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The Role of CT and MR Myelography in Diagnosing Nerve Root Avulsion in Traumatic Brachial Plexus Injuries: A Meta-analysis

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ABSTRACT

The diagnosis of nerve root avulsion in traumatic brachial plexus injuries is important to help the surgeon pre-operatively decide which specific surgery to be performed. The goal of the study was to conduct a meta-analysis comparing Computed Tomography (CT) myelography and Magnetic Resonance (MR) myelography in diagnosing nerve root avulsion in traumatic brachial plexus injuries. The authors endeavored a systematic review and meta-analysis of the literature to determine the diagnostic accuracy of CT and MR myelography in the diagnosis of nerve root avulsion in traumatic brachial plexus injuries. A structured search of literature was conducted in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines to include all relevant articles. The assessment of the methodological quality of articles was reviewed in accordance to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool. Data was extracted for construction of two-by-two contingency tables. Meta- analysis was performed if there were 3 or more studies belonging to either CT or MR myelography. This study showed that MR myelography has higher sensitivity and specificity than CT myelography in diagnosing nerve root avulsion in traumatic brachial plexus injuries.

Key words: Diagnostic, CT myelography, MR myelography, brachial plexus, meta-analysis, nerve root avulsion

INTRODUCTION

Brachial plexus injury is an uncommon consequence of birth trauma, vehicular accidents or other sports-related injuries. Majority of these cases require immediate diagnosis and surgical intervention especially if they involve penetrating trauma or global brachial plexus palsy which if not addressed adequately, may result in life-long neurologic morbidities including intractable pain with motor, sensory and autonomic dysfunctions[1]. Studies have shown that early repair of these injuries results in better neurologic outcomes[2,3]. It is therefore imperative that the precise anatomy of the injured brachial plexus be accurately delineated thru advanced imaging techniques to come up with the appropriate surgical procedure to obtain optimal post-operative results.

One of the most important types of brachial plexus injuries is nerve root avulsion. It is important to differentiate whether the lesion is pre-ganglionic or post-ganglionic as this has an implication in the patients' prognosis especially after surgery[4]. Anterior roots may be involved with or without the posterior rootlets. On the other hand, the rootlets on C5 and C6 are less commonly avulsed because of their strong fascial attachments with the spine[5].

The diagnostic approach of brachial plexus injuries utilizes an array of electro-physiologic and biochemical studies. The histamine test is a biochemical test that is used to determine whether the injury is pre or post ganglionic. If the lesion is proximal to the dorsal root ganglion, a flare in an unconscious skin area will be elicited. This test has a reliability of 80%[5]. Electro-diagnosis is an important tool to localize the pathology and determine the extent of brachial plexopathies. Its utility extends from the pre to the post-operative period. Some studies have also noted that its use is more appreciated than CT or MRI in the localization of such disorders[6].

The brachial plexus is a complex network of nerves responsible for upper extremity innervation. The rootlets of the cervical roots are arranged in a peculiar manner within the spinal cord, which make them vulnerable to avulsion injuries. They are also devoid of any connective tissue and meningeal coating and they move freely within the intervertebral for amina making them susceptible to nerve damage.

As emphasized, neuroimaging plays an important role in the pre-operative planning of brachial plexus injuries. It is essential to distinguish between intra and extra-foraminal root avulsions as surgical interventions vary depending on the type of injury[7]. CT myelography is used to identify nerve root avulsions with high specificity. It was considered superior to MR myelography in the diagnosis of brachial plexus injuries, however, it was considered an invasive technique and predisposes patients to risks of infection, increased exposure to radiation and possible reaction to contrast material[8]. MR myelography, on the other hand, has the advantage of being non-invasive and studies have shown that its predictive value is comparable to that of CT myelography. It has also been shown to be superior to CT myelography in identifying pseudo-meningoceles, which emphasizes the latter, by super positioning the multiple images by three-dimensional reconstruction on MR myelography[8].

While the currently accepted gold standard for the diagnosis of brachial plexopathies is CT myelography, MR myelography has shown promising advantages over the former. However, there are no large-scale studies, which provide a head-on comparison between these two neuroimaging modalities. In this study, the aim was to conduct a meta-analysis comparing CT myelography and MR myelography in diagnosing nerve root avulsion in traumatic brachial plexus.

