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Comparing electrical stimulation with and without ultrasound guidance for phenol neurolysis to the musculocutaneous nerve

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Abstract

Background—Ultrasound guidance is increasingly being used for neurolytic procedures that have traditionally been done with electrical stimulation (e-stim) guidance alone. Ultrasound visualization with e-stim guided neurolysis can potentially allow adjustments in injection protocols that will reduce the volume of neurolytic agent needed to achieve clinical improvement.

Objective—This study compared e-stim only to e-stim with ultrasound guidance in phenol neurolysis of the musculocutaneous nerve (MCN) for elbow flexor spasticity. We also evaluated the ultrasound appearance of the MCN in this population.

Design—Retrospective review

Setting—University hospital outpatient clinic

Participants—Adults (N=167) receiving phenol neurolysis to the MCN for treatment of elbow flexor spasticity between 1997 to 2014 and adult control subjects.

Methods—For each phenol injection of the MCN, method of guidance, volume of phenol injected, technical success, improved range of motion at the elbow post-injection, adverse effects, reason for termination of injections and details of concomitant botulinum toxin injection were recorded. Ultrasound appearance of the MCN, including nerve cross-sectional area and shape were recorded and compared between groups.

Main Outcome Measures—Volume of phenol injected and MCN cross-sectional area and shape as demonstrated by ultrasound

Results—The addition of ultrasound to e-stim guided phenol neurolysis was associated with lower doses of phenol when compared to e-stim guidance alone (2.31 mL vs 3.69 mL, $p<.001$). With subsequent injections, the dose of phenol increased with e-stim guidance ($p<.001$), but not with e-stim and ultrasound guidance ($p=.95$). Both methods of guidance had high technical

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success, improved ROM at elbow post-injection and low rates of adverse events. In comparing the ultrasound appearance of the MCN in patients with spasticity to normal controls, there was no difference in the cross-sectional area of the nerve, but there was more variability in shape.

Conclusions—Combined e-stim and ultrasound guidance during phenol neurolysis to the MCN allows for a smaller volume of phenol to be used for equal effect both at initial and repeat injection. MCN shape was more variable in individuals with spasticity; this should be recognized in order to successfully locate the nerve to perform neurolysis.

Introduction

Spasticity is a common complication of central nervous system disorders, including spinal cord injury, traumatic brain injury, stroke, cerebral palsy and multiple sclerosis. Elbow flexor spasticity in these populations may cause pain, increased difficulty with self-care tasks, and gait imbalance due to oblige arm positioning. Neurolysis of the musculocutaneous nerve (MCN) with alcohol or phenol is an accepted method of treatment for elbow flexor spasticity [1,2]. Traditional methods for targeting the MCN for phenol neurolysis include a blind approach with use of anatomic landmarks or electrical stimulation (e-stim) needle guidance [1].

Use of ultrasound for imaging of peripheral nerves and for guidance of neuromuscular procedures is an area of growing interest. Two small studies of 8 and 10 patients described the use of ultrasound guidance for neurolysis to the MCN to treat spasticity [3,4]. However, these papers made no comparison to traditional methods of guidance. During e-stim guidance alone (e-stim), nerve localization is blind and tenuous requiring many small needle movements with varying stimulation intensities in order to find the nerve. Once the nerve is optimally located, a generous volume of phenol is rapidly injected before the positioning is lost. The subsequent layering of the neurolytic agent is unknown with this technique as the injectant may surround the nerve, but it may also disperse away from the nerve to nearby muscle tissue. The addition of ultrasound to e-stim guidance (e-stim+US) provides direct visualization of the nerve, allowing injection protocols to use smaller aliquots of phenol to surround the nerve in a process termed hydrodissection. Hydrodissection ensures that the fluid is placed around the targeted structure with minimal dispersion. This inherent advantage of e-stim+US may result in lower total volumes of injected phenol, potentially limiting surrounding tissue fibrosis that could cause pain or joint contracture, and make future injections more challenging.

