Objective: To establish appropriate reference values of upper extremity nerve conduction studies (NCS) at the Del Valle University Hospital, from Colombia.

Methods: Two hundred and twenty-two (N = 222) healthy volunteers were recruited. Latencies, amplitudes and conduction velocities from the Median, Ulnar, and Radial nerves were performed following recommendations from Buschbacher and Prahlow. Then, according to the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) task force for reference value establishment, analyses of variance were run where each electrophysiological parameter from every nerve tested was used as dependent variable, to define which characteristics have to be kept for the model. Percentiles 3 and 97 from each of the parameters were derived. Finally, a multivariate quantile regression analysis model was tested.

Results: Sensory percentiles were 2.8–3.5 ms, 18.9–120.8 μV, and 40.0–50.0 m/s for the Median, 2.1–2.9 ms, 10.4–106.9 μV, and 41.0–58.0 m/s for the Ulnar, while 2.6–3.5 ms, 11.3–69.9 μV, and 39.0–54.0 m/s for the Radial nerve. The same parameters for motor function were 2.8–3.9 ms, 4.6–15.0 mV, and 49.0–68.0 m/s for the Median, while 2.3–3.5 ms, 3.9–11.5 mV and 51.0–70 m/s for the Ulnar nerve.

Conclusions: Values of latency, amplitude, and conduction velocity of sensory and motor functions from upper extremity nerves among Colombians are similar to equal parameters, obtained by comparable studies of populations alike.

Significance: This is the first study to establish reference values for upper extremity NCS carried out following the AANEM recommendations in a South American population.

1. Introduction

Since 1939, when studies of nerve conduction velocity determinants were pioneered (Hursh, 1939), the number of these factors has only increased. Nowadays, it is well known how certain demographic characteristics such as age (Stetson et al., 1992; Kommalage and Gunawardena, 2013), gender (Stetson et al., 1992; Hennessey et al., 1994; Kommalage and Gunawardena, 2013), height (Rivner et al., 1990), and body mass index (Buschbacher, 1998) have a role in the determination of conduction velocity studies. Finger width (Stetson et al., 1992), laterality (Kommalage and Gunawardena, 2013), arm length (Hennessey et al., 1994), and proximality of measurements (Ongun and Oguzhanoglu, 2016) also play a part among the anthropometric ones. Others like temperature (Rutkove, 2001), and nerve’s histologic characteristics such as myelin thickness and internode distance (Waxman, 1980), or fiber diameter (Ritchie, 1982) and number (Waxman, 1980; Benatar et al., 2009), have been known to also influence results of nerve conduction studies (NCS).

Thus, the values chosen as references for human NCS affect not only the validity of clinical diagnoses, but also the inclusion to or exclusion of subjects from research studies. Despite the importance of these values, no universally accepted reference values exist. Also, the statistical approaches...
commonly used remark worth related to either measures of central tendency such as the average, or of dispersion such as the standard deviation, underestimating the importance of individual characteristics as some have noticed (Benatar et al., 2009). Nonetheless, the most updated reference values for human NCS published by the American Association of Neuromuscular and Electrodiagnostic Medicine – AANEM (Chen et al., 2016), still do not follow its own recommendations stated at the task force for quality of NCS reference value establishment (Dillingham et al., 2016).

Therefore, the main goal of this study was to establish appropriate reference values of upper extremity NCS for our clinical neuro-physiology laboratory at the Del Valle University Hospital (HUDV), from Cali, Colombia. These values are going to be calculated having into consideration their variation with age, gender, height, body mass index, occupation, hand dominance, and body temperature, according to the conclusions of the AANEM task force to establish NCS values (Dillingham et al., 2016). However, we are also going to bear in mind the particular mixed ethnic background, described for the segment of Colombia’s population living in this area of the country (Ossa et al., 2016).

