



Responsiveness of the Boston Carpal Tunnel Questionnaire and predictive factors in night splinting for Carpal Tunnel Syndrome. A cohort study

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Introduction

Carpal Tunnel Syndrome (CTS) is the most frequently diagnosed nerve compression of the upper extremity and is often managed through surgery, injection or night splinting.¹ Despite its high prevalence, limited research has been conducted to determine the preferred treatment options under different circumstances.^{2,3} Surgery is successful more often than splinting^{4,5} and demonstrates slightly greater improvements.¹ However, surgery also entails higher social costs (health care and sick leave).⁶ It would be beneficial to predict for which patient low-cost splinting is equally effective as the more invasive surgery. And on the other hand, for which patient splinting only yields delayed surgery. This study aims to

enable patients to make an informed choice for treatment. For this, two things are needed: first, that we can reliably compare different treatments using the same outcome measure. And second, that we can better predict how an individual patient will respond to a specific treatment. First, as outcome measure, The Boston Carpal Tunnel Questionnaire (BCTQ) is widely recommended for the evaluation of CTS treatment.^{7,8} The BCTQ is a diagnosis-specific Patient Rated Outcome Measure (PROM) with two subscales: the Symptom Severity Scale (SSS) and the Functional Status Scale (FSS).⁹ The BCTQ has good psychometric properties¹⁰, is more responsive than other PROMs^{11,12}, is translated into Dutch¹³, and subsequently validated.¹⁴ However, its responsiveness is almost

Abstract

Background and purpose | The Boston Carpal Tunnel Questionnaire (BCTQ) was developed to evaluate carpal tunnel treatment. However, its responsiveness is almost exclusively studied for surgical treatment. Furthermore, limited research has been conducted into what factors predict the effect of night splinting for carpal tunnel syndrome (CTS). Therefore, this study aims to determine the responsiveness of the BCTQ for night splinting and create insight into which patients benefit from night splinting.

Methods | Seventy-eight patients (eighty-five hands) were analysed in a prospective cohort study. The BCTQ was completed at baseline and six weeks. Symptom relief was assessed at six weeks and six months. Success was defined as not having surgery and experiencing symptom relief. Responsiveness was assessed through hypotheses testing and the area under the ROC-curve (AUC) at six weeks. Logistic regression was used to determine predictive factors at six months.

Results | After six weeks, 60% of the participants experienced improvement; at six months, this was 49%. Seven out of eight hypotheses were accepted and the AUC was 0.83, confirming responsiveness. Also, patients with no or slight numbness or tingling at night and a higher self-efficacy for pain were more likely to benefit from night splinting. A model with these two factors was statistically significant ($p < 0.05$) and correctly classified 73% of the cases. The AUC was 0.79.

Conclusions | The BCTQ-DLV is responsive for evaluating night splinting for CTS, indicating its usefulness both in clinical practice and in scientific research. Factors that predicted the effect of night splinting were the severity of numbness or tingling at night combined with pain self-efficacy.

exclusively studied for surgical treatment.^{10–12} Since the responsiveness of an instrument depends on the type of intervention, it is important to examine whether the BCTQ is responsive enough to evaluate splinting.¹⁵ Therefore, the first goal of this study is to assess the responsiveness of the BCTQ for night splinting.

Second, better insight into factors that predict the effect of carpal tunnel treatment can support patients to make a well-informed treatment choice. Regarding surgery, extensive research has been undertaken into which factors are related to treatment outcome. Findings vary from no predictive variables¹⁶, to a variety of factors like duration¹⁷, age^{17,18}, grip strength¹⁷, night waking¹⁹, a family history of CTS¹⁹, sex^{18,19}, comorbidity^{19,20}, severity of CTS^{18,20}, hand dominance¹⁹ or psychological factors like pain catastrophizing²¹, anxiety or depression.²⁰ Regarding splinting, a systematic review that merged all non-surgical treatment modalities found no evidence that any of the investigated factors had predictive value.³ In the absence of conclusive research, multiple recommendations were formulated, based on expert's opinion.^{22,23} Therefore, the second aim of this study is to determine which factors predict if a patient with CTS will be likely to benefit from night splinting.

Methods

Study design and setting

A prospective cohort study was undertaken to answer both research questions. Data were collected between November 2021 and August 2024 in the St Antonius Hospital in Nieuwegein and Utrecht.

