RESEARCH ARTICLE

Factors Associated with Requesting Magnetic Resonance Imaging during the Management of Glomus Tumors

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Abstract

Background: The characteristic clinical presentation of glomus tumors and the low negative predictive value of the magnetic resonance imaging (MRI) raise the question whether MRI improves their management. Therefore, this study aimed to investigate whether MRI improved the management of glomus tumors.

Methods: In total, 87 patients with a histologically confirmed glomus tumor were treated over a 25-year period and analyzed retrospectively. Multivariable logistic regression analysis was used to evaluate the independent predictors of an MRI request during the management of glomus tumors.

Results: According to the results, the patients who were treated by orthopaedic surgeons were more likely to have an MRI during the management of a glomus tumor.

Conclusion: The role of an MRI during the management of a glomus tumor is unclear. Orthopaedic surgeons are more likely to request an MRI. Furthermore, visible lesions with characteristic symptoms probably do not benefit from MRI. However, it may help to be sure that the highest-quality MRI is used with the best possible coil for the finger.

Level of evidence: IV

Keywords: Diagnosis, Glomus tumor, Magnetic resonance imaging, Soft tissue neoplasms, Upper extremity

Introduction

Glomus tumors are uncommon benign vascular neoplasms composed of cells resembling smooth cells of the neuromyoarterial glomus bodies (1, 2). The term glomus tumor was historically used to refer to a tumor called paraganglioma which was composed of cells with a neuroendocrine origin descending from neural crest cells (3). Glomus tumors are usually located in areas of the skin that are rich in glomus bodies, such as the subungual regions of digits or the deep dermis of the palm, wrist, forearm, and foot (4, 5). Totally, 75% of all glomus tumors occur in the hand, of which half is subungual; however, they can occur in other sites, such as the nose, lung, gastrointestinal tract (i.e., trachea, stomach, colon), genitourinary tract, shoulder, sacral region, parasternal region, thigh, knee, and leg (1, 4-8).

Glomus tumors often remain undiagnosed or are misdiagnosed for up to 15 years before treatment (on average 3.3 to 5 years) (6, 9-13). An average of 2.5

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physicians (range: 0-7) evaluate a patient before the diagnosis of a glomus tumor is confirmed (14). Regardless of location, complete surgical excision provides the relief of symptoms (15-17).

Glomus tumors have a characteristic symptom triad of cold hypersensitivity, intense paroxysmal pain, and localized point tenderness (2, 6, 17, 18). Variations in clinical presentation and nonspecific symptoms make the diagnosing of the glomus tumors difficult (11). Glomus tumors can mimic clinical symptoms of arthritis, neuromas, or gout (12). Alternative diagnoses included in the differential diagnosis mainly consist of cysts, lipomas, melanomas, or angiomas (5). They are often small and difficult to observe (13). Therefore, glomus tumors are often evaluated with magnetic resonance imaging (MRI). The glomus tumors are known as slightly hypo-intensive to slightly hyper-intensive signals on T1-weighted MRI and hyper-intensive on T2-weighted images. In particular, the T1-weighted image after gadolinium injection shows a strong enhancement (11, 19, 20).

The MRI is believed to be the most useful non-invasive diagnostic test that is utilized to diagnose glomus tumors. It has a positive predictive value (PPV) of 97% (6, 15). However, the negative predictive value is 20% because some glomus tumors are not detected on MRI (6, 11, 15, 17, 21, 22). Radiologists have great difficulty with the diagnosis of glomus tumor on MRI when there are pathologically or anatomically atypical features, no bone erosion, and no relevant clinical history (17). The characteristic clinical presentation (particularly when the tumor is visible) and the low negative predictive value raise the issue of whether MRI improves the management of a suspected glomus tumor.

This retrospective study addresses a primary null hypothesis in which there are no factors, such as clinical presentation or location of the tumor to be associated with obtaining an MRI during the management of glomus tumor. In addition, it is hypothesized that there are no factors associated with obtaining an MRI for glomus in the upper extremity.

Materials and Methods

Study Cohort

This study was approved by the Institutional Review Board of Massachusetts General Hospital, Boston, United States of America. In order to identify adult patients with a histopathologically confirmed glomus tumor, a computerized search was performed using the pathology database in the Massachusetts General Hospital, Boston, United States of America, from January 1990 until February 2015. The searched keywords included “glomus”, “glomus tumor” or “glomangioma” (n=240 adult patients).