2. Materials and methods

2.1. Participant’s selection

Visitors to the HUDV were personally asked by interviewers, if they were interested in participating on this research project. The group of interviewers was encompassed by students of the Universidad del Valle undergraduate programs of medicine, physical and occupational therapy, and were coordinated and trained by the investigators. Once visitants, who usually were companions to patients gave their approval, they were evaluated by a sub-group of interviewers to judge if they would match the inclusion criteria for the study. The recruitment took place during the period between October of 2015 and December of 2016. The inclusion criteria were defined as being 18 years of age or more, having no lifetime condition (inherited or acquired) that would predispose to a neuropathy diagnosis, or having any occupation (or work-related issue) that would make participants prone to have an entrapment neuropathy of the upper extremities, mainly carpal tunnel syndrome (CTS). The lifetime conditions subjects were asked included but were not limited to diabetes mellitus, hypothyroidism, chronic renal failure, and demyelinating diseases. Subjects were also interrogated about previous consumption of medications, particularly certain antibiotics, anti-tubercular, or chemotherapy agents, phenytoin or hydralazine, as well as chronic ingestion of alcohol or consueltudinary use of illicit drugs like glue sniffing. All these chemical compounds can produce drug induced neuropathy (Grosset and Grosset, 2004).

2.2. Subjects’ evaluation

All subjects who met inclusion criteria and agreed to participate were also applied a survey to rule out occupational hazards that could predispose to CTS. The survey was based in an instrument contained in an official document created for this same purpose, by the Colombian Ministry of Social Protection (Gutierrez, 2011; Burt et al., 2011). In addition, a short questionnaire about neuropathy symptoms restricted to the upper extremities, this time based on the first four sections of the Total Neuropathy Score (Cornblath et al., 1999) was applied to participants. If subjects had no occupational hazard, such as manipulation of toxic substances or use of heavy machinery and presented no symptoms of neuropathy in the upper extremities were allowed to participate in the study.

Those who qualified according to the two surveys, would undergo a standard neurologic exam focused in the upper extremities, which included: Tinel and Phalen tests, examination of superficial pain sensibility with the Semmes-Weinstein monofilament, and vibration sensibility testing of the upper extremities evaluated using a 128 Hz tuning fork (Goldberg and Lindblom, 1979). If the focused neurologic exam was normal, participants were invited to sign the written informed consent, which officially included them into the study. Subjects who had at least one positive finding in any of the two surveys, or the focused neurologic exam, were disqualified from their participation. Then, participants were given an appointment for NCS of the upper extremities to be carried out the next day by one of the Physical and Rehabilitation Medicine attendings of this clinical service, who usually perform this test at the HUDV. This study follows recommendations for research of the Helsinki’s declaration of human rights and had been previously approved by the ethics committee of the HUDV, as well as by the internal review board of The Universidad del Valle.

2.3. Neuro-conduction studies (NCS)

Participants were evaluated in the sited position, and neuroconduction studies of the Median, Ulnar and Radial nerves were performed at the left upper extremity in all subjects, to minimize the effect of hand dominance (Zambelli et al., 2010). Skin temperature was measured at the beginning of the testing with a battery operated K-type thermocouple of Chrome-Aluminum, for –50 to ~ 1300 °C (RS Components®, Stock No. 206–3722; Medifactory International, MFI BV, Heerlen, The Netherlands). For sensory studies, antidromic stimulation was performed with a standard Cadwell™ stimulator’s probe of 2.5 cm between electrodes and with the cathode positioned distal to avoid a possible anodal blockade (Kanbayashi et al., 2019; Wee et al., 2000). For the recording, digital-clips (MFI BV, FC-294 type) were used at the 2nd finger for the Median, while at the 5th digit for the Ulnar, and at the base of the thumb for the Radial nerve. Comparative Median/Ulnar recordings were taken from the 4th finger. For motor studies, stimulation was performed with the same type of stimulator’s probe than for the sensory studies, to the abductor pollicis brevis and abductor digiti minimi minimum muscles for the Median and Ulnar nerves testing, respectively. Standard stainless-steel surface, round electrode pairs (Cadwell® x1.0 cm of diameter) were used for the motor recordings, and the muscle-belly method was used for the muscles’ location. In all cases the ground used was a 3.0 × 3.0 cm surface metal electrode located in the back of the hand or forearm. We used a Cadwell® machine, type 12.1, version 1.2 equipped with Sierra™ wave software, 11.0.116, version 4.84 (The Cadwell® Corporation Inc. through their distributor in Colombia).