The appearance of the MCN under ultrasound has been described extensively in healthy subjects [5,6,7,8], including reference values for the cross sectional area (CSA) [5,6,9,10]. However, ultrasound appearance of the MCN in disease states has rarely been reported. In 7 patients with MCN neuropathy diagnosed by electromyography, ultrasound findings showed a fusiform neuroma in 5 cases, focal swelling in 1 case and no abnormality in 1 case [6]. It is conceivable that spasticity could alter the ultrasound appearance of the MCN due to increased muscle tone of the elbow flexors. Such changes in nerve appearance would need to be appreciated during e-stim+US injections in order to successfully and expeditiously visualize the nerve.

The aim of this study is to retrospectively compare our experience using e-stim+US guidance to e-stim guidance alone for phenol neurolysis of the MCN in participants with elbow flexor spasticity. Secondly, we aim to evaluate its appearance and CSA in participants with spasticity compared to normal controls.

Methods

Participants

The study protocol was approved by the Institutional Review Board of our institution. A retrospective review of medical charts of all patients consecutively treated in our outpatient spasticity clinic from January 1997 to September 2014 was performed. Participants were included in the study if: 1) They were at least 18 years old at initial review and 2) they underwent phenol neurolysis of the MCN to treat elbow flexor spasticity. Medical charts were reviewed for each participant and the following data were recorded: age, gender, diagnosis, number of injections and reason for terminating injections.

For each injection, the following data were recorded: date of injection, method of guidance, volume of phenol injected, side of injection, if the injection was technically successfully, if the injection was qualitatively successful (range of motion (ROM) at the elbow was improved post-injection) and any adverse effects. It was also recorded if the participant underwent injection with botulinum toxin at that same visit and if so, the type of toxin, the total dosing and the dose to the elbow flexor muscles (biceps brachii, brachialis and brachioradialis). When available, the change in Modified Ashworth Scale (MAS) and elbow ROM pre- and post-injection were also extracted. For each participant, the reason for discontinuing injections was recorded if applicable.

Comparison of Methods of Guidance

Technique with E-stim Guidance

When using e-stim guidance alone, the participant was positioned supine with the affected arm closest to the practitioner. If possible, the arm was abducted to 90 degrees and externally rotated to 90 degrees with the elbow flexed. However, underlying spasticity often limited arm abduction. The head of the biceps was palpated in the upper arm. At this point, a 37 or 50mm monopolar injectable needle was inserted. The nerve stimulator was set at 10mA of current and the needle was advanced and repositioned multiple times until the proper motor response (elbow flexion) was seen. The stimulator was turned down in increments with further repositioning of the needle until the elbow flexion response was seen at the target threshold. Ideally, this was 1mA, but at times a higher stimulus threshold was used due to positioning challenges. After meticulously moving the injectable electrode to get an ideal location at the lowest possible stimulus threshold, 1.0 cc of 6% sterile aqueous phenol was injected. The stimulator was turned back on and if the motor response was still observed, another 1.0 cc was injected until the motor response was extinguished. The needle would then be repositioned if necessary and the protocol described above was repeated. The injection was terminated when no further response was elicited and reduction in elbow flexor tone was appreciated. As described, this localization was time consuming, uncomfortable for many patients and challenging for the practitioner as the targeted

stimulation could easily be lost with small needle movements. Therefore, our protocol used 1.0cc aliquots of phenol aimed at extinguishing nerve excitability quickly before localization was lost. After the injection, it was noted whether elbow ROM was improved.

Technique with Ultrasound and E-stim Guidance

For phenol neurolysis of the MCN with e-stim+US guidance, the participant was positioned as described with the e-stim only technique. A GE LOGIC e ultrasound machine (GE Healthcare, Wauwatosa, WI, USA) was used with a 12 MHz linear array transducer. The probe was placed on the arm at the level of the pectoralis major tendon insertion on the humerus, in transverse view to the course of the axillary artery. The vertical angle of the transducer was maintained perpendicular to the nerve and the probe was placed on the skin with the minimum pressure necessary to obtain proper image quality. From this location, the practitioner scanned distally to the point of the best visualization of the MCN in the proximal upper arm.

