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Preoperative State Anxiety, Acute Postoperative Pain, and Analgesic Use in Persons Undergoing Lower Limb Amputation

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Abstract

Objectives: The current study examined the relationship between preoperative anxiety and acute postoperative phantom limb pain (PLP), residual limb pain (RLP), and analgesic medication use in a sample of persons undergoing lower limb amputation.

Methods: Participants included 69 adults admitted to a large Level 1 trauma hospital for lower limb amputation. Participants' average pain and anxiety during the previous week were assessed prior to amputation surgery. RLP, PLP, and analgesic medication use were measured on each of the 5 days following amputation surgery.

Results: Results of partial-order correlations indicated that greater preoperative anxiety was significantly associated with greater ratings of average PLP for each of the 5 days following amputation surgery, after controlling for preoperative pain ratings and daily postoperative analgesic medication use. Partial correlation values ranged from .30 to .62, indicating medium to large effects. Preoperative anxiety was also significantly associated with ratings of average RLP only on postoperative day 1, after controlling for preoperative pain ratings and daily postoperative analgesic medication use ($r = .34$, $p < .05$). Correlations between preoperative anxiety and daily postoperative analgesic medication dose became non-significant when controlling for pre- and post-amputation pain ratings.

Discussion: These findings suggest that anxiety may be a risk factor for acute post-amputation PLP and RLP, and indicate that further research to examine these associations is warranted. If replicated, the findings would support research to examine the extent to which modifying preoperative anxiety yields a reduction in post-operative acute PLP and RLP.

Keywords

anxiety; chronic pain; amputation

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Introduction

Pain, both chronic and acute, is a common problem following acquired limb loss [1]. It is estimated that chronic phantom limb pain (PLP), or pain felt in the portion of the limb that has been amputated, is experienced by approximately 60-85% of persons with amputation[2,3,4–8]. Although previously believed to be considerably less common than PLP, several studies indicate that chronic residual limb pain (RLP), or pain in the portion of the leg remaining after amputation, is frequent and may occur in over 70% of persons with lower limb amputation[3,9,10]. The onset for both types of pain is typically during the acute recovery phase. Depending on the study, acute RLP is reportedly experienced by 57-100% of persons immediately following amputation.[5,11,12] The onset of PLP is generally within the first week after surgery and experienced by between 72-85% of patients immediately following amputation[5,13]. Importantly, persons who do not experience PLP during this acute recovery phase generally do not develop it later[12,14].

Research also suggests that acute pain following amputation surgery may be an important factor associated with the development of chronic pain in persons with amputation[15]. The findings from several studies provide preliminary empirical support for this hypothesis. For example, Nikolajsen et al.[16] found that the presence of PLP 1 week after amputation was significantly associated with the presence of PLP at 3 and 6 months post-amputation. Additionally, the findings from a study by Hanley et al.[17] indicated that the intensity of PLP during the acute recovery phase (days 4 and 5 following amputation) significantly predicted PLP intensity at 6 and 12 months post-amputation. The same pattern of findings was observed regarding the relationship between the intensity of acute and chronic RLP.

Given the importance of acute post-operative pain as a risk factor for chronic pain, research has attempted to identify modifiable risk factors for pain following amputation. This line of research has the potential to yield valuable information about the prevention of pain following amputation. A number of studies have demonstrated that pain prior to amputation is associated with pain in the acute recovery period following amputation surgery[12,17–19]. Such findings have, in part, prompted researchers to examine whether administration of epidural anesthesia preoperatively and perioperatively may reduce the incidence and/or severity of PLP and RLP following amputation[16,20–22]. Unfortunately, such studies have yielded inconsistent findings; we do not yet know if this approach is generally effective, effective for some patients and not others, or if the beneficial effects of preventative analgesia that have been identified in some studies are simply due to random variations in post-operative pain[23–25]. Thus, further research is not only needed to study the effects (and identify possible moderators) of these interventions, but also on identifying other potentially malleable risk factors for the development of pain following amputation.

