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Letter to the Editor

## Exploring relationships between pre-operative median nerve echointensity and short-term outcomes of carpal tunnel release – A retrospective review

Carpal tunnel syndrome (CTS) is a common mononeuropathy, accounting for 90 % of all upper extremity entrapment neuropathies (Chen et al., 2016). Nevertheless, the success rate of carpal tunnel release (CTR) varies widely, ranging from 27 % to 100 % (Bland et al., 2014). While multiple studies have proposed various clinical factors as the predictors for successful CTR outcomes, there is no clear consensus in the literature.

Nerve echointensity (EI) has been gaining attention to indicate intraneural pathology where reduced EI represent intraneural edema (Fisse et al., 2019). A recent study by Fisse et al. demonstrated hypoechoic nerves remained stable or even improved over time with treatment (Fisse et al., 2019). While hypoechoic median nerves are noted in CTS, their relationship with surgical outcomes remains unclear (Kerasnoudis et al., 2019). Our study aimed to assess the association between preoperative nerve EI and CTR surgery outcomes.

Following approval by the Duke Institutional Review Board, we investigated patients with CTS who underwent CTR within 4 months of median nerve ultrasound study conducted between June 1, 2021, and May 1, 2022. CTS diagnosis was established through clinical evaluation by neurologists or hand surgeons, and confirmed by either electrodiagnostic or ultrasound criteria. CTS severity was graded as mild, moderate, or severe based on established electrodiagnostic criteria (Stevens, 1997). When there was isolated sonographic evidence of CTS without meeting the electrophysiologic criteria, it was defined as "borderline". Nerve EI was measured using the black-white fraction method (0100) in Image J software (National Institutes of Health, Bethesda, Maryland, USA) (Fisse et al., 2019) by two independent reviewers (Fig. 1). Ultrasound was performed with either a 12 MHz (Sierra NMUS1; Cadwell, Kennewick, Washington, USA) or 15–6 MHz matrix linear array transducer (LOQIQ; GE Healthcare, Boston, Massachusetts, USA).

Surgical outcomes were assessed based on retrospective chart review of visits taking place 2–6 weeks post-surgery where history taking/physical exam and testing are conducted to evaluate the surgical outcomes. The clinical record was examined for the presence of symptoms (numbness/tingling, pain, limited function) adapted from Boston Carpal Tunnel Questionnaire (BCTQ) domains.(Levine et al., 1993) "Complete resolution" was defined when none of these symptoms were present. Otherwise, it was "incomplete resolution". Two independent reviewers evaluated the surgical outcomes and inter-rater reliability was measured. Subsequently, a third reviewer determined the outcomes in the event of disagreement. All three reviewers were blinded to ultrasound data.

We identified 79 median nerves in 71 patients. Sixty (84.5 %) patients underwent median nerve evaluation via the lower resolution ultrasound system (12 MHz). Table 1 presents patient characteristics, median electrophysiological and sonographic data, as well as surgical information. In the 12 MHz group, no significant differences were observed in mean EI between those with complete and incomplete resolution post-surgery (80.1 and 78.4 for complete and incomplete resolution, respectively: mean difference (95 % CI) = 1.65 (−2.277, 5.574), $p = 0.40$). This held true for each side (right: $p = 0.43$, left: $p = 0.68$). A multivariable logistic regression, adjusting for age, gender, and diabetes, found no association between median nerve EI and complete versus incomplete resolution (OR = 1.01, 95 % CI = 0.99–1.02, $p = 0.488$). Mean EI did not differ across CTS severity groups ($p = 0.456$). Inter-rater reliability was excellent for outcome assessment and EI measurement (97.0 % agreement, kappa = 0.93, ICC 0.919). Only two cases required the 3rd reviewer to determine the outcomes. In the 15 MHz group, six of 12 CTR patients achieved complete resolution (Table 1), with no significant mean EI difference between complete and incomplete resolution (mean difference (95 % CI) = 5.48 (−17.46, 6.51), $p$-value = 0.33).

In summary, our study further confirms that sonographic risk factors for incomplete recovery in the early post-operative period after CTR remain elusive. Regarding the clinical significance of median nerve intraneural edema in CTS, Holzapfel *et al.* reported an increase in nerve EI post-successful CTR, suggesting that reduced intraneural edema contributes to better outcomes. (Holzapfel et al., 2022) Tagliafico *et al.* showed that median nerve EI could distinguish mild and severe CTS, indicating its potential in severity assessment.(Tagliafico et al., 2010) Combining the work of these three studies including ours, it might be reasonable to say that EI can assist with determining the severity of CTS and normalization of EI can be expected after successful CTR; however, the reduced EI prior to CTR is not a predictor for poor outcomes. Thus, patients with reduced EI on preoperative ultrasound need not be counseled to expect incomplete relief of symptoms after surgery.