The practitioner inserted a 37 or 50mm monopolar injectable needle using an in-plane approach from lateral to medial. The nerve stimulator was set at 10mA of current initially to ensure that the target produced the proper motor response (elbow flexion) and then turned down incrementally to 1mA. However, unlike the e-stim only protocol, if the nerve was visualized and there was a proper motor response, the threshold stimulus did not require precise adjustments to the lowest stimulation since visualization with ultrasound was the most important localization for the injection. Often the stimulator was turned off to avoid arm movement when injecting to allow precise placement of the injectant using ultrasound. The goal of ultrasound guidance was to layer the neurolytic agent around the nerve via hydrodissection and avoid fluid dispersion to nearby muscle tissue and blood vessels. Hydrodissection can be achieved with smaller aliquots using 0.25cc of 6% sterile aqueous phenol at a time. The injection was repeated until the practitioner had hydrodissected the nerve, creating a target sign around it (Figure 1). The post-injection evaluation was the same as described in the e-stim only technique.

Comparison of ultrasound appearance of the MCN—This additional study protocol was approved by the Institutional Review Board of our institution. Normal controls provided written informed consent. We compared saved ultrasound images of the MCN in patients with spasticity prior to phenol neurolytic injection to ultrasound images collected from normal controls recruited for comparison.

Spasticity group

We retrospectively searched the archive of ultrasound images to find saved images of patients with spasticity undergoing phenol neurolysis of the MCN for the first time. From these saved images, the best visualization of the MCN was used in the analysis. Based on arm positioning, we attempted to image the nerve at the same relative location since all images were recorded by 1 physician. We did not include subsequent injections because scarring of the nerve from the injection theoretically could cause changes in size or appearance. Additional data including weight, height and body mass index (BMI) was extracted from the medical charts where available.

Normal controls

Normal controls over the age of 18 were recruited from May to June, 2016. Recruitment ended when the number of controls recruited was the same as the number of patients with ultrasound images available to review. Controls were age and gender matched to patients. Exclusion criteria were 1) history of neurologic disease 2) history of surgery to the right upper arm or 3) unexplained pain or weakness in upper arm or elbow. Demographic data including age, gender, height and weight were collected at the time of enrollment. BMI was calculated as the weight in kilograms divided by the square of the height in meters [11]. The ultrasound images were obtained using the standard protocol described above.

Measurements

For each image of the MCN, two independent reviewers measured the CSA by tracing around the hyperechoic rim and the mean value was calculated. The shape of the nerve was described as triangular, round, oval or flat. The nerve was considered round if the x and y axes were approximately equal (Figure 2-A). It was considered flat if one axis was greater than two times as long as the other axis (Figure 2-B). It was considered triangular if there was a 3 cornered appearance (Figure 2-C). It was considered oval if the x and y axis were asymmetrical, but it was not flat or triangular (Figure 2-D). In cases where the reviewers differed, the first reviewer's description was used. A single reviewer measured the distance from the surface of the skin to the nerve and from the nerve to the axillary artery. Distance from the surface to the nerve was measured from the surface of the skin to the center of the nerve, parallel to the ultrasound beam. Distance between the axillary artery and the nerve was measured from center of the nerve to center of the artery.

Statistical Analysis

For the analysis of each unique participant's first injection, the participants were divided into those whose first injections were done using e-stim+US guidance versus those whose injections were done using e-stim guidance alone. The age, gender, diagnosis, adverse effects, mean volume of phenol, mean total units of botulinum toxin injected, technical success, qualitative success and mean units of botulinum toxin injected to the elbow flexors for each method of guidance were described. For all analyses regarding botulinum toxin, only those subjects injected with onabotulinumtoxinA were included, as this represented the vast majority of patients and toxin units were not comparable between types. The methods of guidance were compared using either a chi-square test or t-test where appropriate. Volume of phenol and units of botulinum toxin were analyzed as continuous variables. No transformation was applied.

For both groups, the change in MAS and elbow ROM pre and post-injection and the reason for termination of injections was described, but because this data was only available in a small subset of participants, no comparison was done between groups.

To assess injections over time, participants were excluded if they had injections done on both sides. Using linear generalized estimating equations (GEE) models with clustered robust standard errors to adjust for within-subject correlation over time, we compared the volume of phenol, the total amount of botulinum toxin, and the amount of botulinum toxin

to the elbow flexors between comparison groups defined on the injection level as e-stim+US guidance versus e-stim guidance alone.

In analyzing the ultrasound images of the MCN, demographic characteristics (age, gender, height, weight, BMI), and nerve measurements and shape were compared between patients and controls. For nerve CSA, interrater reliability was checked via intraclass correlation coefficient (ICC). For descriptions of shape (oval, round, flat, or triangular), Cohen's kappa was used.