The exclusion criteria included patients whose pathology reports mentioned glomus cells or glomus tumor, but did not identify a glomus tumor (n=16), patients with a paraganglioma (a distinct tumor that is sometimes referred to as”glomus tumor”; n=51) and a recurrent and/or persistent glomus tumor (n=34), and those who were treated outside of one of our institutions (n=52). This resulted in a final cohort of 87 patients with a primary presentation of a glomus tumor for further analyses. The mean±SD age of the patients was 49±15years (age range: 20-86 years,) and 52% of the cases were male [Table 1].

In total, 62% of all glomus tumors (n=54) were located in the upper extremity, of which 55% (n=30) were subungual. In addition, 33 glomus tumors were identified outside the upper extremity, mostly in the leg (n=23, 70%), but also in the back, penis, cheek, trachea, gastric wall, ovary, chest, and flank [Table 2].

The most common presentations were a painful and non-discolored palpable spot, nodule, or mass (n=38, 44 %), a painful and discolored (i.e., blue, red, purple or grey) palpable nodule or mass (n=36, 41%), or a non-painful and discolored mass or swelling (n=9, 10%).

The patients with a glomus tumor of the penis suffered from increasing urinary frequency, urgency, and incontinence. Moreover, the patients with a tracheal glomus tumor had intermittent hemoptysis. In two patients, the glomus tumor was an asymptomatic incidental finding identified on the evaluation of a pathology specimen (i.e., one stomach tumor and one ovarian tumor).

Statistical Analysis

Explanatory variables included demographic characteristics (i.e., name, gender, and the age at the time of diagnosis), clinical symptoms (i.e., visible tumor, pain, point tenderness, paroxysmal pain, and cold hypersensitivity), department of care provider (i.e., dermatology, orthopaedic surgery, plastic surgery, general surgery, urology, and other), and anatomical location of the tumor. Additionally, the size (largest dimension) affected side, and clinical symptoms (i.e., painful nail bed, point tenderness, cold hypersensitivity, and paroxysmal pain) were reviewed in patients with a glomus tumor only in the upper extremity since these variables generally do not apply to glomus tumors located outside the upper extremity.

The response variable was the number of glomus tumors that was managed with or without MRI. The patient characteristics were summarized as frequencies (n) and percentages (%) for categorical variables. In case of normal distribution of the data, the continuous variables were summarized using mean and SD; otherwise median and interquartile range were employed to summarize the data. Moreover, Fisher’s exact test, Student t-test, and Mann-Whitney U test were used in bivariate analysis.

All variables with a *P-value* ≤ 0.10 in the bivariate analysis as well as clinically relevant variables were imported into multivariable logistic regression models to evaluate the independent predictors of an MRI request during the management of glomus tumors. The exact logistic regression and Hosmer–Lemeshow goodness-of-fit test were employed to analyze the subgroup and assess how well the model fits the data, respectively. *P-value* less than 0.05 was considered statistically significant, and data were analyzed using STATA 13 (StataCorp LP, College Station, Texas, United States of America).

Table 1. Baseline characteristics and bivariate analysis of all pathologically confirmed glomus tumors: factors associated with the request of *MRI during the management of glomus tumors in all pathologically confirmed glomus tumors

		Total (N=87; 100%)	No MRI (N=60; 69%)	MRI (N=27; 31%)	*P-Value*
		Mean (SD)	Mean (SD)	Mean (SD)	
Age at the time of Diagnosis		49 (15)	49 (16)	49 (13)	0.86
		N (%)	N (%)	N (%)	
Gender	Male	45 (52)	35 (78)	10 (22)	0.10
	Female	42 (48)	25 (60)	17 (40)	
Tumor location	Upper Extremity	54 (62)	38 (70)	16 (30)	0.81
	Other	33 (38)	22 (67)	11 (33)	
Department	Orthopaedics	44 (51)	22 (50)	22 (50)	< 0.001
	Non-orthopaedics[1]	43 (49)	38 (88)	5 (12)	
Visible tumor	Yes	72 (83)	51 (71)	21 (29)	0.54
	No	15 (17)	9 (61)	6 (39)	
Painful tumor	Yes	74 (85)	51 (69)	23 (31)	0.99
	No	13 (15)	9 (69)	4 (31)	
Indication for MRI or diagnostic excision	Painful, discolored	36 (41)	27 (75)	9 (25)	0.76
	Painful, non-discolored	38 (44)	24 (63)	14 (37)	
	Non-painful, discolored	9 (10)	6 (67)	3 (33)	
	Other	4 (5)	3 (75)	1 (25)	

Abbreviations: MRI: Magnetic Resonance Imaging; n, number of patients; SD, Standard Deviation; NA, Not applicable; IQR, Interquartile Range; NR, Not reported

[1] Including dermatology (n=19), general surgery (n=8), internal medicine (n=2), plastic surgery (n=9), thoracic surgery (n=1), urology (n=2), other (n=1).