MATERIALS AND METHODS

Prospective, retrospective, randomized and non-randomized studies which utilized CT and MR myelography for the diagnosis of traumatic nerve root avulsion brachial plexus injury were included in this review. Unpublished and ongoing studies were also looked into. Neonates and adult patients less than 70 years old were included. There was no restriction as to the type and mechanism of how the brachial plexus injury was incurred, the respective comorbidities of the patients and the strength of magnetic field used for MRI.

Studies that made use of at least 16-slice CT scan were included. Axial, coronal and sagittal views were used as references for interpretation. Only images obtained pre-operatively were included in this study. Only studies which looked into root avulsions after traction injuries of the brachial plexus were included. The diagnosis of root avulsion was based on the absence of either one (partial) or both rootlets (complete) and the presence of pseudo meningocele[4,8]. Mechanisms may be from obstetric or other forms of traumatic avulsion injuries.

The gold standard for the diagnosis of nerve root avulsion is still surgical exploration. Only studies wherein brachial plexus exploration was done with exposure of the retroclavicular and infraclavicular areas were included for review. The criteria for the diagnosis of total avulsion intra- operatively include: 1) the dorsal root ganglion was identified outside the intervertebral foramen, 2) the intervertebral foramen was empty and 3) there was normal appearing nerve with no response to electrical stimulation on exploration[7]. For partial root avulsion, intraspinal exploration was also done.

In accordance to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines, an extensive literature search was done in MEDLINE (PubMed), EMBASE (Elsevier), Cochrane Register of Diagnostic Test Accuracy Studies, PubMed Central (PMC), BioMed Central and Europe PMC. The following Medical Subject Headings (MesH) terms were used in the search: 'brachial plexus injury', 'nerve root avulsion', 'myelography', 'CT myelography', 'Computed Tomography Myelography', 'CTM', 'MR Myelography', 'Magnetic Resonance Myelography', 'MRM', 'Magnetic Resonance Imaging', 'MRI' and 'diagnostic accuracy'. Filters were not used to include as many articles as possible since preliminary search pointed out only few studies on this area. Searching was done from May to October 2016.

The authors independently extracted data using a data collection form. Extracted data include study design, sample

Table 1: Methodological criteria used to assess the quality of studies investigating diagnostic accuracy of CT myelography and MR myelography (QUADAS)

Item		
1.	Patient selection	
	A.	Risk of Bias
		Was a consecutive or random sample of patients enrolled? Was a case-control design avoided?
		Did the study avoid inappropriate exclusions?
		Could the selection of patients have introduced bias?
	B.	Concerns regarding applicability
		Are there concerns that the included patients and setting do not match the review question?
2.	Index test	
	A.	Risk of Bias
		Were the index test results interpreted without knowledge of the results of the reference standard?
		If a threshold was used, was it pre-specified?
		Could the conduct or interpretation of the index test have introduced bias?
	B.	Concerns regarding applicability
		Are there concerns that the index test, its conduct, or interpretation differ from the review question?
3.	Reference standard	
	A.	Risk of Bias
		Is the reference standards likely to correctly classify the target condition?
		Were the reference standard results interpreted without knowledge of the results of the index tests?
		Could the reference standard, its conduct, or its interpretation have introduced bias?
	B.	Concerns regarding applicability
		Are there concerns that the target condition as defined by the reference standard does not match the question?
4.	Flow and timing	
	A.	Risk of Bias
		Was there an appropriate interval between index test and reference standard?
		Did all patients receive the same reference standard? Were all patients included in the analysis?
		Could the patient flow have introduced bias?

size, base line characteristics, type of interventions and neuroimaging outcomes. A two-by-two table was constructed which constitute the values of true positives, false positives, false negatives and true negatives to be pooled in the meta-analysis.

Methodological quality of the included studies was assessed independently by two review authors and disagreement on study quality was resolved by a third review author. Methodological quality of selected studies was assessed using a modified version of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist[9]. This tool was used to assess the risk of bias using four domains namely patient selection, index test, reference standard and flow and timing. These domains were ranked as high, low, or unclear risk (Table 1).