Demographic characteristics and nerve measurements and shape were evaluated using Chi-square analysis, Fisher's Exact Test or T-test, where appropriate. Furthermore, correlations between nerve CSA and demographic characteristics were tested using Chi Square analysis or T-test.

In all analyses, two-sided p-values < .05 were considered statistically significant. All analysis was carried out in IBM SPSS version 24 (IBM Corp., Armonk, NY). Observations with missing data were excluded from analysis.

Results

Baseline Subject Characteristics

Of the patients evaluated during this study period, 167 participants met inclusion criteria. For the patients' first injection, 46 used e-stim+US and 121 used e-stim localization. E-stim was used almost exclusively from 1998–2008. There was a period of overlap from 2009–2011, as e-stim+US was introduced to the practice. E-stim+US guidance has been used exclusively since 2012. There was no significant difference in age, gender or diagnosis between groups (Table 1).

Comparison of Methods of Guidance for First Injections

The e-stim+US group had a significantly lower volume of phenol injected than the e-stim group (2.31 mL vs 3.69 mL, $p < .001$) (Table 1, Figure 3) during the first injection. Adverse effects were similar between groups. (Table 1).

Injections were reported as technically successful and post injection elbow ROM was reported as improved nearly universally regardless of method of localization (99% technically successful and 99% with improved elbow ROM post injection for both methods of guidance).

Further outcome measures were available only in a small subset of injections with this retrospective review. 12% had MAS documented pre and post injection ($n=24$ in e-stim group, $n=4$ in e-stim+US group) and 17% had change in elbow ROM documented in degrees ($n=9$ in e-stim group, $n=11$ in e-stim+US group). Both groups showed improvement in MAS (1.52 with e-stim guidance and 1.75 with e-stim +US guidance) and elbow ROM post-injection (31.1 degrees with e-stim guidance and 40.9 degrees with e-stim+US guidance), but the small sample size precluded statistical comparison. Only 3 injections were recorded as unsuccessful and these were all in the e-stim group. Documented reasons for terminating

injections included: 1) adverse effects 2) treatment not effective 3) injections technically challenging and 4) sustained benefit from prior injection, but again the small numbers precluded statistical comparison (Table 2).

For botulinum toxin, the total toxin dose, the dose to elbow flexors and the percentage of participants receiving toxin to the elbow flexors were similar between groups for the first phenol injection (Table 1).

Comparison of Methods of Guidance over Time

Of the 167 participants, 11 were excluded due to bilateral MCN nerve injections that would make tracking of the same nerve injected over time difficult to study. For the remaining participants, there were 421 injections and 274 used e-stim and 147 used e-stim+US. E-stim+US continued to be associated with lower doses of phenol than e-stim only with repeated injections ($p<.001$, Figure 4). Furthermore, with subsequent injections, the dose of phenol increased in the e-stim group ($p<.001$), whereas it did not increase in the e-stim+US group ($p=.95$) (Figure 4).

Total dose of botulinum toxin increased with each subsequent injection ($p<.001$), but dose to elbow flexors was stable ($p=.77$). Neither total dose nor dose to elbow flexors was associated with method of guidance ($p=.22$ and $p=.78$ respectively).

Comparison of Ultrasound appearance of the MCN

Ultrasound images in the spastic limb were available in 33 individual patients undergoing their first MCN phenol injections of which 29 had an identifiable nerve that allowed measurement. In 2 patients, only the motor branch was visualized and in 2, the nerve could not be identified. The left arm was scanned in 69%. For 3 patients, weight and height information were not recorded. In 14, the artery was not visible in the saved image.

We scanned 29 arms on 29 healthy controls. The MCN was visualized and measured in all controls. There was no significant difference between groups in age, gender, height, weight or BMI. There was no significant difference between patients and normal controls in CSA, distance to surface, or distance to artery indicating that the relative scanning location was similar between patients and controls (Table 3). There was a difference in nerve shape between the 2 groups with normal controls almost universally being described as 'oval' or 'triangular', while the patients with spasticity had more 'round' and a few 'flat' nerves ($p<.001$, Table 3).

