbance remains elusive. Although evidence shows that pain and sleep exhibit a
- 121 circular relationship with one another (i.e. pain causes sleep disturbance and sleep
- disturbance intensifies pain), [16-19] opioids used to concomitantly treat both pain and
- secondary sleep disorders are not always successful. [20,21]
- 124
- 125 Opioid receptors in the brain are located in the same nuclei that are active in sleep 126 regulation and abnormal sleep architecture has been reported as a characteristic feature of 127 opioid use, with a reduction of rapid eve movement (REM), slow wave sleep stages, and 128 overall sleep quality. [18,20,22] Opioid use in OSA patients can be particularly 129 troublesome, as opioids not only impair arousal, but can worsen airway obstruction, even 130 in non-OSA patients. [21,23,24] Thus, alternative multimodal pain management 131 approaches are recommended to minimize the need for opioids for OSA patients. These 132 include: regional or local anesthesia when appropriate, continuous peripheral nerve 133 blockade, and non-opioid analgesics such as acetaminophen and NSAIDS. [15,23,25-27] 134 Recent evidence also supports use of low-dose ketamine or adjuvant clonidine injections 135 to potentiate local or regional nerve blocks. [23,28,29] Finally, conservative measures 136 aimed at decreasing postoperative pain and inflammation such as icing, elevation, and 137 compression should be emphasized, especially upon discharge home.
- 138
- 139 Sedative-Dependent Sleep Disorders

140 The use of short-acting sedative-hypnotics, particularly non-benzodiazepine sedative

141 hypnotics (NBSH, e.g. zolpidem), for treatment of insomnia has increased markedly in

- 142 recent decades. [30] Generally intended to treat short-term insomnia, NBSH
- 143 discontinuation may precipitate rebound insomnia, lasting up to weeks in extreme cases, or

144 after taking a single dose. [31-33] Thus, the dependency potential is relatively high. [34-36]

- 145 Use of zolpidem as a postoperative sleep aid or pain-adjuvant has recently been described
- 146 following knee and shoulder surgery with reported success in improving sleep quality and
- 147 function, while decreasing opioid requirements, pain and fatigue. [37-39] However, none of
- 148 these studies reported patient outcomes beyond the acute treatment period. [37-39] Its

- similar utility in hand surgery has not been reported. Perhaps surprisingly, antihistamines
- 150 used as sleep aids may warrant similar caution. [41] A recent survey of patients who took
- 151 the commonly-used sedative H1 antihistamine doxylamine found the majority of patients
- used the medication daily for at least six months, including 77% who experienced rebound
- insomnia when attempting to discontinue use. [41] These findings suggest that sedative
- 154 hypnotics and antihistamines should be used with judiciously in hand surgery patients
- 155 with sleep disorders.
- 156

## 157 Sleep Disorders Associated with Mental, Neurologic, or Other Medical Disorders

158 This second category includes a variety primary medical disorders that *secondarily* involve

159 sleep disturbance or excessive sleepiness as a major clinical feature, [9] including several

- 160 hand and upper extremity conditions.
- 161

## 162 Carpal Tunnel Syndrome

163 Insomnia is a nearly universal finding in patients with carpal tunnel syndrome (CTS), often 164 serving as the primary motivating factor for seeking surgical care. [42-48] Although the mechanism linking these two conditions is unclear, McCabe and colleagues reported that 165 166 patients with CTS are more likely to prefer sleeping on their side compared to control 167 patients. [42-44] The authors acknowledge, however, that these associative findings do not 168 necessary prove causation. In an effort to further characterize the severity of sleep 169 disturbance in CTS patients. Patel et al prospectively studied patients with CTS and found 170 that 78% of patients met the threshold for poor sleep quality using the Pittsburgh Sleep 171 Quality Index (PSQI), a validated sleep-quality outcome measure. [46,49,50] The authors 172 also noted a positive correlation between CTS-related functional impairment and severity 173 of sleep symptoms. [46] The authors did not study the potential association of preoperative 174 electrodiagnostic findings with sleep symptom severity, nor did they investigate the 175 potential therapeutic effect of median nerve decompression on sleep symptoms. Both of 176 these associations may warrant further study, as the ability to predict relief of sleep 177 symptoms following decompressive surgery would allow clinicians to better tailor 178 management for CTS patients whose primary complaints are sleep-related.