To our knowledge, one risk factor for the development of pain following amputation that has not previously been investigated in persons undergoing amputation is preoperative anxiety. This is surprising given that anxiety has received considerable attention in the broader postoperative pain literature, including its relationship to acute post-operative pain and to chronic post-surgical pain (CPSP). The link between greater pre-operative anxiety and an increased risk for developing CPSP has been documented in a number of studies [26,27,28,29],

but findings to date are somewhat equivocal. For example, in their systematic review, Hinrichs-Rocker[30] and colleagues conclude that data to date are “inconclusive” regarding the impact of pre-operative anxiety on the development of CPSP. In a more recent and more comprehensive meta-analysis of the topic, Theunissen and colleagues[28] found that a small majority of studies evidenced a significant relationship between greater pre-operative anxiety and the development of CPSP, with no studies evidencing the reverse relationship. Taken together, this literature remains preliminary and calls for more attention.

A more consistent link has been evidenced between pre-operative anxiety and increased acute postoperative pain ratings in persons undergoing a variety of surgical procedures, including elective abdominal hysterectomy[31], radical mastectomy[32], breast cancer surgery[33], and colorectal surgery[34]. In addition, Kalkman et al.[19] found that preoperative state anxiety, when measured as anxiety specific to anticipation of surgery versus a general measure of state anxiety, was a significant independent predictor of severe postoperative pain (VAS > 7/10) in a large sample of persons undergoing a wide array of surgical procedures (i.e., opthalamic, laparoscopic, ENT, abdominal, and orthopedic surgeries). A review of studies that utilized the State-Trait Anxiety Inventory[35] (STAI) to assess preoperative state anxiety indicated moderate effect sizes for the relationship between preoperative anxiety and postoperative pain ratings in studies with significant findings[36].

However, a closer examination of the literature reveals that findings are somewhat equivocal in this literature, as well, as there are those who have failed to find a relationship between state anxiety and post-operative pain for procedures such as elective abdominal surgery[18] and laproscopic tubal ligation[37]. A few studies have also shown that higher levels of preoperative anxiety are associated with increased need for analgesia to achieve deep sedation during surgery[38], as well as analgesic medication use following surgery[32,39,40]. Whether this increased analgesic use is simply a proxy for higher postoperative pain levels, or whether it has an independent relationship with preoperative anxiety, is not clear.

At present, it is unknown whether the findings regarding the associations between preoperative state anxiety and postoperative pain and analgesic use are generalizable to persons who have undergone amputation. This question is worthy of investigation, as state anxiety prior to amputation could potentially be reduced via a variety of psychopharmacological and psychosocial interventions. Thus, research in this area could identify additional strategies for preventing and/or reducing the onset of chronic pain problems and analgesic use following amputation.

The current study’s objectives were to examine the relationship between preoperative anxiety and acute postoperative PLP and RLP, as well as analgesic medication use, in a sample of persons undergoing lower limb amputation. We hypothesized that higher levels of preoperative anxiety would be associated with greater acute PLP and RLP, as well as increased use of analgesic medication, even after controlling for preoperative pain levels.

Materials and Methods

Participants

Patients approached to participate included adults consecutively admitted to a large Level 1 trauma hospital in the Northwest United States who were scheduled for lower limb amputation and were recruited for a randomized control trial comparing the effects of perioperative epidural anesthesia on post-amputation phantom and residual limb pain. Inclusion criteria for the study included: (1) being scheduled for amputation surgery; (2) sufficient cognitive skills to understand the informed consent form and complete self-report measures; (3) at least 18 years of age; (4) English speaking; and (5) a permanent home address for follow-up purposes. Exclusion criteria included: (1) significant lower limb phantom pain on the same or opposite side of the scheduled amputation subsequent to a previous amputation; and (2) a medical condition in which epidural anesthesia would be contraindicated. For the purpose of the current paper, data from all subjects who participated in the randomized control trial were pooled, as the results of the trial indicated no treatment effects for perioperative epidural anesthesia on subsequent phantom or residual limb pain.

Procedures

Participants were assessed at the following intervals: (1) prior to amputation surgery (except in cases of emergent amputation when it was not possible to conduct interviews); (2) on each of the 5 days following amputation surgery; (3) and at 1, 6, 12, and 24 months post-amputation. Pre-amputation interviews were conducted within the 2 weeks prior to amputation (median = 2 days, range = 0 – 14 days before surgery). The current paper examines data collected prior to amputation and during the acute recovery phase (i.e., post-operative days 1 through 5). Pre-amputation assessments were completed during in-person interviews conducted by one of the study investigators. A research nurse or research psychologist conducted assessments during the 5 days following amputation. Amputation history, including the date of surgery, location, and reason for amputation, was obtained from hospital medical records.