The unit of analysis was the brachial plexus, particularly the number of nerve root avulsions detected either as partial, complete, or with the presence of pseudo meningocele in individual patients. Sensitivities and specificities for each study were calculated based from the two-by-two tables constructed. Pooled sensitivity and specificity for CT myelography and MR myelography was calculated with confidence level for all calculations set to 95% and using a continuity correction of 0.5 if applicable. Test for equality of sensitivities and specificities were also performed. Forest plot was generated to represent the precision of sensitivity and specificity in each study as well as their variability across studies. From this, the heterogeneity can be inspected. The authors have intended to study the effects of co-variates, such as: age group, patient built, strength of magnet and sequence used for MR myelography and slice thickness and detector size for CT myelography in the specificity, sensitivity, or both if three or more studies were available for each study.

Statistical analysis: Paired sensitivities and specificities were plotted in summary Receiver-Operator Curve (ROC) plot reflecting the summary ROC curves for both CT and MR myelography. The parameter estimates for the HSROC model by Rutter and Gatsonis were derived from SAS software and were utilized to plot the summary ROC curves in Rev Man 5.3 software. Areas under the summary ROC curves were also computed.

RESULTS

Searching the different search portals identified a total of 816 studies. There were no studies assessed from clinical trial registries. After removing duplicate studies and irrelevant records, a total of 26 studies were retrieved. Twenty studies were then excluded as they did not meet the inclusion and exclusion criteria (Fig. 1). The data extracted from the six studies comprised of 444 nerve roots of which 228 were examined using CT myelography and 216 were analyzed using

Table 2: Summary table of extracted data

Author	Year	Outcome	TP	FP	FN	TN
Abdel Ghany *et al.*[11]	2011	Nerve root avulsion on CT Myelography	16	0	4	0
Abul-Kasim *et al.*[3]	2010	Nerve root avulsion on MR Myelography	13	2	2	17
Yamazaki *et al.*[12]	2007	Nerve root avulsion on CT Myelography	23	1	4	20
Gasparotti *et al.*[13]	1997	Nerve root avulsion on MR Myelography	33	3	4	58
Nakamura *et al.*[10]	1997	Pseudomeningocele on MR Myelography	14	0	2	84
		Nerve root avulsion on MR Myelography	16	5	1	62
		Pseudomeningocele on CT Myelography	16	1	0	83
		Nerve root avulsion on CT Myelography	15	6	2	61
Walker *et al.*[14]	1996	Nerve root avulsion on CT Myelography	20	1	3	52

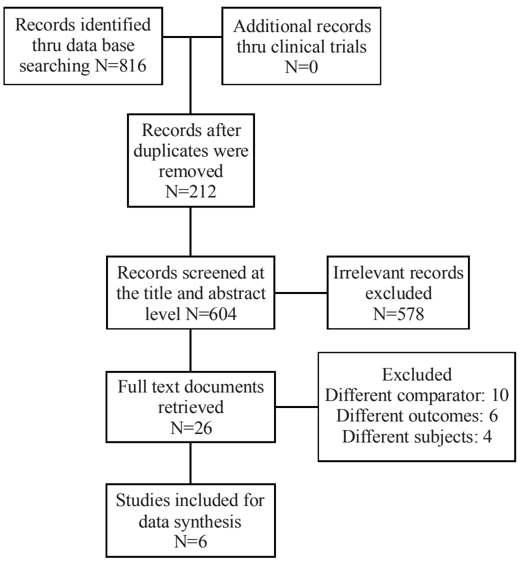

Fig. 1: Prisma flow diagram shows the summary of searching process

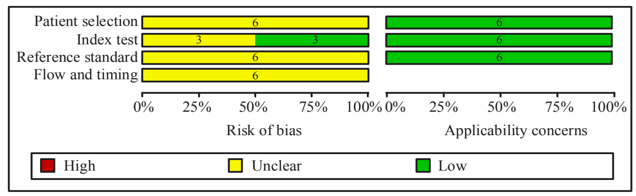

Fig. 2: Methodological quality graph shows review authors' judgments about each methodological quality item presented as percentages across all included studies