For the sensory studies of the Median and Ulnar nerves the stimulation was performed 14 cm proximal to the active electrode, while at 12 cm for the ones to the Radial. A sweep-speed of 2 ms/division and equipment sensitivity of 20 µV/division were used for visualization of these recordings. The band-pass filters were set-up at 10 Hz to 10 kHz for these studies. For the motor studies of the Median and Ulnar nerves, the distal stimulation was carried out 8 cm proximal to the active recording electrode, while the proximal stimulation at different places. For the Median nerve, the proximal stimulation was performed at the internal aspect of the Biceps brachialis insertion tendon. The proximal places of stimulation for the Ulnar nerve were located 1.5 cm distal or 7.5 cm proximal to the mid-point of a straight line from the condilum to the epi-condilum of the respective elbow, with this subtending an arc of approximately between 45 and 90 degrees of flexion. For motor studies, the band-pass filter setting used was the same than for the sensorial ones, while the sweep speed was 5.0 ms/division and the equipment sensitivity of 5 mV/division for visualization.
The stimulus duration used was 0.2 ms for all cases, and the intensity was progressively increased until a supramaximal level was obtained. Sensory latencies were measured from the stimulus artifact to the peak of the action potential, while motor ones to its origin. Amplitudes were all measured from baseline to peak. The conduction velocity for the sensory studies was automatically calculated by the equipment, while for motor studies introduction of the distance (in cm) between the proximal and distal points of stimulation, measured from each of these points used to stimulate, was required on each subject. All the parameters and distances were used according to recommendations for NCS of the upper extremity (Buschbacher and Prahlow, 2006).

2.4. Statistical analysis

The Shapiro-Wilk test was used to test the data for normality. Group differences were established by student-t statistics between the means of continuous variables, while by chi-square statistics between percentages for discrete ones. Once all the data was successfully obtained, independent one-way analyses of variance were performed for each one of the three most important electrophysiological parameters obtained (amplitude, latency and conduction velocity) from each one of the three nerves tested, Median, Ulnar and Radial. Thus, sensory and motor parameters were used as dependent variables in order to establish what demographic variables were significant, in order to keep them for the definitive models. Then, multiple quantile regression analyses of these variables were performed (Peng et al., 2009). The quantiles chosen to express the reference value intervals were percentiles 3, and 97, for each one of the electrophysiological variables mentioned above, from each of the nerves evaluated. The statistical significance (p) accepted for all tests was established at p ≤ 0.05. All statistical analyses were made using the commercially available SAS 9.4® (TS1M6) statistical software version SAS/STAT 15 for the Windows® platform (University of New South Wales Department of Information Technology, under license No. EASS49899 from The SAS Institute Inc., Cary, North Carolina, USA).

3. Results

Three hundred and two subjects were invited by the interviewers to participate in the study during the period between October of 2015 and December of 2016. Two of the individuals approached still did not have 18 years of age. Of all individuals targeted, seventy-eight (26%) were excluded from their participation because they completed at least one exclusion criterium. Fourteen subjects (4.7%) suffered of at least one of the diseases representing a risk factor for neuropathy, and the first survey detected 16 (5.3%) individuals who had issues related either to manipulation of heavy machinery, toxic substances, or a profession which made them prone to develop a CTS. The second survey identified 14 (4.7%) people with symptoms of compression neuropathy in the upper extremities. Additionally, 8 (2.7%) possible participants were found to have at least one sign related either to a cervical radiculopathy, or a brachial plexopathy according to the focused neurologic exam. Thirteen subjects (4.3%) never attended the appointment to have their NCS performed. Three persons (1%) resigned from the study because did not tolerate the electrical stimulation, and 10 subjects (3.3%) were excluded after performing the NCS, because they had asymptomatic, electrophysiological findings of a CTS diagnosis. Thus, the final number of participants of this study were two hundred and twenty-two (N = 222).