Measures

Demographic and amputation-related information.—Demographic questions assessed age, gender, and ethnicity. Amputation-related questions assessed the primary reason for amputation and whether the amputation was above or below the knee.

Preoperative anxiety.—During pre-amputation interviews, participants were asked to rate their anxiety on a 0 (“no anxiety”) to 10 (“worst possible anxiety”) scale in response to the following question: “Please circle the one number that best describes your anxiety or nervousness over the past week.” Elkins et al.[34] used a similar 0-10 numeric rating scale to assess preoperative state anxiety in a sample of persons scheduled for colorectal surgery and found that the measure correlated strongly (r = .64, $p < .0001$) with the State subscale of the State-Trait Anxiety Inventory.

Preoperative pain.—During pre-amputation interviews participants were asked to rate their average pain during the past week in the leg scheduled to be amputated, on a 0-10

Numerical Rating Scale (NRS), where 0 = “no pain” and 10 = “pain as intense as I could imagine.” Such 0 – 10 scales have demonstrated their validity as measures of pain by their strong association with other measures of pain intensity, as well as by their responsivity to pain treatments[41]. The end-points for this scale were adapted from the pain intensity items of the Graded Chronic Pain Scale[42].

Postoperative phantom and residual limb pain.—On each of the 5 days following amputation surgery, participants were asked to rate their average PLP and RLP (over the past 24 hours) on the same 0-10 NRS used to assess pain during pre-amputation interviews. PLP was defined as “pain in the missing portion of your leg” and RLP was defined as “pain in the portion of the leg left remaining after the amputation.”

Postoperative analgesic medication use.—Patient controlled analgesia (PCA) was available to all participants and was started in the Post Anesthesia Care Unit (PACU). The use of PCA is consistent with standards of practice and also provided a reliable and feasible method for measuring the amount of opioids used post-operatively. The use of PCA and all analgesic medications on days 1 through 5 following amputation was recorded and the amount of medication used was converted to standard morphine equivalents wherever possible.

Statistical analyses

Preliminary analyses were conducted to examine the relationship between demographic variables as possible covariates in the main analyses. These included bivariate correlations and independent samples t-tests to examine the relationship between age and gender, respectively, to RLP and PLP on each of the post-operative days.

To examine the associations between preoperative anxiety and acute post-amputation PLP, RLP, and analgesic medication use, we conducted a series of zero-order and partial correlation analyses. Partial correlations were examined to determine the associations between preoperative anxiety and each of the outcome measures after controlling for the effects of other important factors (i.e., preoperative pain and daily post-amputation analgesic medication use).

We also examined the overlap between the existence of RLP and PLP on each post-operative day using chi-square analyses, dividing participants by the presence and absence of each pain type on each day.

Results

Description of the sample

Two of the 89 cases of adults consecutively admitted for lower limb amputation during the time of this study were under the age of 18 and an additional 16 participants did not have sufficient time to complete interviews prior to surgery due to the emergent nature of their amputations. Of the remaining 71 patients who did complete pre-amputation interviews, 2 did not answer the question regarding pre-amputation anxiety, leaving a total of 69 possible patients eligible for participation in the current analyses (about 78% of the sample of 89

consecutive cases). Because of missing data on any single assessment day (e.g., PLP on post-amputation day 1), the following analyses include sample sizes ranging from 43 to 67 participants. All participants were included in at least one analysis, thus the demographics reported below represent all 69 eligible participants.

The sample was predominantly male (70%) and Caucasian (80%) and had a mean age of 43.9 years (SD = 12.37; range, 24-72). The primary reason for amputation was traumatic injury (67%), usually the late result of failure at limb salvage. The second most frequent reason was diabetes (16%), followed by infection and vascular disease (both 4%), gangrene (1%), congenital anomalies (1%), and other (3%). There were two participants for whom amputation etiology was missing (3%). The majority of amputations were below the knee amputations (74%). For further information regarding pain and anxiety characteristics of the sample, please see Table 1.

Preliminary Analyses

Preliminary analyses included examination of demographic covariates and distributions. Skewness of the distributions of pre-operative anxiety and each of the five post-operative ratings of RLP and PLP were examined. No distributions evidenced significant skew (all values ≤ 1.2). Additionally, preliminary analyses revealed no statistically significant relationships between age and gender (all ps>.05) on RLP and PLP on any of the post-operative days. No demographic covariates were included in the primary analyses.