The Intraclass Correlation Coefficient to measure interrater reliability between the 2 independent reviewers was .81 in the normal controls and .87 in the spasticity patients. Likewise, for the descriptions of shape, the Cohen's kappa statistic was .81 in normal controls and .90 for patients with spasticity. This indicates high interrater reliability for both nerve CSA measurements and shape description.

Discussion

We hypothesized that the injection protocol using e-stim+US would allow hydrodissection of the MCN nerve resulting in lower phenol doses. Indeed, our data demonstrate that the volume of phenol used in first injections is significantly reduced using e-stim+US as compared to e-stim alone. With repeated injections, volume of phenol increased over time using e-stim alone, but not using e-stim+US. The mean volume injected with e-stim+US in our study is comparable to the volume of local anaesthetic reported in the anesthesiology literature of 2.30mL to completely surround the MCN using ultrasound [12] and even less than the 2.9mL mean volume of phenol used in the previous study of 10 hemiparetic stroke patients [3]. Several factors may explain the advantage of e-stim+US. With ultrasound guidance, one can visualize the injectant surrounding the nerve, minimizing fluid dispersion to nearby muscle and blood vessels. With e-stim only, no such feedback exists. Also, the ability to use smaller aliquots allows termination at a lower effective dose. It is important to note that though the dose of phenol used with e-stim+US was lower than with e-stim, clinical effectiveness was equivalent. Finally, even though a muscle twitch with e-stim at low current suggests the needle tip is close to the nerve, the needle can be oriented in a way that spreads injectant away from the nerve and this can only be appreciated with ultrasound. The ability to maintain stable, non-escalating doses of phenol with e-stim+US, but not with e-stim only is also an advantage. Repeat phenol neurolysis to the MCN nerve can become more challenging as scarring occurs to the nerve and surrounding tissues from the effects of phenol. E-stim+US guidance may reduce surrounding tissue changes with the smaller doses utilized and can better achieve nerve localization even in the presence of tissue fibrosis.

Ultrasound guidance for MCN blocks has previously been described in 2 studies with good results. In 6/8 patients, Lee performed intraneural phenol injection with ultrasound guidance alone and achieved a longer effective duration (>400 days) [4]. In another study of 10 hemiparetic stroke patients who underwent e-stim+US guided alcohol neurolysis to the MCN, reduction in elbow flexor tone was observed immediately in all 10 patients and maintained at 2 month follow up [3]. It seems intuitive that identifying the nerve and visualizing needle placement would improve localization, compared to use of anatomic landmarks or blind electrical stimulation probing. This is especially true in the case of the MCN, in which variable anatomy has been described [13]. However, neither of these studies directly compared different methods of guidance.

There was a low incidence of reported dysesthesias, swelling or other adverse effects in both groups. The low reported rate of dysesthesias with either method of guidance falls at the low end of the previously reported range of 2-32% [14]. This may be explained by the retrospective review of the medical record; if the participant had transient dysesthesias that were not reported, this would have been missed. There was no difference in botulinum toxin dosing to the elbow flexors related to method of guidance. However, no matter the method of guidance, the total dose to the elbow flexors was relatively low compared to other studies in which onabotulinumtoxinA was used for the treatment of elbow flexor spasticity [15,16,17]. This dose included toxin to the brachioradialis, which is not innervated by the MCN and thus would not be treated by phenol neurolysis. This suggests that phenol

injections to the MCN had a dose sparing effect to the elbow flexors and potentially allowed toxin to be utilized in other muscle groups.

To perform successful e-stim+US guided phenol neurolysis to the MCN, the practitioner must be able to identify the nerve in individuals with spasticity. In our clinical experience, the nerve can be harder to identify under ultrasound in individuals with spasticity. To understand the reasons for this, we compared the ultrasound appearance of the nerve in patients with spasticity to normal controls. As expected, the nerve was more difficult to identify in patients with spasticity. In our post hoc ultrasound image review, it could not be identified in 4 patients with spasticity, compared to successful visualization in all normal controls. In terms of MCN size, there was no significant difference between the spasticity and normal control groups and mean CSA values for both were within range of previously reported normal controls [5,6,9,10]. With regards to shape, there was greater variation in the spasticity group compared to normal controls where it was most commonly oval or triangular. This could be caused by the hypertonicity of the surrounding muscles or by the positioning limitations related to spasticity.