Ethical approval

The study was approved by the Research & Development department of the recruiting hospital (Registration number R&D/Z21.030). All participants provided written informed consent.

Participants

We included a consecutive sample of adult patients, diagnosed with CTS, referred to the Hand Therapy Department for night splinting and able to complete questionnaires in Dutch. We excluded patients who received an injection less than one year prior to the first visit, or who had a carpal tunnel release in the affected hand before.

Data collection

The translated and validated BCTQ-DLV^{13,14} was used as primary outcome to investigate responsiveness. The following participant characteristics were assessed: age, gender, duration of symptoms, involvement of the dominant hand, bilateral complaints, comorbidities, BMI, type of work, receiving workers' compensation and psychological status. Psychological status was assessed with the Dutch translation of the Pain Self-Efficacy Questionnaire (PSEQ-DLV).^{24,25} Symptom relief was recorded on a 5-point Likert scale (much improved, somewhat improved, stayed the same, somewhat worsened, much worsened). Furthermore, progression to surgery or injection was recorded. Data were collected with REDCap and missing data were prevented by setting each field to required.

Procedure

Patients referred to hand therapy were screened for eligibility and invited to participate. At baseline, patient's characteristics and the BCTQ were completed, and patients received a thermoplastic or prefabricated wrist splint (thumb and MCP joints were not immobilised) with the instruction to wear the splint each night for six weeks. Prolonged splint wear after this period was left to the patient's preference. Patient education about CTS and the rationale of splinting was given during the first visit, but no additional treatment or exercises were provided. After six weeks and six months, treatment effect was evaluated. First, we verified if patients progressed to surgery or injection; subsequently, if no other treatment than splinting was received, patients recorded symptom relief and completed the BCTQ-DLV.

Statistical analyses

Patient characteristics were described based on the assessment of a normal distribution by the Kolmogorov-Smirnov-test. Failure was defined as either having surgery or injection, planning to have surgery or injection, or experiencing unchanged or worsened symptoms. Only those who experienced symptom relief with no other treatment than splinting were counted as success. We used the 6-week measurements to assess responsiveness and the 6-month measurements to determine predictive variables.

Responsiveness

Responsiveness is the ability of an instrument to detect clinical change when this occurs and is often defined as effect size (ES) or standardised response mean (SRM), where a higher value represents a larger treatment effect. ES is calculated by the difference in means (before and after intervention) divided by the standard deviation of means before intervention. The SRM divides the mean change by the standard deviation of the change scores. ES and SRM are specific for the type of treatment and the investigated sample.¹⁵ A larger treatment effect is expected from surgery than splinting¹; consequently, a lower ES/SRM is expected for conservative treatment. Also, the change score, ES and SRM in the success group are expected to be higher than in the failure group. Additionally, the ES and SRM tend to be higher for the SSS than the FSS.¹⁰

Based on these expectations from previous research, we formulated eight concrete hypotheses a priori to examine responsiveness. We applied the minimum clinically important difference that was used in the most recent Cochrane review to evaluate change scores.¹ We extracted reference values for ES and SRM from two studies that compared different questionnaires for CTS within a surgical sample.^{11,12} This resulted in the following hypotheses:

1. Overall ES and SRM (SSS) < 1.5^{11,12}
2. Overall ES and SRM (FSS) < 0.6^{11,12}
3. SRM and ES for the SSS are higher than for the FSS¹⁰
4. SRM and ES (BCTQ) in the success group are 0.2 points higher than in the failure group
5. Δ SSS > 1 for the success group¹
6. Δ SSS < 1 for the failure group¹
7. Δ FSS > 0.7 for the success group¹
8. Δ FSS < 0.7 for the failure group¹

Additionally, we calculated the area under the receiver

operator characteristics curve (AUC). According to the most recent COSMIN manual for systematic reviews of PROMs, we agreed that either 75% of the results should be in accordance with the hypotheses or the AUC should be > 0.7, to accept the responsiveness of the BCTQ-DLV as sufficient.²⁶ Furthermore, the minimal clinically important difference (MCID) was calculated to verify when a change in symptoms is actually experienced as meaningful for a patient.²⁷ Multiple approaches are available to calculate the MCID, explaining the variety of previously published values.^{1,5,10} Anchor-based methods are regarded as gold standard²⁷; therefore, experiencing somewhat or much symptom relief was used as an anchor to calculate the MCID of the BCTQ, by calculating the between-patient score changes (the difference between the mean scores of the success and failure group) and by determining the threshold from the ROC analysis at six weeks.²⁷