Overlap Between Residual Limb Pain (RLP) and Phantom Limb Pain (PLP)

Chi-square analyses, dividing participants by the presence and absence of each pain type (RLP and PLP) at each time point following surgery, revealed a significant relationship between pain types on the first day following surgery ($X^2 = 3.10$, p = .05), as well as the 5^{th} day ($X^2 = 4.10$, p - .04), while the overlap in these pain types was insignificant on post-operative days 2-4 (all ps >.05). Of note is the small sample size within the current study, resulting in a violation of minimal cell sizes, which artificially inflates the chi-square value and increasing the Type I error rate.

Phantom limb pain (PLP)

Results of zero-order correlations indicated that preoperative anxiety was significantly associated with ratings of average PLP for each of the 5 days following amputation surgery (see Table 2). Specifically, higher levels of preoperative anxiety were associated with more severe PLP after surgery. This association remained significant for each of the 5 days following surgery even after controlling for preoperative pain ratings and daily postoperative analgesic medication use, suggesting that this is a robust finding. Partial correlation values ranged from .30 to .62, indicating moderate to large effects. Please note that post-amputation daily PLP and RLP ratings were not obtained from 7 participants, thus there were ultimately 63 potential participants eligible for analyses involving daily post-amputation pain ratings. Due to missing data, total sample sizes for these analyses range from 43 to 53.

Residual limb pain (RLP)

Preoperative anxiety was also significantly associated with ratings of average RLP for each of the 5 days following surgery (see Table 3). As with PLP, zero-order correlation values indicated that higher levels of preoperative anxiety were associated with greater RLP (rs ranged from .26-.50). However, partial correlation results indicated that preoperative anxiety was only significantly associated with ratings of average RLP on postoperative day 1 after controlling for daily preoperative pain ratings. Moreover, partial correlations between preoperative anxiety and daily average RLP were insignificant after controlling for both preoperative daily pain ratings and daily analgesic medication use. Again, please note that post-amputation daily PLP and RLP ratings were not obtained from 7 participants, thus there were ultimately 63 potential participants eligible for analyses involving daily post-amputation pain ratings. Due to missing data, total sample sizes for these analyses range from 43 to 53.

Analgesic medication use

Zero-order correlations indicated that preoperative anxiety was significantly associated with analgesic medication use for each of the 5 days following surgery (see Table 4). Higher levels of preoperative anxiety were associated with higher daily doses of postoperative analgesic medication (rs ranged from .25-.33). However, the correlations between preoperative anxiety and daily postoperative analgesic medication dose became non-significant when controlling for only pre-amputation pain ratings, as well as when controlling for both pre-amputation pain ratings and post-amputation daily RLP and PLP pain ratings. Due to missing data, total sample sizes for these analyses range from 42 to 66.

Discussion

The current study sought to examine the relationship between pre-amputation state anxiety and post-operative acute phantom and residual limb pain, as well as post-operative analgesic use, in a sample of persons admitted for lower limb amputation. The most robust finding is that higher state anxiety was significantly related to greater post-amputation acute phantom limb pain (PLP) during 5 consecutive days post-amputation, even after controlling for preoperative pain and daily post-operative analgesic use. Interestingly, anxiety was not significantly related to post-amputation residual limb pain (RLP) after controlling for pre-operative levels of pain and post-amputation analgesic use. Anxiety was also unrelated to post-amputation analgesic use after controlling for post-amputation daily ratings of PLP and RLP and pre-operative levels of pain. This is the first study to examine the relationship between pre-operative anxiety and post-operative pain and analgesic use in a sample of persons undergoing amputation. These findings, as well as recommendations for future research, are discussed below.