#### 180 Rheumatoid Arthritis and Other Inflammatory Arthropathies

181 Sleep disturbances in patients with Rheumatoid Arthritis (RA) are multifactorial,

182 codependent on pain, fatigue, and depression. [51-53] In a prospective analysis of RA

183 patients seen at an outpatient clinic, Løppenthin et al reported that 61% met criteria for

184 poor sleep using the PSQI. [52] Westhovens et al found that RA disease activity showed

185 significantly positive correlation with worsening sleep symptoms, [53] while Fragiadaki et

- al reported improvement in sleep symptoms in a series of 15 RA patients treated with
- 187 tocilizumab, [54] together suggesting that primary management of underlying RA activity
- 188 may serve as an optimal strategy for co-managing sleep symptoms. Recent evidence has

also demonstrated a significant association between psoriatic arthritis and sleep disorders,

190 particularly OSA and insomnia. [55-58] Although etanercept was reported to improve

191 insomnia symptoms in patients with psoriatic arthritis, treatment with adalimumab did not

show a therapeutic effect on patients' OSA symptoms. [57,58] Patients with both psoriatic

193 arthritis and OSA who are to undergo hand surgery should be managed according to the

194 OSA principles discussed earlier.

- 195
- 196

#### 197 Additional Management Considerations

Given the potential adverse effects associated with sedatives and opioid pain medication,
alternative treatment modalities for concomitant sleep disturbance and acute

200 postoperative pain warrant further discussion. Gamma-aminobutvric acid (GABA)

201 analogues gabapentin and pregabalin may have utility for treating concomitant pain and

sleep symptoms, either as primary therapeutic or adjuvant agents. [59,60] Gabapentin has

203 previously been shown as an effective treatment for both pain and sleep disturbance in CTS

204 patients, [61] although this finding has been both supported and refuted in more recent

- studies. [62,63] Pregabalin shows promise in the concomitant treatment of sleep and pain
- symptoms, albeit in patients with fibromyalgia, for which it is FDA-approved. [64,65] While
- 207 neither medication is currently FDA-approved for neuropathic pain associated specifically
- 208 with conditions of the upper extremity, further investigation to that end could be

209 worthwhile. [59]

211 Another promising agent for use in hand surgery is exogenous melatonin. Although its 212 sleep-promoting characteristics are widely-reported, melatonin possesses numerous 213 additional benefits which suggest an ideal role as a therapeutic agent in hand surgery. [66] 214 In vitro studies on chondrocytes demonstrate that melatonin is chondrogenic and 215 promotes matrix synthesis, and can also serve as a rescue agent for chondrocytes that are 216 exposed to damaging pro-inflammatory or cytotoxic factors. [67-69] In an animal model of 217 median nerve injury, sleep deprivation made rats more vulnerable to nerve injury-induced 218 neuropathic pain, while melatonin reversed nerve injury-induced hypersensitivity. [70] In 219 the lone clinical study evaluating its efficacy in hand surgery, melatonin was found to 220 improve tourniquet tolerance while decreasing opioid requirement in patients receiving 221 regional anesthesia intravenously. [71] Given this therapeutic potential and limited 222 adverse effect profile, use of melatonin in hand surgery certainly warrants ongoing trial 223 and further investigation.