A comparison of the characteristics between the groups of subjects included and excluded from the study showed the mean age (t = 235.515; degrees of freedom – d.f. = 1,221; p < 0.0001) and hand dominance (F value – F = 6.361; d.f. = 1,221; p = 0.012) had different statistically significant differences (see Table 1). The gender ratio was 0.98 with 110 females (49.6%) and 112 males (50.4%). Participants had an average age (plus or minus SD) of 40.04 ± 14.6 years, with a range from 18 to 81. Their average weight was 67.61 ± 11.95 kgs, with a height of 1.64 m ± 18 cm. The average body mass index was 24.72 ± 3.25 kg/m², and the temperature found was always above 32 °C when starting the procedure, with a mean (range 35.0–38.2 °C) of 36.17 ± 0.63 °C.

After performing all the initial independent one-way analysis of variance for each one of the electrophysiological parameters (amplitude, latency and conduction velocity) obtained from each of the nerves evaluated (Median, Ulnar and Radial) as dependent variables, it was found that height and temperature were significant (p < 0.05) in at least 58.8% of these analyses, while age and gender in at least 41.2% of them. Thus, height, temperature, age and gender were the variables to keep for the multiple quantile regression analyses.

The values of the estimated percentiles 3, 50, and 97 for each one of the electrophysiological parameters, evaluated from each one of the 3 nerves tested (Median, Ulnar, and Radial), as well as the values of the most important factors from each one of the mul-

| Characteristic | Value (units) | Participants(N² = 222) | Excluded(N = 78) | Probability test (value) | p² |
|---------------|--------------|------------------------|-----------------|--------------------------|----|
| Age: Average (years) | 40 | 47 | t' (235.515) | <0.0001 |
| Range (min - max) | (18–81) | (18–77) | χ² | 0.06 |
| Gender: Female n(%)/f | 110 (49.6) | 49 (64.5) | F | 0.398 |
| Male n (% | 112 (50.4) | 27 (35.5) | | |
| Ethnicity: African n (%) | 35 (15.8) | 16 (22.5) | | |
| Indigenous n (%) | 9 (4.0) | 2 (2.8) | | |
| Hispanic n (%) | 21 (9.5) | 9 (12.7) | | |
| Mixed n (%) | 157 (70.7) | 44 (62.0) | | |
| Hand dominance | Right n (%) | 205 (92.3) | 56 (80.0) | F | 0.012 |
| Left n (%) | 11 (5.0) | 12 (17.1) | | |
| Ambidextrous n (%) | 6 (2.7) | 2 (2.9) | | |

(items): N: Total number of subjects by group.
(²): t: Probability value under the student-t distribution.
(²): t: Probability value under the F distribution.
(²): χ²: Probability value under the chi-square distribution.
(²): %: Percentage.
The values of the calculated percentiles 3, 50, and 97 did not show significant differences when the population sample was divided either by gender, or by age according to if subjects were younger and/or older than 40 years of age. However, there were important differences when the population was stratified according to decades of their ages. These values are shown in Table 3.