Predictive factors

Univariate analysis using chi-square or Fisher’s exact test for categorical variables and Student’s t-test or Mann-Witney U-test for continuous variables was used to identify potential predictive factors for success of splinting at six months. Variables were selected for inclusion in a multivariable logistic regression model if they reached a significance level of $p < 0.2$ on univariate analysis testing and counted at least five observations in each category. When variables were interrelated, such as comorbidity in general versus a specific comorbidity, or the FSS subscale versus the entire BCTQ, the variable with the greatest significance was included, to mitigate collinearity. A stepwise selection approach was used to create the final model, evaluating the contribution of each variable at every step. The decision to keep or remove variables was based on their statistical significance within the model. Based on the number of cases, it was agreed to include a maximum of three variables, to avoid overfit. Log-likelihood, Akaike and Bayesian information criteria were calculated for each logistic regression to compare models and goodness of fit was assessed through the AUC. Analysis was conducted in RStudio version 2023.09.1.

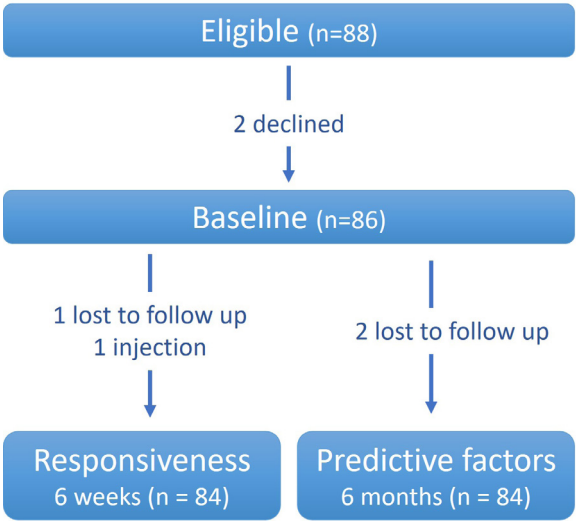


Figure 1 Flowchart of patient recruitment

Table 1 Patient characteristics

Characteristic	N = 85 ¹
Age	60 (14)
Gender (Female)	62 / 85 (73%)
Bilateral complaints	52 / 85 (61%)
Dominant hand (also) affected	74 / 85 (87%)
Duration	12 (5, 24)
Duration > 6 months	55 / 85 (65%)
Comorbidity present	52 / 85 (61%)
Trigger finger	24 / 85 (28%)
Diabetes	9 / 85 (11%)
Rheumatic condition	32 / 85 (38%)
Thyroid condition	6 / 85 (7.1%)
Neurological condition	10 / 85 (12%)
Pregnant	2 / 85 (2.4%)
BMI	27.7 (24.1, 31.2)
BMI > 30	26 / 85 (31%)
Type of work	
Physically light work	43 / 85 (51%)
Physically moderate work	29 / 85 (34%)
Physically heavy work	13 / 85 (15%)
Receiving workers' compensation	
No	29 / 85 (34%)
Partially, due to these complaints	2 / 85 (2.4%)
Yes, due to these complaints	3 / 85 (3.5%)
Yes, due to other complaints	16 / 85 (19%)
Not working	35 / 85 (41%)
PSEQ score at baseline	3.80 (1.72)
BCTQ score at baseline	2.91 (0.87)
SSS score at baseline	3.07 (0.87)
FSS score at baseline	2.69 (1.02)

¹ Mean (SD); n / N (%); Median (IQR)