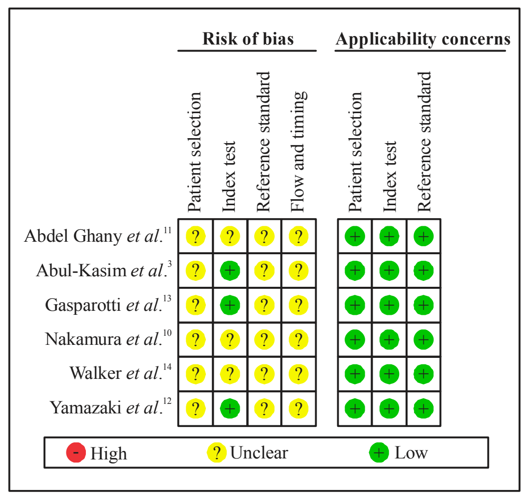

Fig. 3: Methodological quality graph shows review authors' judgments about each methodological quality item for each included study

MR myelography[3,10-14]. Only Nakamura analyzed the diagnostic accuracy of CT and MR myelography in terms of findings of pseudo meningocele only as a separate finding (Table 2)[10].

A total of eighty-four patients with age ranging from 3 months to 67 years old were included with a mean age range of 22 to 29 years old. At least 56 males and 13 females comprised the population of the studies and at least 40 of these subjects have complete brachial plexus palsy while at least 31 of them have either upper or lower brachial plexus palsy. The studies were conducted from 1996 to 2011 in different countries in single center set-up. The characteristics of the individual studies are presented in Table 3.

All of the studies dealt with traumatic nerve root avulsions wherein most of them were incurred in motorcycle vehicular accidents, while in the pediatric population, most were related to obstetric birth injuries. All of the included studies have used a combination of at least two imaging modalities: CT Myelography, MR Myelography, or Myelography in examining their subjects. Only Abdel Ghany *et al.*[11] had utilized CT Myelography with axial, coronal and oblique projections as single imaging modality in all of their patients.

All six studies were assessed to have unclear risk of bias in terms of patient selection, reference standard and flow and timing. Three studies had unclear bias while the rest have low risk of bias in terms of index test. All of them were deemed to have no problems with regards concerns on applicability in terms of patient selection, index test, reference standard and flow and timing (Fig. 2, 3).

All studies have pre-specified imaging thresholds. However, Abdel Ghany *et al.*[11] and Yamazaki *et al.*[12] shared the same

Table 3: Characteristics of studies included

Author	Year	Place	Single or multi-institutional	Study design	Reference standard	Imaging	Type of injury	Population	Imaging thresholds
Abdel Ghany *et al.*[11]	2011	Egypt	Single	Prospective	Surgical exploration and clinical tests	CT myelography axial, coronal and oblique views	Traumatic and obstetric root avulsion	3 months to 5 years	Pseudomening-ocele Abnormal ventral/dorsal nerve roots
Abul-Kasim *et al.*[3]	2010	Sweden	Single	Retrospective	Surgical exploration	MR myelography, CT myelography , or both	Traumatic root avulsion	15 to 61 years	Abnormal ventral, dorsal nerve roots, or both Pseudomening-ocele CSF leakage along nerve root Bleeding near the nerve root exit Signal changes near nerve root exit
Yamazaki *et al.*[12]	2007	Japan	Single	Prospective	Intra-operative findings of: direct observation of the nerve roots, evoked spinal cord potentials of each nerve root, choline acetyltransfera-se activity measurement	CT Myelogrpahy coronal, oblique coronal and axial views Myelography	Traumatic root avulsion	15-56 years	Pseudomening-ocele Abnormal ventral/dorsal nerve roots
Gasparotti *et al.*[13]	1997	Italy	Single	Prospective	Surgical exploration and Intraoperative somatosensory evoked potential	3D MR Myelography CT Myelography Myelography	Traumatic root avulsion	17 to 46 years	Nerve root avulsion and Traumatic meningocele
Nakamura *et al.*[10]	1997	Japan	Single	Prospective	Surgical exploration	CT myelography Axial and sagittal MR myelography Myelography	Traumatic root avulsion	16 to 38 years	Traumatic pseudomening-ocele Injured nerve root Abnormal nerve-root sleeve
Walker *et al.*[14]	1996	USA	Single	Prospective	Surgical exploration and Intraoperative somatosensory evoked potential for each injured nerve root	CT Myelography Myelography	Traumatic root avulsion(mot-or vehicle accident and birth)	18 months to 67 years	Nerve root avulsion traumatic pseudomening-ocele or deformity of the subarachnoid space

