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

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1 **Title:**
2 Evaluation and Management of Sleep Disorders in the Hand Surgery Patient
3

4 **Running Title:**
5 Sleep Disorders in Hand Surgery
6

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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
55 role of hand surgeons in the recognition and management of sleep disorders that are most
56 common in hand surgery.

57

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,
61 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
66 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
68 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
76 surgery: (1) *dysomnias* which are disorders that produce excessive sleepiness or difficulty
77 in initiating or maintaining sleep and (2) sleep disorders associated with other medical
78 disorders. [9] A more inclusive outline of general sleep disorders is presented in [Figure 1](#).

79

80 ***Intrinsic Dysomnias***

81 Intrinsic dysomnias 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 dysomnia 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
93 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
96 In addition to patients with a known diagnosis of OSA, surgeons are often tasked with
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 fared 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
122 disturbance intensifies pain), [16-19] opioids used to concomitantly treat both pain and
123 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 eye 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

149 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
152 used the medication daily for at least six months, including 77% who experienced rebound
153 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
165 mechanism linking these two conditions is unclear, McCabe and colleagues reported that
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.

179

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
186 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
189 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
192 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**

198 Given the potential adverse effects associated with sedatives and opioid pain medication,
199 alternative treatment modalities for concomitant sleep disturbance and acute
200 postoperative pain warrant further discussion. Gamma-aminobutyric acid (GABA)
201 analogues gabapentin and pregabalin may have utility for treating concomitant pain and
202 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
205 studies. [62,63] Pregabalin shows promise in the concomitant treatment of sleep and pain
206 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]

210

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

240 A second limitation of the current evidence regarding sleep disorders in hand surgery is
241 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
251 sleep and hand disease.

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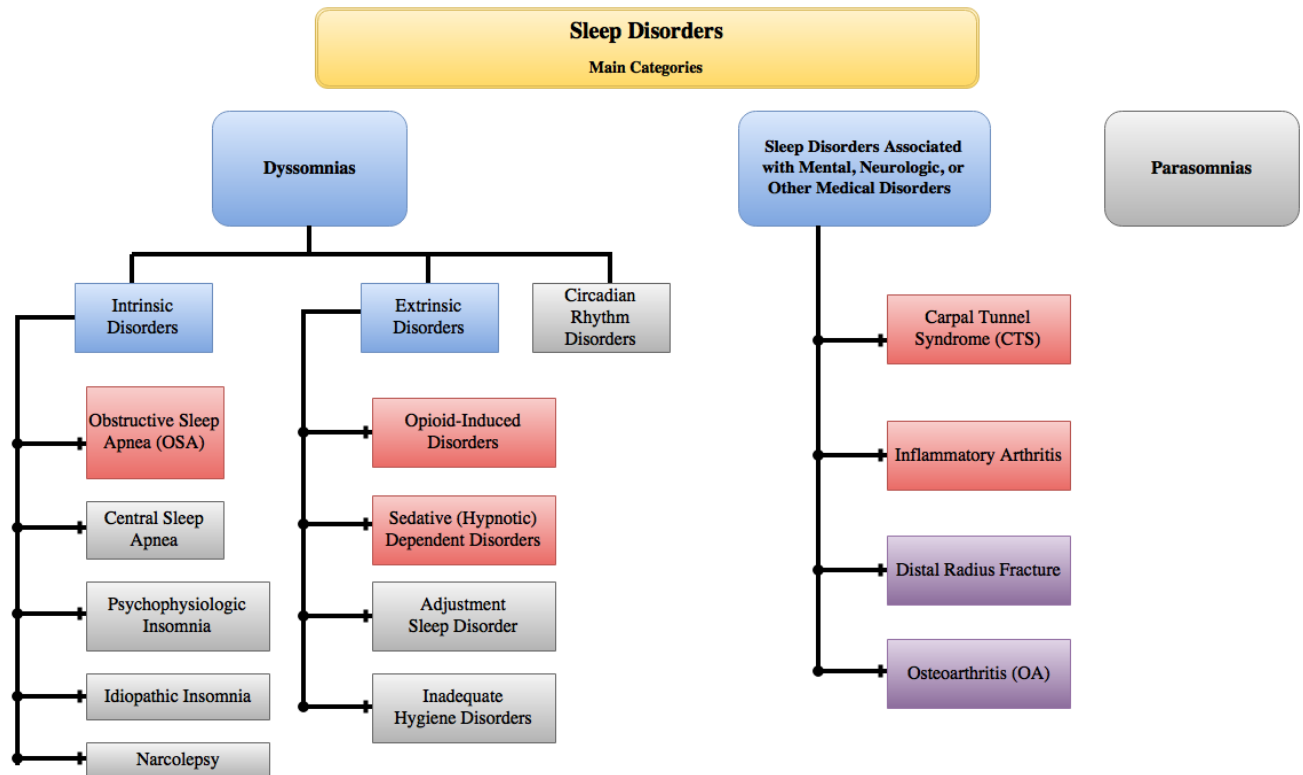
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521 **Figure 1.** Flow chart outlining the key types of sleep disorders relative to hand surgery in
 522 the context of a broader overview of all sleep disorder categories. The first level represents
 523 the three main categories of sleep disorders. 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.



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Table 1. STOP-BANG Questionnaire to assess for risk of Obstructive Sleep Apnea (OSA). The first section (STOP) consists of four history or symptom-related questions for the patient to answer, while the second section (BANG) consists of four items that may be objectively measured by the clinician. Answers of “Yes” to any question or measure results in a point, while “No” does not result in a point. Patients with total scores of 0-2, 3-4 and 5-8 points are considered low, intermediate, and high risk of having OSA, respectively.

Question or Variable	YES	NO
STOP		
Do you SNORE loudly (louder than talking or loud enough to be heard through closed doors)?	1	0
Do you often feel TIRED , fatigued, or sleepy during daytime?	1	0
Has anyone OBSERVED you stop breathing during your sleep?	1	0
Do you have or are you being treated for high blood PRESSURE ?	1	0
BANG		
BMI more than 35kg/m ² ?	1	0
AGE over 50 years old?	1	0
NECK circumference > 16 inches (40cm)?	1	0
GENDER: Male?	1	0

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