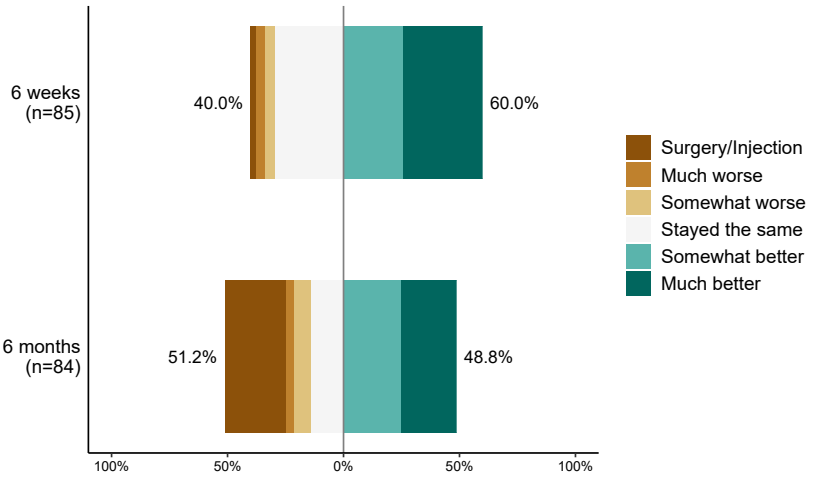


Figure 2 Symptom relief at six weeks and six months

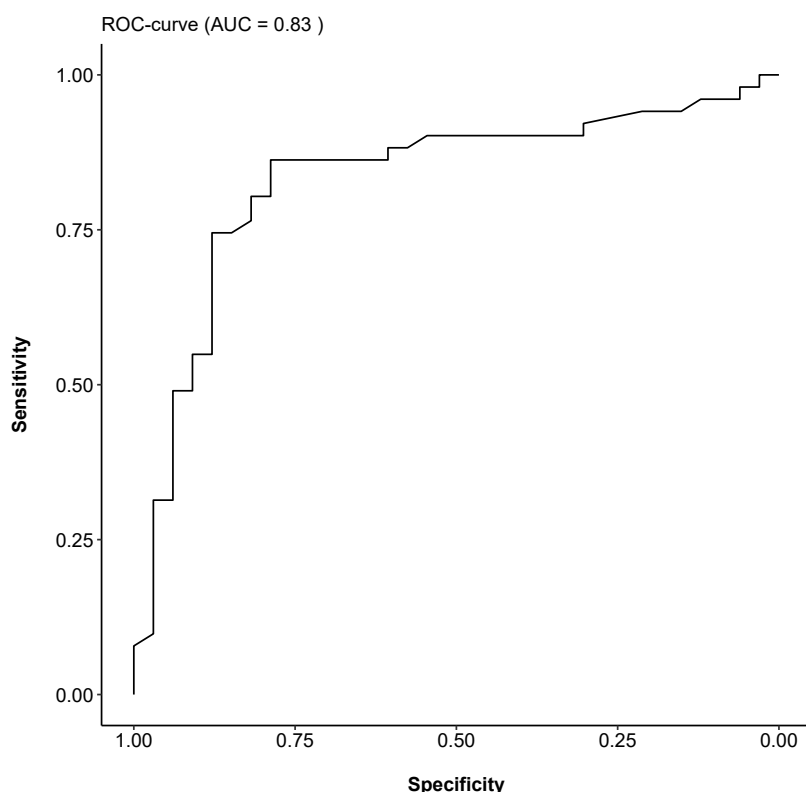


Figure 3 ROC curve of the BCTQ responsiveness

Sample size

With a power of 95% and $\alpha = 0.05$, 14 participants are needed to detect an effect size of 0.4. Power was calculated based on the standard deviation of change from a previous study.¹⁴ A sample size of 50-99 patients is adequate for hypotheses testing.²⁸ With 80 participants and a 40%-60% distribution of outcomes, a model with a maximum of three variables can be created.

Results

A total of 81 unique patients were eligible. Seven patients were referred again with CTS on the other hand and were screened twice, resulting in 88 eligible hands. At six weeks and six months, 84 complete measurements were available (**figure 1**). Patient characteristics are shown in **Table 1**. After six weeks, 60% of the participants experienced improvement and at six months, this was 49% (**figure 2**).

Responsiveness

BCTQ scores at baseline and at six weeks are presented in **Table 2**, with the ES and SRM for both the entire sample and the success versus failure group separately. Based on these outcomes, seven out of eight hypotheses were accepted (**Table 3**). The AUC of the BCTQ was 0.83 (95% CI [0.74-0.93]). Furthermore, the MCID calculated from between-patient change scores was 0.89. Based on ROC analyses, the MCID threshold for experiencing symptom relief was 0.40 with an accuracy of 83%.