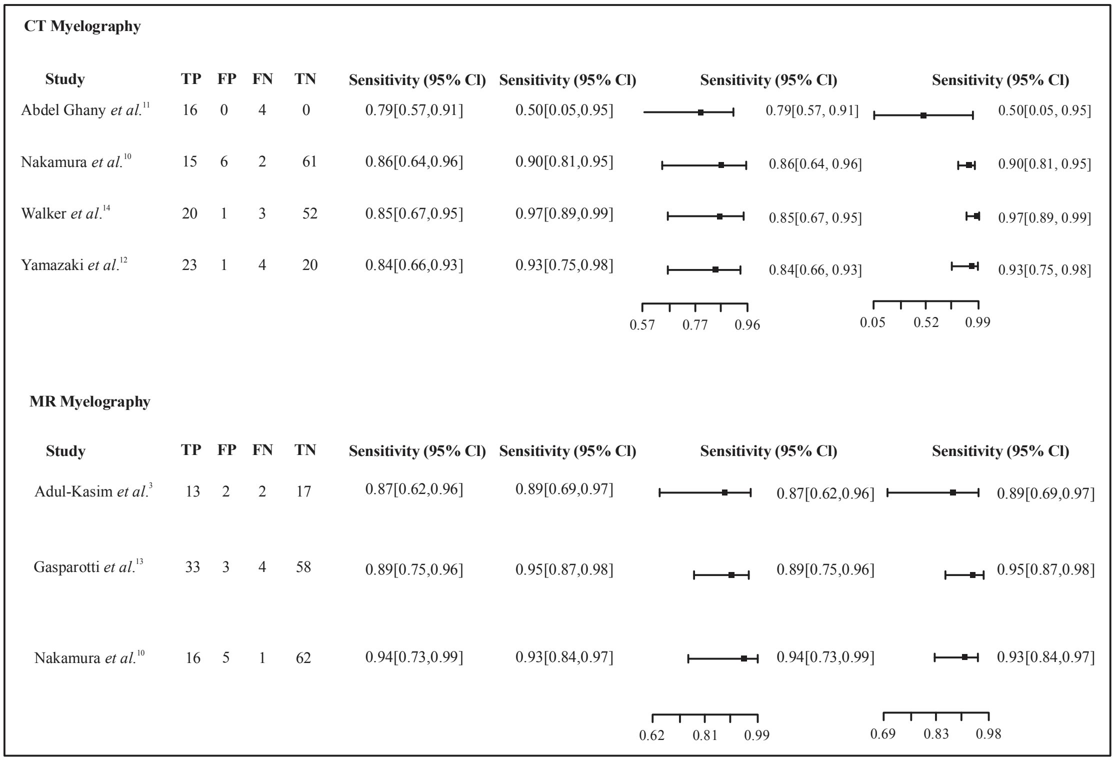

Fig. 4: Forest plot of the paired sensitivity ad specificity values for CT myelography or MR myelography compared to a reference standard in the diagnosis of traumatic nerve root avulsion

threshold with the former adapting the latter's concept. They classified CT myelographic diagnosis of root avulsion based as follows: A(+); ventral root can be recognized, A(-); ventral root cannot be recognized, P(+); dorsal root can be recognized, P(-); dorsal root cannot be recognized, M(+); meningocele can be recognized, M(-); meningocele cannot be recognized. A nerve root was considered avulsed from the spinal cord when either ventral or dorsal roots were unrecognizable on axial view, while on coronal and oblique coronal views, nerve roots were considered avulsed when the number or size of rootlets was decreased or the roots were absent. The sensitivities and specificities of individual studies for CT myelography and MR myelography were computed from the number of true positives, false positives, true negatives and false negatives extracted in the individual studies. These were plotted in a forest plot for easier visualization (Fig. 4). For CT myelography with four primary studies, test for equality of sensitivities yielded: X-squared=0.5275, df=3, p-value=0.913. Since the p-value (0.913) is larger than the level of significance of .05, the null hypothesis of homogeneity was not rejected. The four studies have substantial similarity in sensitivity. The test for equality of specificities on the other hand showed that: X-squared=5.071, df=3, p-value=0.167. Since the p-value (0.167) is larger than the level of significance of 0.05, the null hypothesis of homogeneity was not rejected. The four studies have substantial similarity in specificity. For MR myelography with three primary studies, test of equality of sensitivities yielded: X-squared=0.5241, df=2, p-value=0.769. Since the p-value (0.769) is larger than the level of significance of 0.05, the null hypothesis of homogeneity was not rejected. The three studies have substantial similarity in sensitivity. The test for equality of specificities on the other hand demonstrated: X-squared=0.8033, df=2, p-value=0.669. Since the p-value (0.669) is larger than the level of significance of 0.05, the null hypothesis of homogeneity was not rejected. The three studies have substantial similarity in specificity.