In order to perform a successful neurolytic block, it is important for the practitioner to recognize that the MCN may be more difficult to identify under ultrasound in individuals with spasticity and careful positioning is needed. It is also important to recognize that the MCN may have a different shape and appear unexpectedly round or flat in this population compared to healthy normal subjects.

Limitations

Limitations of this cohort study include the retrospective nature that resulted in an unbalance number of participants between groups, incomplete quantitative outcome measures (post-injection MAS and degree improvement in elbow ROM), possible underreporting of adverse events and absence of power analysis. Future prospective studies confirming the primary findings would be helpful to recommend e-stim plus US guidance as the standard of care for phenol neurolysis to the MCN.

Conclusions

For treatment of elbow flexor spasticity, the addition of ultrasound to e-stim guidance is beneficial when performing phenol neurolysis to the MCN. E-stim+US guidance allows for smaller total volumes of phenol both at first injection and with repeat injections because direct visualization results in hydrodissection without dispersion to nearby tissue. The MCN can be more difficult to identify in individuals with spasticity because of variable shape. Understanding these differences in this population can help practitioners to perform this procedure successfully.

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Figure 1. Transverse (short axis) ultrasound image of in-plane approach of the needle (black arrow) injecting phenol around musculocutaneous nerve (between arrowheads), creating a target sign (white arrow). *Aa* axillary artery; *H* humerus

Figure 2.

Transverse (short axis) ultrasound images of musculocutaneous nerves (between arrowheads) in the axilla and upper arm, demonstrating the variable shape of the nerve. A) round B) oval c) flat d) triangular. *Aa* axillary artery; *Av* axillary vein; *H* humerus. These four scans were obtained in different volunteers or patients.

Figure 3.
Comparison of volume of phenol injected by method of guidance for first injections

Figure 4.
Comparison of volume of phenol injected by method of guidance over subsequent injections

Table 1

Comparison of methods of guidance in first phenol injection to the MCN

		E-Stim Only (n=121)	Ultrasound and E-Stim (n=46)	p value
Age (SD)		53 (18.4)	55 (14)	.49
Gender (female)		61 (50.4%)	25 (54.3 %)	.78
Diagnosis	Stroke	70 (57.9%)	33 (71.7%)	.11
	TBI	24 (19.8%)	7 (15.2%)	
	SCI	4 (3.3%)	4 (8.7%)	
	Cerebral Palsy	16 (13.2%)	1 (2.2%)	
	MS	4 (3.3%)	1 (2.2%)	
	Other	3 (2.5%)	1 (2.2%)	
Volume of Phenol mL (SD)		3.69 (1.5)	2.31 (0.893)	<.001
Total Botulinum Toxin Units (SD)		378 (109)	381 (105)	.87
Total Toxin to Elbow Flexors Units (SD)		68.1 (45)	58.4 (38)	.40
Number receiving Toxin to Elbow Flexors		59 (54.1%)	20 (45.5%)	.33
Adverse Effects	Dysesthesias	5 (4.1%)	2 (4.3%)	.49
	Swelling	2 (1.7%)	1 (2.2%)	
	Other	1 (0.8%)	2 (4.3%)	

Table 2

Reasons for Discontinuing Injections

	E-stim Only (121)	Ultrasound and E-stim (46)
Adverse Effects	1 (0.8%)	1 (2.2%)
Sustained Benefit	7 (5.8%)	10 (21.7%)
Technically Challenging	5 (4.1%)	5 (10.9%)
Treatment Not Effective	2 (1.7%)	2 (4.3%)

Table 3

Nerve measurements and characteristics

		Normal Controls (n=29)	Spasticity (n=29)	p-value
Nerve area mm ² (SD)		6.76 (1.95)	6.21 (1.78)	.27
Distance to surface cm (SD)		1.49 (0.44)	1.35 (0.36)	.18
Distance to artery cm (SD)		1.34 (0.62)	1.44 (0.58)	.62
Nerve Shape	Triangular	14 (48.3%)	8 (27.6%)	.001
	Oval	14 (48.3%)	8 (27.6%)	
	Round	0	10 (34.5%)	
	Flat	1 (3.4%)	3 (10.3%)	