Predictive factors

Univariate regression was used to determine potential factors for a predictive model (**Table 4**). Variables with a significance of $p < 0.2$ were selected, which included PSEQ and BCTQ baseline scores, bilateral complaints and

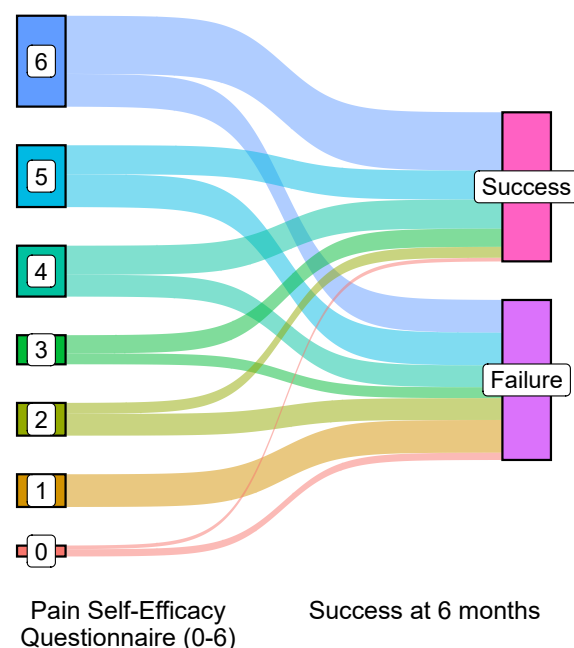


Figure 4 Sankey plot of PSEQ-2 score at baseline to success at 6 months

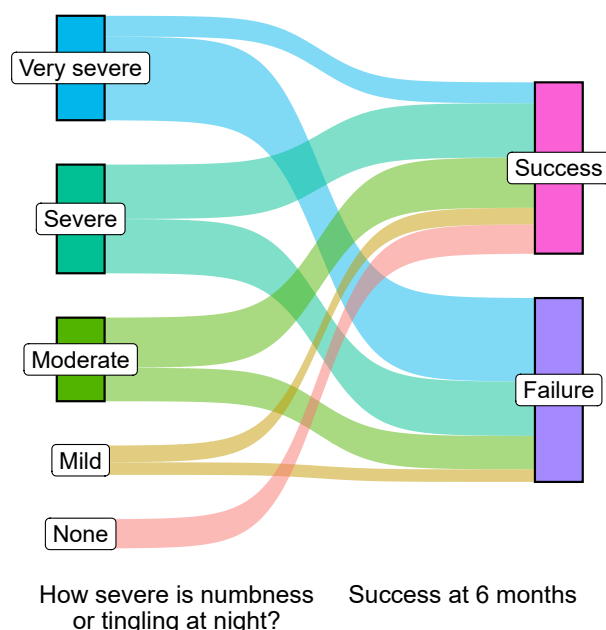


Figure 5 Sankey plot of tingling at night at baseline to success at 6 months

This study demonstrated that the BCTQ is responsive for evaluating night splinting in patients with CTS

comorbidity (specifically rheumatic conditions). The PSEQ and BCTQ were stronger predictors than bilateral complaints and comorbidity. Regarding the PSEQ, the entire questionnaire and both the published short versions were compared.^{25,29,30} The PSEQ-2 with item 8 and 929 was found to be the strongest predictor and was selected as first variable in the stepwise selection process. The BCTQ was significantly correlated with the outcome at six weeks in the univariate analysis, both on subscale and on item level. However, on subscale level, it did not contribute significantly to a predictive model with the PSEQ, due to its correlation with the PSEQ (Pearson's $r = 0.62$). On item-level, numbness or tingling