The pooled sensitivities and specificities were plotted in a Receiver-Operator Curve (ROC) (Fig. 5). The summary receiver operator curve for CT myelography and MR myelography was fitted using the HSROC model by Rutter and Gatsonis whereby the parameters were computed from SAS software and inputted into Rev Man 5.3 software to derive the curve.

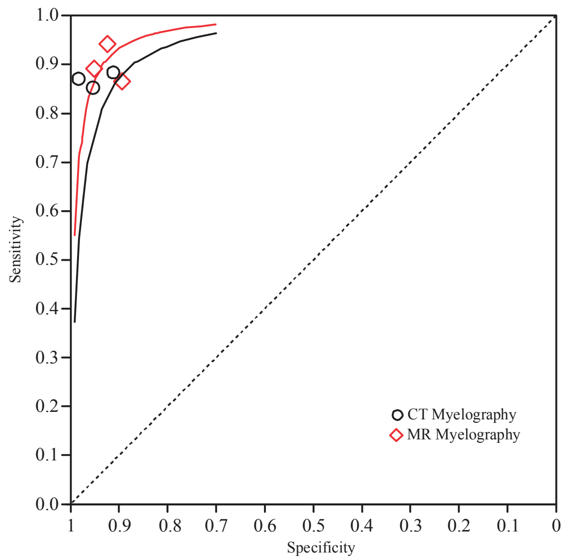

Fig. 5: Pooled estimates of sensitivity and specificity for CT myelography or MR myelography compared to a reference standard in the diagnosis of traumatic nerve root avulsion

Area under the curve (AUC) was also computed. The higher the AUC, the better was the diagnostic ability with the highest value at 1.00 or 100%. For CT myelography, AUC was 0.857 while for MR myelography the AUC was 0.858.

DISCUSSION

The diagnostic accuracy of CT myelography and MR myelography in the diagnosis of nerve root avulsion in traumatic brachial plexus injuries may help the surgeon decide on which kind of surgery to utilize for a particular injury. Only three studies have used both modalities[3,10,13]. Furthermore, only one study had the data in both modalities been extracted since the reference standard used was the one specified in this meta-analysis, which was surgical exploration[10]. In the other study, only the data for MR myelography was utilized since CT myelography was also used as adjunct reference standard apart from the surgical findings[13]. The third study had only used both modalities in two subjects, the rest of the subjects had undergone MR myelography. Hence, the data for this was extracted for this meta-analysis[3]. The unit of analysis in the study was the brachial plexus. Particularly, the number of individual nerve roots that were avulsed in a single subject. No subjects in the studies were utilized as controls. The control in the interpretation of the results on the injured side was the contralateral uninjured side[10,14]. In the QUADAS assessment this was raised with contention, however as is with any radiologic study assessment, having the contralateral side as control is not tantamount to having another subject as control, which pertains to one of the items in the QUADAS.

It is advised that case-control studies in diagnostic accuracy reviews should not be included because these have been proven to increase 2- or 3-fold higher estimates of diagnostic accuracy compared with cohort studies with consecutive sampling. In these studies the disease status, determined by reference standard, is already known before the index test is performed[13]. Most of the studies have acceptable reference standard of surgical findings or exploration coupled with intraoperative Somatosensory Evoked Potential (SEP) findings. Some authors advocate that hemilaminectomy be done to inspect the cervical roots due to inconclusive radiological findings. This is due to the fact that nerve action potential studies only assess the dorsal and not the ventral rootlets[4].