- 224
- 225

#### 226 Current Limitations and Future Directions

227 Due to the complex interplay of sleep with pain, psychiatric disorders, social factors, and 228 other associated conditions, the evaluation of sleep disorders in the hand surgery patient is 229 rarely straightforward. In a recent study by Peters and colleagues, the authors attempted 230 to determine a relationship between sleep disturbance and upper-extremity disability, and 231 found that psychological factors such as ineffective coping strategies were more likely to 232 predict arm disability than sleep symptoms. [72] The authors discussed the possibility that 233 sleep disturbance was also the product of these psychological factors, suggesting a 234 bidirectional relationship. Their study exemplifies the challenging nature inherent to 235 determining underlying pathology and causal relationships regarding sleep disturbances. 236 This is echoed by Shulman et al, who found that sleep disturbance following distal radius 237 fracture at long-term follow-up was more dependent on mental health than on functional 238 status. [73]

239

A second limitation of the current evidence regarding sleep disorders in hand surgery is

with respect to the heterogeneity of the patient populations studied; a shortcoming fully

- 242 acknowledged by Peters and colleagues. [72] In their study fractures, soft-tissue injuries,
- 243 and degenerative conditions were all treated as equivalent upper extremity disabilities.
- 244 Furthermore, CTS and cubital tunnel syndrome were lumped together although there is no
- 245 current literature that describes sleep disorders in patients with cubital tunnel syndrome.
- 246 Similarly, in their study of melatonin's utility in improving tourniquet tolerance and
- 247 decreasing opioid requirements, Mowafi and Ismail did not stratify or match patients based
- 248 on condition or procedure. [71] Future studies using larger, more homogenous patient
- 249 cohorts, would be critical to fully understanding the relationships between sleep disorders
- 250 and hand pathologies, and developing precise and effective regimens to treat coexisting
- sleep and hand disease.
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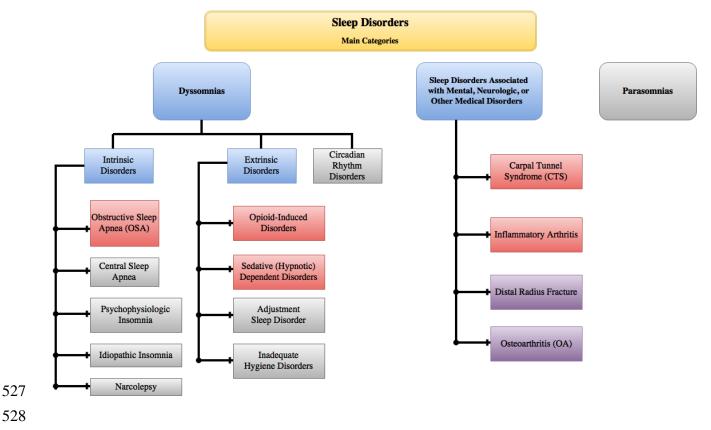
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- 521 **Figure 1.** Flow chart outlining the key types of sleep disorders relative to hand surgery in
- 522 the context of a broader overview of all sleep disorder categories. The first level represents
- 523 the three main categories of sleep disorders. Note that boxes in grey are not relevant to this
- 524 discussion, those in red highlight the key types of sleep disorders known to be related to
- 525 hand surgery patients, and those in purple represent conditions that are likely to be
- 526 associated with sleep disorders based on current evidence.



**Table 1.** STOP-BANG Questionnaire to assess for risk of Obstructive Sleep Apnea (OSA).

531 The first section (STOP) consists of four history or symptom-related questions for the

532 patient to answer, while the second section (BANG) consists of four items that may be

533 objectively measured by the clinician. Answers of "Yes" to any question or measure results

534 in a point, while "No" does not result in a point. Patients with total scores of 0-2, 3-4 and 5-

535 8 points are considered low, intermediate, and high risk of having OSA, respectively.

536

529

Question or Variable	YES	NO
STOP		
Do you <b>SNORE</b> loudly (louder than talking or loud enough to be heard through closed doors)?	1	0
Do you often feel <b>TIRED</b> , fatigued, or sleepy during daytime?	1	0
Has anyone <b>OBSERVED</b> you stop breathing during your sleep?	1	0
Do you have or are you being treated for high blood <b>PRESSURE</b> ?	1	0
BANG		
BMI more than 35kg/m2?	1	0
AGE over 50 years old?	1	0
<b>NECK</b> circumference > 16 inches (40cm)?	1	0
GENDER: Male?	1	0