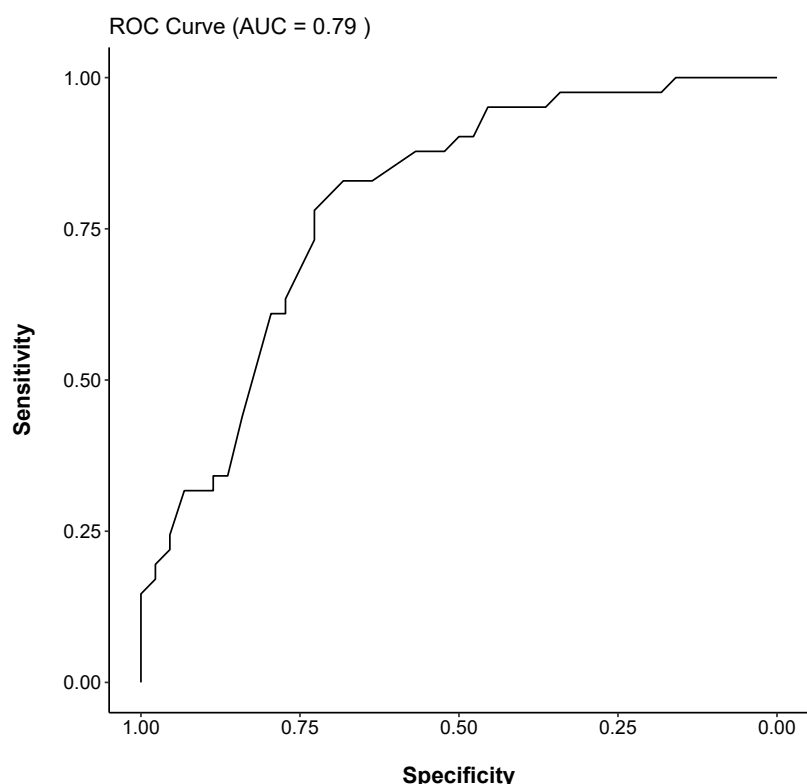


Figure 6 ROC curve of the prediction model 'numbness or tingling at night and self-efficacy versus success at 6 months'

at night was the strongest predictor and significantly contributed to a model with the PSEQ-2.

Logistic regression was used to analyse the relationship between numbness or tingling at night (SSS-9), pain self-efficacy (PSEQ-2) and success with night splinting.

It was found that, holding all other predictor variables constant, the odds of night splinting success occurring increased by 1.50 (95% CI [1.14, 2.06]) for each point increase in pain self-efficacy (figure 4) and decreased with 0.43 (95% CI [0.25, 0.67]) for one point increase in numbness or tingling at night (figure 5). Both variables significantly ($p < 0.05$) contributed to the model. Adding a third variable did not improve the model. The model correctly classified 73% of the cases with a sensitivity of 73% and a specificity of 73%. To examine how well this model predicted splinting success, we compared the predicted probabilities with the actual splinting success; the AUC was 0.79 (95% CI [0.70-0.89]) (figure 6).

Discussion

This study demonstrated that the BCTQ is responsive for evaluating night splinting in patients with CTS. Furthermore, it revealed that patients with less severe nocturnal complaints and a higher pain self-efficacy are more likely to benefit from night splinting.

Definition of success

Evaluation of CTS treatment knows a wide variety of outcome measures and success is defined in various ways: improvement on the BCTQ, progression to surgery or patient's satisfaction.³ To answer both research questions, the sample was divided into a success and failure group. We chose not to use the BCTQ-score to define success, as the responsiveness of the scale was subject to the first

research question. Furthermore, we strived to determine for whom splinting was sufficient as sole treatment and improvement on the BCTQ does not automatically imply that no further treatment is needed. No progression to surgery as only criterium for success was thought to bias the result in favour of splinting: those who did not benefit from splinting but did not want surgery either, would be incorrectly counted as success. Therefore, symptom relief was added to the definition of success. Both somewhat and much improved symptoms were included, as we discovered that many participants (often with rheumatic comorbidity) rated their improvement as 'somewhat improved', explaining that they no longer woke up at night, that tingling and numbness were absent, but that pain was still present in, for example, the CMC-I joint. We concluded that it was difficult for patients to distinguish between CTS complaints and untreated comorbidities. As a result, we defined success for night splinting as somewhat and much improved symptoms in combination with not progressing to surgery nor injection.

Responsiveness

The responsiveness of the BCTQ was evaluated firstly in terms of expected treatment effect and secondly in terms of ability to distinguish between improved and not-improved patients. The treatment effect was evaluated by ES and SRM, which are highly contextualised indicators that relate to the investigated treatment modality.¹⁵ Therefore, a responsive outcome measure should not only detect effect, but should also represent the real amount of change and not over- or underestimate the treatment effect.²⁶ Since previous research has shown a

Table 2 BCTQ change scores with effect size (ES) and standardised response mean (SRM)