Table 2. Distribution of all glomus tumor locations throughout the whole body

Upper extremity	N (%)	Lower extremity	N (%)	Other	N (%)
Subungual	30 (35)	Knee	8 (9)	Back	2 (2)
Finger	11 (13)	Thigh	7 (8)	Penis	2 (2)
Arm (inclusing wrist and elbow)	8 (9)	Toe	3 (3)	Cheek	1 (1)
Hand	3 (3)	Leg	2 (2)	Gastric wall	1 (1)
Shoulder	1 (1)	Ankle	1 (1)	Ovary	1 (1)
Not reported	1 (1)	Foot	1 (1)	Chest	1 (1)
		Buttock	1 (1)	Flank	1 (1)
				Trachea	1 (1)
Total	54 (62)	Total	23 (26)	Total	10 (12)

Results

Patients who were treated by orthopaedic surgeons were more likely to have an MRI during the management of a glomus tumor, compared to those treated by other specialists regardless of the presentation or location [*P<0.001*, Table 1]. According to the results of the logistic regression, an orthopedic surgeon provider was the only factor associated independently with requesting an MRI during the management of a glomus tumor (adjusted OR

7.6, 95% CI 2.5 – 23, *P<0.001*).

Among patients with upper extremity glomus tumors, the females (n=31, 57%, *P=0.034*), patients without paroxysmal pain (n=7, 13%, *P=0.019*), and patients with an orthopaedic surgeon provider (n=34, 63%, *P<0.001*) were more likely to have an MRI [Table 2]. In the subgroup of glomus tumors in the upper extremity, patients who were treated by orthopedic surgeons (OR 18, 95% CI 2.6 – >1000, *P=0.001*) were more likely to have an MRI during the management of a glomus tumor, when adjusted for gender, visible tumor, and paroxysmal pain [Table 3].

Table 3. Baseline characteristics and bivariate analysis of pathologically confirmed glomus tumors in the upper extremity: factors associated with the request of MRI during the management of glomus tumors in all pathologically confirmed glomus tumors

		Total (N=54; 100%)	No MRI (N=38; 70%)	MRI (N=16; 30%)	*P-Value*
		Mean (SD)	Mean (SD)	Mean (SD)	
Age at the time of diagnosis		49 (16)	51 (17)	45 (11)	0.22
Size		Median (IQR)	Median (IQR)	Median (IQR)	
	Largest dimension (cm)[1]	0.5 (0.2 - 0.7)	0.5 (0.3 - 0.75)	0.5 (0.4 - 0.7)	0.66
Gender		N (%)	N (%)	N (%)	
	Male	23 (43)	20 (87)	3 (13)	0.034
	Female	31 (57)	18 (58)	13 (42)	
Specific tumor location	Subungual	30 (56)	19 (63)	11 (37)	
	Other[2]	23 (43)	18 (78)	5 (22)	0.37
	NR[1]	1 (2)	1 (100)	0 (0)	
Department	Orthopaedics	34 (63)	18 (53)	16 (47)	< 0.001
	Non-orthopaedics[3]	20 (37)	20 (100)	0 (0)	
Affected side	Left	31 (57)	22 (71)	9 (29)	
	Right	22 (41)	15 (68)	7 (32)	0.99
	NR (excl. from analysis)	1 (2)	1 (100)	0 (0)	
Visible tumor	Yes	42 (78)	31 (74)	11 (26)	0.31
	No	12 (22)	7 (58)	5 (42)	
Painful nail bed	Yes	26 (48)	17 (65)	9 (35)	
	No	5 (9)	3 (60)	2 (40)	0.99
	NR[1]	23 (43)	18 (78)	5 (22)	
Point tenderness	Yes	53 (98)	37 (70)	16 (30)	0.99
	No	1 (2)	1 (100)	0 (0)	
Cold hypersensitivity	Yes	15 (28)	8 (53)	7 (47)	0.11
	No	39 (72)	30 (77)	9 (23)	
Paroxysmal pain	Yes	7 (13)	2 (28)	5 (72)	0.019
	No	47 (87)	36 (77)	11 (23)	
Indication for MRI or diagnostic excision	Painful, discolored	28 (52)	21 (55)	7 (44)	
	Painful, non-discolored	25 (46)	16 (42)	9 (56)	0.68
	Asymptomatic, discolored	1 (2)	1 (3)	0 (0)	