Overall, the positive unique association between pre-amputation anxiety and post-amputation acute PLP versus RLP, above and beyond pre-operative pain and post-operative analgesic use, emerged as the most curious finding of the current study. Our findings of a significant association between pre-operative anxiety and acute post-operative pain are consistent with numerous other studies that have identified this association for other surgical

procedures[18,33,37,38,43,44]. Nonetheless, this is the first study to examine this association in persons undergoing amputation who, unlike other populations examined, may experience at least two distinct types of post-operative pain. Along these lines, these findings suggest that the association between pre-operative state anxiety and pain in this population may differ as a function of the *type* of postoperative amputation pain examined. This is further corroborated by the finding that the presence of RLP and PLP significantly overlapped on only two of five post-surgical days in the current sample, thus suggesting that pain pathways may differ for PLP and RLP. This latter finding is tentative and warrants replication in light of the small sample size in the current study. While speculative, the unique relationship between pre-operative anxiety and PLP could be explained by the unique confluence of primarily central nervous system processes that underlie the development of PLP and acute anxiety, including a complicated restructuring of cortical structures that is associated with the development of PLP[45]. Thus, it might be possible that the CNS processes that underlie the experience of anxiety reflect, or are factors influencing, the central nervous system processes contributing to PLP. This hypothesized relationship is further supported by literature examining the impact of anticipatory anxiety on perceived pain intensity[46]. Specifically, Lin and colleagues[46] found that the anterior insula, considered part of a "salience network" within the brain (p. 42), plays a central role in integrating anticipatory anxiety for an oncoming stimulus into the pain experience itself. Specifically, they found that heightened pre-stimulus threat (e.g., experimentally induced dental pain), and thus heightened pre-pain anticipatory anxiety, was linked with both heightened activity in the anterior insula and perceived acute pain intensity. Support for this finding may also be found in the literature linking psychological processes and the exacerbation and triggering of PLP[47,48]. More research is needed to both unravel the relationship among these processes as well as to replicate the current findings.

Likewise, the fact that pre-operative state anxiety did not predict post-operative RLP, versus PLP, is somewhat inconsistent with prior research linking pre-operative state anxiety with acute postoperative pain[19,31,32,34,38,43,44]. However, while the literature has established a compelling relationship between these variables for many surgical procedures, this has not been replicated in all studies, including studies examining persons undergoing laparoscopic tubal ligation[37], abdominal surgery[18] and persons underdoing numerous inpatient surgeries[19]. Moreover, Kalkman et al.[19] found that the type of state anxiety measured emerged as an important consideration. Specifically, state anxiety, as measured by the STAI[35], was not predictive of post-operative acute pain, but anxiety specific to the procedure, as measured by the Amsterdam Preoperative Anxiety and Information Scale[49] (APAIS), was a unique predictor of post-operative acute pain.

What emerges from this somewhat equivocal literature, when considered in light of the findings of the current study, is the possibility that the role that pre-operative state anxiety plays in post-operative acute pain may depend upon the nature of the pre-operative anxiety (e.g., anxiety about the procedure itself) or, perhaps, the type of pain incurred by the procedure. Along these lines, the type of state anxiety measure used in the current study may be important when considering these discrepant findings. The current study utilized a 0-10 scale to assess "anxiety in the past week". What this measure fails to identify is what participants are anxious about. Perhaps it matters if heightened anxiety is about anticipation

of a certain type of pain (PLP), fear of pain more broadly, or anticipation of the procedure itself. The target of one's anxiety may have a differential impact on one's experience of acute post-operative PLP and RLP pain. This calls for future research to examine the possible differential impact of specific types of anxiety (e.g., fear of pain versus fear of the procedure) on post-operative acute pain experiences.

Finally, the results of the current study revealed no significant associations between preoperative state anxiety and postoperative analgesic use. This finding is inconsistent with the literature that has found a positive relationship between pre-operative anxiety and post-operative analgesic use for other surgical procedures[32,39,40,44,50]. One possible explanation of these inconsistent findings is that there are variables that emerge for persons undergoing a planned amputation that upstage the potential impact of anxiety on analgesic use. For example, persons undergoing a planned amputation, including those in the current study, a majority of whom were undergoing amputation as a result of failed limb salvage, often experience pre-operative pain in the limb to be amputated. The presence of pain prior to surgery may impact pain expectancies during the post-surgical period, which, in turn, may impact how one copes with and perceives its intensity. Moreover, this is consistent with the work of others who have linked expectancies with alterations in pain intensity, further corroborated by concurrent changes in related brain activity[51]. One may anticipate that pain expectancies will vary widely for persons undergoing amputation whose limb pain prior to surgery also varies widely.