### 4. Discussion

To the authors' knowledge, this is the first study of reference values for upper extremity NCS carried out following the recommendations of the AANEM (Billingham et al., 2016) in the Latin American area, which has also been published in the English language literature. Our results are closely congruent with two different studies recently published, done in populations very similar to ours.
(Hidalgo et al., 2009; Ortiz-Corredor and López-Monsalve, 2009). The first of these studies recorded the same parameters that we did, but it did not follow the AANEM methodology, and was carried out in Honduras (Hidalgo et al., 2009). The second of these studies took place in our country’s capital Bogotá, but it just looked at some of the same electrophysiological parameters we did. It measured only distal motor and sensory latencies from the Median and Ulnar nerves, because, this work was performed with a completely different purpose. Also, although this study was carried out in a population of our own contemporaries, Colombians living in the Andean zone of the country where this study took place, have not only a different ethnic background (Ossa et al., 2016), but the geographical difference between that central and elevated city, is abysmal with ours located in the warmer seashores of the Pacific ocean of Southwestern Colombia, making our temperatures always higher (Ortiz-Corredor and López-Monsalve, 2009). It is however noticeable, that we found significant influence of age (Stetson et al., 1992; Kommalage and Gunawardena, 2013; Hennessy et al., 1994), and height (Rivner et al., 1990) but not of body mass index, as well as negative correlation between height and velocity as several other studies carried out in very different areas of the world, such as the ones from North America (Benatar et al., 2009; Chen et al., 2016) or Asia (Fong et al., 2016) have recently informed.

Among the strengths of our study we have: 1. The especial care taken to select a population sample of real healthy participants for the study, manifested in the diverse, multiple and sequential screening measures employed, such as even considering occupational risk factors for CTS (Gutierrez, 2011; Burt et al., 2011). 2. The representation in the population sample of all types of ethnic backgrounds existent in the inhabitants of this zone. This characteristic makes this study effectively representative of the population from this area of the country. 3. The inclusion in the models of several covariates, as well as 4. The novel type of statistical techniques used during this study. To notice, the multiple quantile regression analysis is not only versatile and easy to apply, but in fact, it has been established that can be utilized with data which does not follow a Gaussian, normal distribution (Peng et al., 2009; Staffa et al., 2019). Also, instead of what happened in the past with this situation and other statistical techniques, there is no need to manipulate the data obtained during attempts to its transformation/normalization. 5. We did not find highly different reference values than the American ones that we currently use in our laboratory (DeLisa, 1982).

It is also important to highlight, not only that by finishing this study our results are going to fill a vacuum that has existed in the medical literature of our country for a long time, but very likely our results are going to become reference values for upper extremity NCS of a vast area of Colombia. It is also noticeable, these reference values were developed according to recommendations of the AANEM for the acquisition of these type of ciphers, but also in agreement with its last task force on this issue (Dillingham et al., 2016).

One of the limitations of this study was to try finding healthy subjects in the segment of the population older than 60 years old. Although, we consider this a normal situation in a developing country with predominance of younger population, we had to specifically target these participants and were able to recruit only 8% of the population sample from this age stratum.

Of note, one of the most important limitations when recording upper extremity NCS its the low interrater reliability values of Ulnar nerve conduction velocity measurements (Schuhfried et al., 2017) as well as change in the amplitude of the action potentials recorded, also especially among those carried out at the Ulnar nerve (Johnsen et al., 2006). The reason being is, the elbow and shoulder positions must be standardized and held during the execution of the tests. If this is not properly done, the great length of reserve of this nerve can be responsible for changes in the value of its velocities between 0.8 and 2.9 m/s (Hsu and Robinson, 2019). In our case, we had exactly this problem with the first subjects evaluated, until we find out a way to keep the position of these two important joints steady but comfortable, with the help of foam pillows during the time participants were being evaluated.

In conclusion our study supports the AANEM’s task as probably the best current publication of how to correctly establish reference values for nerve conduction studies. The methods suggested on this publication are not only simple and easy to apply, but they produce results such as the ones we obtained, in agreement in general to international studies, and closely correlated to most of the studies performed in similar populations.

Authorship statement

All authors contributed equally to the design, planning, interviewers’ training, data analysis, writing and correction of this study. Unfortunately, Miss Cantor and Dr. Habeych were not able to be present for the data collection. The performance of the neuro-conduction studies was carried out by Drs. EAE, SPG, CA de los RG, and ALM.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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