The results obtained in the meta-analyses showed homogenous and high sensitivities and specificities for both CT myelography and MR myelography in the diagnosis of nerve root avulsions. One advantage of MR myelography is that it better visualizes pseudo meningoceles or traumatic meningoceles, which form after dura is torn with subsequent in-flow of cerebrospinal fluid (CSF) and eventual closure of the tear[11,12,15]. Since MR myelography utilizes the CSF in generating myelogram-like images to visualize the bracahial plexus, artifacts caused by CSF pulsation, patient movement and inclusion of vertebral arteries and plexuses affect visualization of the brachial plexus[10]. Newer MR myelography sequences were developed to offset these problems. In particular, the 3DCISS (3-dimensional constructive interference in steady state) sequence minimizes artifacts secondary to pulsatile CSF flow by acquiring the sequence with flow compensation[16]. Likewise, the use of gradient echo sequences (turbo flash) improves visualization due to its high sensitivity to minimal bleedings at the nerve root exit[10]. The strength of magnet also affects the quality of the MR myelography image. A 3T MRI offers better spatial and temporal resolution but a 1. 5T MRI, as preferred by some in brachial plexus imaging, provides lesser susceptibility artifacts[17]. For CT myelography, only two studies, indicated the number of slice specification of the machine which was 16-slice helical CT scan[11,12]. The advantages of CT myelography compared to MR myelography include: better revelation of partial nerve root avulsions, preferred for use in claustrophobic patients, elimination of cerebrospinal fluid flow artifacts and excellent visualization of bony structures[17]. In addition, high resolution multiplanar reconstructions can be used to increase detection of nerve root avulsion either partial or complete. In the axial view, it allows perception and differentiation between ventral and dorsal rootlets. In the coronal view, it provides judgment of the image of the ventral rootlets while in the oblique coronal view, it gives good resolution of the dorsal rootlets[18]. For this review, only two studies had utilized multiplanar views in the conduct of CT myelography[11,12]. And only the data for axial view were extracted for the two-by-two contingency table since this view allows visualization of both dorsal and ventral rootlets in one image. The disadvantages of CT myelography are: being an invasive procedure; high radiation exposure; risk adverse reaction to contrast material; intraprocedural complications (epidural/subdural hematomas); post procedural complications (headache, seizures, nausea and vomiting); and radiation beam hardening artifacts[17]. These complications are not apparent on MR myelography on the other hand since it does not use contrast material but instead rely on the CSF to generate myelogram-like images. Also, in infants, MR myelography has the advantage of better projecting the intrinsic signal intensity and integrity of the spinal cord than CT myelography[8]. Another advantage of MR myelography is that it can be used in the acute phase of the injury while its not the case in CT myelography since lumbar puncture and use of contrast agent may carry a significant risk[10]. Albeit, MR myelography gives better visualization of pseudo meningoceles, the exact time or interval for it to develop after injury is not known[13]. Furthermore, meningoceles may indicate nerve root avulsions but nerve root avulsions may occur without pseudo meningocele formation. Similarly, traumatic meningoceles may present without nerve root avulsions[11,12,15]. All of the studies included for this meta-analysis had imaging thresholds which included traumatic meningocele or pseudo meningocele as a finding considered for nerve root avulsion together with either partial or complete nerve root avulsion. Only one study analyzed nerve root avulsions with pseudo meningocele as a separate finding from partial or complete nerve root avulsion[10]. Other disadvantages of MR myelography are: long acquisition times; multiple planes needed to view entire extent of injury and artifacts due to CSF pulsation as previously mentioned.

CONCLUSION

Based on the results of the meta-analysis done on this paper, MR myelography has higher sensitivity and specificity than CT myelography in diagnosing nerve root avulsion in traumatic brachial plexus injuries. In the selection of a particular imaging modality to be used, the invasiveness and cost of each study could also be considered. Other factors such as patient age group, patient body built and MRI and CT-scan machine specifications may contribute in the decision making process of selecting a particular modality but the effects of these were not explored in this review due to the scarcity of details in the studies with regards to these and also the number of studies themselves are not enough to perform a subgroup analysis.

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