Characteristic	Overall, N = 851	Success, N = 511	Failure, N = 341
BCTQ			
Baseline score	2.91 (0.87)	2.81 (0.87)	3.06 (0.86)
Score at 6 weeks	2.14 (1.00)	1.68 (0.70)	2.84 (0.99)
Δ 0-6 weeks	0.78 (0.88)	1.13 (0.85)	0.24 (0.60)
ES	-0.892	-1.292	-0.280
SRM	-0.891	-1.325	-0.402
SSS			
Baseline score	3.07 (0.87)	3.01 (0.88)	3.16 (0.86)
Score at 6 weeks	2.12 (1.02)	1.60 (0.65)	2.93 (0.97)
Δ 0-6 weeks	0.96 (1.02)	1.42 (0.95)	0.26 (0.67)
ES	-1.105	-1.602	-0.305
SRM	-0.942	-1.491	-0.385
FSS			
Baseline score	2.69 (1.02)	2.52 (1.00)	2.93 (1.00)
Score at 6 weeks	2.16 (1.08)	1.79 (0.91)	2.73 (1.10)
Δ 0-6 weeks	0.53 (0.83)	0.73 (0.87)	0.22 (0.68)
ES	-0.517	-0.730	-0.212
SRM	-0.635	-0.843	-0.320

^aMean (SD)

lower treatment effect for night splinting than for surgery¹, the ES and SRM should reflect this rather than be as high as possible. Hypotheses testing confirmed that the ES and SRM of the BCTQ were in line with the expected treatment effect for night splinting.^{1,10–12} Hypotheses testing as well as the AUC further confirmed that the BCTQ was able to distinguish between the success and failure group in this sample.²⁶ These results imply that the BCTQ is able to detect change in response to various treatment modalities, making it relevant for clinical practice and scientific purposes. In clinical practice, all CTS patients can be evaluated with the same outcome measure, regardless of the type of treatment or practitioner. This enhances communication in integrated health care, where multiple healthcare professionals are involved. In scientific research, different treatment modalities can be reliably compared with the BCTQ as a responsive outcome measure.

Table 3 Hypotheses to assess responsiveness

Hypotheses	Result	Accepted
Overall ES and SRM (SSS) < 1.5	ES (SSS) = 1.105 SRM (SSS) = 0.942	Yes
Overall ES and SRM (FSS) < 0.6	ES (FSS) = 0.517 SRM (FSS) = 0.635	No
ES and SRM (SSS) > ES and SRM (FSS)	1.105 vs 0.517 0.942 vs 0.635	Yes
ES and SRM BCTQ (success) > ES BCTQ (failure) by 0.2	1.325 vs 0.402 1.292 vs 0.280	Yes
ΔSSS (0-6 weeks) > 1 for the success group	ΔSSS = 1.42	Yes
ΔSSS (0-6 weeks) < 1 for the failure group	ΔSSS = 0.26	Yes
ΔFSS (0-6 weeks) > 0.7 for the success group	ΔFSS = 0.73	Yes
ΔFSS (0-6 weeks) < 0.7 for the failure group	ΔFSS = 0.22	Yes

Predictive factors

Various factors were analysed to identify those that predict the effectiveness of night splinting, with PSEQ and BCTQ baseline scores emerging as significant predictors. Psychological status can be assessed with a multitude of instruments and for this study we selected the Pain Self-Efficacy Questionnaire (PSEQ-DLV).^{24,25} The PSEQ assesses self-efficacy, which is a person's belief in their capability to master a situation.³¹ The PSEQ was selected because of its focus on patients' strengths and resilience, which aligns with the concept of positive health.³² PSEQ scores were only analysed on a (sub)scale level, since self-efficacy is an abstract concept.³⁰ This is measured by multiple items, which are not clinically relevant at item level. The BCTQ on the other hand, consists of a variety of concrete symptoms like tingling, numbness, muscle weakness, pain or nightly complaints, that might individually relate to the success of splinting and was therefore also analysed at item level. In the selection of variables for the model, we searched for BCTQ items that were not only statistically significant, but also clinically meaningful. We critically assessed if items strongly related to the overall concept of the questionnaire and did not build upon a previous question. Univariate

regression revealed that especially numbness or tingling at night was strongly correlated with treatment result. This item was considered highly connected with the overall aim of the questionnaire and also remains meaningful as an isolated question. Additionally, nocturnal numbness is one of the two symptoms in the CTS-6 evaluation tool, emphasizing its clinical importance.³³ Consequently, the severity of numbness and tingling at night together with pain self-efficacy are both clinically relevant factors that predict the success of night splinting for a patient with CTS. This can contribute to the process of shared decision making by providing health care professional and patient with clear indicators of the odds of night splinting success.