Future Research

Overall these findings offer a number of directions for future areas of inquiry. The findings suggest the possibility that interventions designed to decrease preoperative anxiety could influence acute postoperative PLP levels; clinical trials of pharmacologic or other interventions to reduce anxiety in the preoperative period yield new ways to reduce chronic post-operative pain. Replication of these findings is encouraged in future research with better measures of state anxiety, preferably the STAI[35]. Another important area of future research is the examination of the potential differential impact of pre-operative state versus trait anxiety on post-amputation pain. Future studies could also include more long-term measures of pain prior to amputation given the potential impact of pain expectancies. There is some evidence that persons with greater pain in their amputated limb prior to surgery are more likely to develop PLP[17]. Finally, one may consider the importance of examining other pre-operative psychological indices, including pain-related catastrophizing[52], given the robust literature linking this psychological process with pain intensity in other pain populations[53], as well as in amputation pain[54].

Study Limitations

The current study has several limitations. First, as discussed earlier, a single item measure was used to assess preoperative state anxiety (average anxiety in the prior week). Although a similar 0 to 10 rating scale has previously been found to correlate strongly with the State scale of the State-Trait Anxiety Scale (STAI) in a surgical population[34], future research in this area could benefit from using a more well-validated anxiety measure, like the STAI[35], which has been used often in similar research to date. Moreover, as stated earlier, it is not

possible, from our measurement of anxiety, to discern if we are tapping into state versus trait anxiety. This distinction is potentially very important and a weakness of the current study. It is also not possible from the current study to conclude that anxiety, however measured, prior to amputation would have a similar relationship to chronic RLP or PLP as it does with acute post-operative pain. Future studies are needed to examine the long-term trajectory of pain following amputation, relative to pre-operative state and trait anxiety. Second, the sample size was relatively small and only included persons with lower limb amputation. Research is needed with larger samples, affording the inclusion of a broader range of pain experiences, as well as samples of persons with upper limb amputation. Larger samples will help determine whether these findings are generalizable to the broader population of persons with acquired limb loss and to establish the replicability of these findings. Third, pre-amputation data could not be collected from nearly 20% of the study's sample due to the emergency nature of their amputation surgeries. Therefore, the current findings represent the relationship between preoperative anxiety and post-amputation pain and analgesic use for individuals participating in *planned* amputation surgeries. It is unknown whether the findings are characteristic of persons undergoing emergency amputation surgeries. Arguably, persons who undergo emergency amputations may experience higher levels of anxiety prior to amputation surgery than those who undergo planned surgeries and their pre-operative levels and duration of pain intensity may be quite variable. Likewise, anticipation of a planned amputation may yield more prolonged periods of anxiety and represent physical maladies with comorbid protracted pain. Therefore, we can only speculate about the possible impact of the temporal nature of anxiety, given the limitations of the current sample. Additionally, we did not obtain information about different types of anesthesia used by participants, thus we were unable to evaluate the extent to which this may predict pain after amputation, thus a possible covariate. Lastly, preoperative anxiety was significantly associated with all outcome measures when examining zero order correlations, however these findings were rendered non-significantly related to residual limb pain and analgesic use when controlling for other factors (i.e., preoperative pain, daily opioid equivalent medication dose). Therefore, it is somewhat unclear whether preoperative anxiety is a meaningful risk factor for acute pain post-amputation, or whether other factors, such as preoperative pain, pose a greater risk for pain following amputation.

Conclusions

Despite the study's limitations, this is the first study of which we are aware to examine the associations between preoperative anxiety and postoperative PLP and RLP and analgesic use following lower limb amputation surgery. The current findings provide preliminary evidence, consistent with the broader literature on preoperative anxiety and postoperative outcomes, that higher levels of anxiety prior to lower limb amputation are associated with greater acute pain intensity postoperatively. These results were most robust for intensity of PLP than for RLP. Given that early onset PLP is a risk factor for chronic PLP, prevention of this problem in the acute post-surgical phase is desirable.