This retrospective study has several limitations. The exact duration of CTS symptoms was not available in most subjects, which could have influenced the study findings. Due to the nature of retrospective design, the surgical outcomes were determined from review of postoperative notes. These lacked standardization in describing patient symptoms. The timing of postsurgical assessment (i.e. 2–6 weeks after surgery) was relatively short compared to previous studies.(Demino and Fowler, 2022) Some patients recover for several months after surgery; thus, some of our "incomplete resolution" patients may have become "complete resolution" patients with longer follow up. Outcomes were analyzed during this time-window as it is the standard practice for

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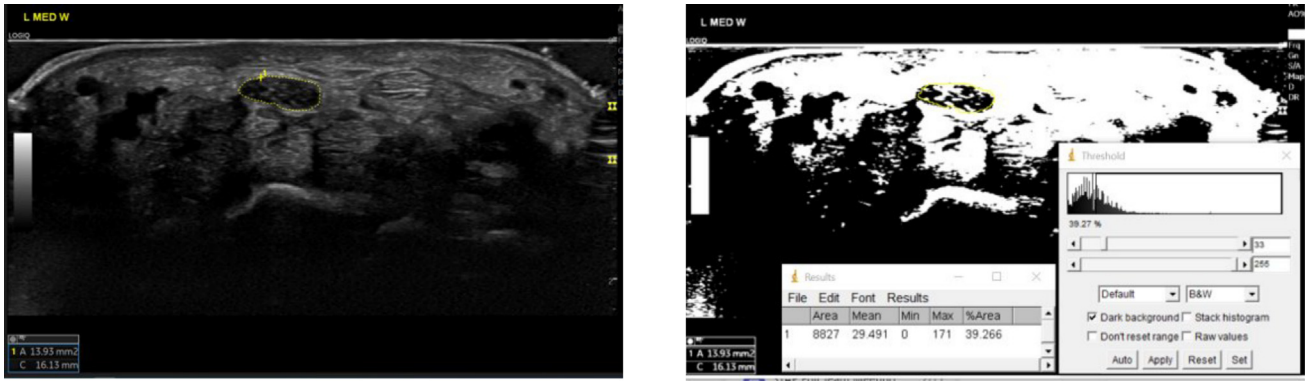


**Fig. 1.** Black-White fraction method. Left: Sonographic image of left median nerve at wrist. Right: Image conversion in Image J software for black-white fraction method.

**Table 1**
Summary of patient demographics and surgical information.

| Characteristics | Number (percentage) or median (range) | |
|---|---|---|
| | 12 MHz Images | 18 MHz Images |
| Number of subjects | 60 | 11 |
| Female | 37 (61.7 %) | 6 (54.5 %) |
| Male | 23 (38.3 %) | 5 (45.5 %) |
| Number of subjects with diabetes | 19 (31.7 %) | 4 (36.4 %) |
| Number of median nerves | 67 | 12 |
| Right | 38 | 9 |
| Left | 29 | 3 |
| Age at CTR surgery (years) | 56.5 (31–91) | 70 (44–86) |
| Severity of CTS | | |
| Borderline | 3 | 0 |
| Mild | 18 | 5 |
| Moderate | 29 | 1 |
| Severe | 17 | 6 |
| Median nerve echointensity | 80.6 (65.4–91.7) | 85.6 (71.8–97.6) |
| Cross-sectional area of median nerve ($mm^2$) | 16.2 (9.4–35.9) | 13.41 (9.0–43.95) |
| Wrist-forearm ratio of cross-sectional area | 2.5 (0.54–6.9) | 1.7 (1.0–5.17) |
| CTR Approach | | |
| Open | 64 | 9 |
| Endoscopic | 3 | 3 |
| Surgical outcomes 2–6 weeks after surgery | | |
| Complete resolution | 44 | 6 |
| Incomplete resolution | 23 | 6 |

CTR – carpal tunnel release, CTS – carpal tunnel syndrome.

postoperative follow-up in our institution. Furthermore, most median nerves (67/78) were evaluated by relatively low-resolution ultrasound system. As the 12 MHz ultrasound device is incorporated with the EMG system and readily available, we routinely use it in our practice for CTS screening. This might not be as sensitive to evaluating the changes of EI as a higher resolution ultrasound system and could have obscured our ability to detect an association between nerve EI and surgical outcomes. Although a similar conclusion was drawn from the sub-analysis of 11 median nerves evaluated by the higher resolution ultrasound system, the sample size was too small to properly assess the relationship between median nerve EI as measured by different US systems and surgical outcomes.

## Disclosure

Yohei Harada is a salaried employee of UCB Pharma and receive stock and stock option from employment. The research presented in this publication was conducted outside of the scope of current role in the company. The views and opinions expressed in this publication are solely those of the authors and do not necessarily reflect the official policy or position of company.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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