Strengths

This study was the first to assess responsiveness of the BCTQ-DLV for splinting, which was done extensively and according to the COSMIN criteria.^{26,28} The confirmed responsiveness of the BCTQ for night splinting is pivotal to its application in clinical practice and scientific research. Also, many studies have focussed on whether splinting is beneficial, or how successful splinting is compared to other treatment modalities.^{1,5} However, in this study we prospectively investigated *for whom* splinting might be advantageous, thereby expanding the evidence regarding night splinting for CTS.³

Limitations

This study has some limitations. First, CTS was diagnosed in various ways, for instance by electromyographic or ultrasound examination or clinical presentation. Second these finding only indicate whether or not splinting is potentially successful; it cannot be concluded that surgery is better for those who do not benefit from splinting. Specifically, patients with a low pain self-efficacy were found to have lower odds of improving with night splinting. However, a low pain self-efficacy is strongly related to psychological factors like pain catastrophizing, anxiety or depression³¹, which are known to impact on surgical treatment results.^{20,21} Consequently, patients with low pain self-efficacy might not benefit from surgery either.¹ Furthermore, we assessed symptom relief, but did not record patient satisfaction. Lastly, these findings should not be interpreted outside the context of secondary care: our sample consisted of patients that were referred by a general practitioner to a specialist, which is mainly done in the more severe cases, for those with longer duration or multiple hand problems. We searched for a reliable referral strategy for this particular group in secondary care. Repeating this study in the context of primary care might reveal different findings.

Recommendations

Based on the findings of this study, several recommendations for future research and for clinical practice are formulated. This study only reveals for whom splinting is beneficial and does not evaluate the outcome of further treatment when night splinting fails. For future studies it is recommended to follow the same patients in their journey along multiple healthcare providers.

Table 4 Univariate regression for success at six months with baseline characteristics with $p < 0.2$ highlighted

Characteristic	p-value
Age	0.9
Gender	0.6
Dominant hand affected	0.7
Bilateral complaints	0.068
Duration	0.9
Comorbidity present	0.2
Trigger finger	0.4
Diabetes	0.3
Rheumatic condition	0.12
Thyroid condition	0.4
Neurological condition	0.4
Pregnant	0.10
BMI	>0.9
Type of work	0.9
Receiving workers' compensation	0.4
PSEQ score	0.004
PSEQ-2 (item 8,9) score	0.002
PSEQ-2 (item 5,9) score	0.007
BCTQ score at baseline	0.003
SSS score at baseline	0.007
FSS score at baseline	0.004
SSS on item level	
1 Pain severity, night	0.053
2 Pain wake-ups	0.2
3 Pain severity, daytime	0.3
4 Pain frequency, daytime	0.7
5 Pain duration, daytime	0.7
6 Numbness	0.022
7 Weakness	0.024
8 Tingling	0.004
9 Numbness/tingling severity, night	<0.001
10 Numbness/tingling wake-ups	0.079
11 Grasping difficulty	0.036
FSS on item level	
1 Writing	<0.001
2 Buttoning	0.014
3 Holding a book	0.045
4 Gripping a telephone	0.060
5 Opening jars	0.025
6 Household	0.034
7 Carrying bags	0.030
8 Bathing and dressing	0.11

For evaluating treatment, we recommend applying the entire BCTQ as a responsive and validated outcome measure. However, out of the BCTQ, numbness or tingling at night is sufficient for predicting the odds of success of night splinting.

The PSEQ addresses self-efficacy, which requires resilience to overcome obstacles.³¹ Resilience plays a pivotal role in the concept of positive health.³² We advocate applying the positive health concept to the care of CTS patients, broadening the perspective to include not only the level of symptoms but also the well-being of the person.

Conclusion

This study found the BCTQ-DIV to be responsive for evaluating night splinting and able to distinguish between patients who experience improvement and those who do not. This enables clinicians to evaluate surgical as well as conservative treatment by means of the BCTQ-DIV. Furthermore, patients with no or slight numbness or tingling at night and patients with a high pain self-efficacy were most likely to benefit from night splinting. Clinicians might use these predictive factors at the time of referral to inform a specific patient of the odds of success of night splinting.

Conflict of Interest statement

Authors received funding from the *Antonius Onderzoeksfonds*.

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JA conceived and carried out the study. JA and TD wrote the study protocol. All authors discussed the results and recommendations. JA wrote a first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version. ■

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