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Table 1

Pain and anxiety characteristics of participants

Variable	Pre-Amputation	POD1	POD2	POD3	POD4	POD5
Phantom Limb Pain	NA	2.98 (3.29)	2.96 (2.92)	2.17 (2.60)	2.40 (2.69)	2.08 (2.28)
No Pain, n (%)		21 (30.4%)	19 (27.5%)	22 (31.9%)	18 (26.1%)	20 (29.0%)
Mild		14 (20.3%)	15 (21.7%)	22 (31.9%)	20 (29.0%)	22 (31.9%)
Moderate		8 (11.6%)	10 (14.5%)	4 (5.8%)	6 (8.7%)	6 (8.7%)
Severe		10 (14.5%)	8 (11.6%)	5 (7.2%)	4 (5.8%)	2 (4.0%)
Residual Limb Pain (Mean, SD)	NA	4.71 (2.91)	4.47 (2.61)	3.54 (2.49)	3.31 (2.33)	3.72 (2.53)
No Pain, n (%)		4 (5.8%)	3 (4.3%)	6 (8.7%)	5 (7.2%)	4 (5.8%)
Mild		23 (33.3%)	21 (30.4%)	31 (44.9%)	27 (39.1%)	28 (40.6%)
Moderate		9 (13.0%)	14 (20.3%)	10 (14.5%)	12 (17.4%)	11 (15.9%)
Severe		16 (23.3%)	15 (21.7%)	7 (10.1%)	4 (5.8%)	7 (10.1%)
Pre-Operative Pain	5.49 (2.56)					
No Pain, n (%)	4 (5.8%)					
Mild	15 (21.7%)					
Moderate	21 (30.4%)					
Severe	29 (42.0%)					
Pre-Operative Anxiety	5.28 (3.35)					
Range	0-10					

Note: Response options for all scales range from 0-10. Mild pain is defined as self-reported pain between 4-6, moderate as 5-6, and severe as 7-10 on the NRS for pain. Sample size varies from 48-54 due to missing data at each time point.

NA = Not applicable; POD = Post-operative day

Table 2

Zero-order and partial correlations between preoperative anxiety and post-amputation phantom limb pain

	Phantom Limb Pain (PLP)				
Variable	**POD1**	**POD2**	**POD3**	**POD4**	**POD5**
Preoperative anxiety (n)	.52*** (53)	.48*** (52)	.62*** (53)	.44*** (48)	.44*** (50)
Preoperative anxiety (n) Controlling for 1. Preoperative pain	.49*** (50)	.38** (49)	.50*** (50)	.30* (45)	.30* (47)
Preoperative anxiety (n) Controlling for: 1. Preoperative pain 2. Daily OE medication dose	.50*** (48)	.34* (47)	.50*** (48)	.31* (43)	.30* (46)

Note: n = 43 - 53 (due to missing data). POD = Post-operative day. OE = Opioid equivalent.

* $p < .05$.

** $p < .01$.

*** $p \leq .001$.

Table 3

Zero-order and partial correlations between preoperative anxiety and post-amputation residual limb pain

	Residual Limb Pain (RLP)				
Variable	**POD1**	**POD2**	**POD3**	**POD4**	**POD5**
Preoperative anxiety (n)	.50*** (52)	.41** (53)	.36** (54)	.26 (48)	.35* (50)
Preoperative anxiety (n)	.37** (49)	.22 (50)	.13 (51)	−.04 (45)	.22 (47)
Controlling for:					
1. Preoperative pain					
Preoperative anxiety (n)	.34* (47)	.15 (48)	.10 (49)	−.07 (43)	.22 (46)
Controlling for:					
1. Preoperative pain					
2. Daily OE medication dose					

Note: n = 43 – 54 (due to missing data). POD = Post-operative day. OE = Opioid equivalent.

* $p < .05$.

** $p < .01$.

*** $p < .001$.

Table 4

Zero-order and partial correlations between preoperative anxiety and post-amputation daily opioid equivalent medication dose

	Daily Opioid Equivalent (OE) Medication Dose				
Variable	**POD1**	**POD2**	**POD3**	**POD4**	**POD5**
Preoperative anxiety (n)	.31* (66)	.33** (66)	.32** (66)	.27* (65)	.25* (64)
Preoperative anxiety (n)	.19 (63)	.20 (63)	.20 (63)	.13 (62)	.07 (61)
Controlling for:					
1. Preoperative pain					
Preoperative anxiety (n)	.22 (46)	.22 (46)	.30* (47)	.19 (42)	.01 (45)
Controlling for:					
1. Preoperative pain					
2. Post-amputation daily PLP					
3. Post-amputation daily RLP					

Note: n = 42 - 66 (due to missing data). OE = Opioid equivalent. POD = Post-operative day. PLP = Phantom limb pain. RLP = Residual limb pain.

* $p < .05$.

** $p < .01$.

*** $p < .001$.