Abbreviations: MRI, Magnetic Resonance Imaging; n, number of patients; SD, Standard Deviation; NR, Not reported

[1] Missings (n=1) and patients with glomus tumors outside the upper extremity (n=33) were excluded from analysis

[2] Including finger (n=11), hand (n=3), arm (i.e., wrist and elbow) (n=8), shoulder (n=1)

[3] Including dermatology, general surgery, and plastic surgery

Discussion

The role of MRI during the management of suspected glomus tumors could be considered an area of debate. It is found in this study that orthopaedic surgeons are more likely to request an MRI during the management of a primary glomus tumor because the tumors at other sites are often palpable or in other ways more obvious. Another reason for the MRI request is attributed to the habits of orthopedic surgeons, some of whom obtain an MRI as a routine (23, 24).

There are some limitations to consider when interpreting this study. First, this study was conducted using the database of the Department of Pathology in our institute at one of the largest hospitals in the region and a quaternary referral center. To some degree, the inclusion of patients who were treated at our institution could improve the generalizability although many of those patients might have been referred for unusual tumors. Secondly, since surgical pathology was used in this study to identify patients, there were no information on suspected patients who were diagnosed with no glomus tumors, which might have led to a selection bias. Additionally, due to the retrospective nature of this review to assess the electronic medical record, some variables may not have been reported consistently. Therefore, it was impossible to analyze hand dominance in the upper extremity and cold hypersensitivity, point tenderness, and paroxysmal pain outside the upper extremity. Furthermore, the characteristics of the MRI equipment and technique were not reported in this study. Additionally, a symptom absent if not reported was considered in this study which might introduce some inaccuracies.

This obtained result that orthopedic surgeons are more likely to order MRI during the management of a glomus tumor is in accordance with the existing data on the current use of MRIs. This is consistent with the observed unwarranted variation of discretionary services (23, 24). Cammisa et al. reported an increased rate of 1.09 in the use of MRI per month in 34 high-volume practice sites between 2007 and 2008 (23). The widespread availability of musculoskeletal MRI changed the diagnostic approach to many orthopedic conditions, perhaps due to the lack of adverse effects combined with increasing patient expectations (25). The decision of whether or not to request an MRI in the assessment of a possible glomus tumor did not include any clinical signs or symptoms making the reasons why care providers request an MRI unclear.

Al-Qattan et al. reported a PPV of 97% for MRI in the diagnosis of glomus tumors as small as 2 mm among 42 patients, whereas Ham et al. (2013) reported a PPV of 100% for finding small mass lesions among 21 patients (Ham et al., 2013) (11, 21). In the same line, Al-Qattan et al. excluded patients with an atypical clinical presentation or other leading diagnoses (21). Specifically, the inclusion of patients with the clinical diagnosis of a glomus tumor may have resulted in an overestimation of the PPV of MRI (17).

The low specificity and negative predictive value of MRI indicate that a negative image does not rule out a glomus tumor (11, 15, 21, 22). Al-Qattan et al reported that 10% of all patients had a non-diagnostic MRI (21). Furthermore, the majority of patients had small size glomus tumors (all 2-3 mm in diameter) which can be related to the lack of detection of the smaller tumors on MRI (3). Consequently, both the surgeon and patient may decide to proceed with surgical exploration despite a negative MRI (14, 21). Particularly, an MRI is useful when the location or size of the lesion is in doubt, or the multifocality of the lesion is to be ruled out (17, 26). Since the absence of relevant clinical history is associated with the lack of true diagnosis by the radiologist, it is important to communicate a clinical suspicion of a glomus tumor during consultation (17).

In our review of 87 cases, the patient characteristics of glomus tumors are consistent with those of the previous case series (12, 15, 17, 20). In this study, no symptoms of cold hypersensitivity and paroxysmal pain in glomus tumors were observed outside the upper extremity. This result is in line with the findings of a study conducted by Shiefer et al. (27). They reported cold hypersensitivity as being present in only one out of 56 patients with extra digital glomus tumors (1.8%) and did not take paroxysmal pain into consideration.

In addition, Chou et al. reported 42% of cold hypersensitivity in their digital glomus tumor cohort (n=33) which was comparable to the rate of 31% (n=18) observed in this study (15). Furthermore, the majority of glomus tumors in this study were located in the upper extremity. This is in accordance with the results obtained from a study by Mravic et al. who reported that 52%, 14%, 13%, and 4% of all glomus tumors were located in the hand, arm, leg, and toe, respectively. On the other hand, it was found in this study that the majority of glomus tumors occurred at hand (60%), leg (including the ankle and knee) (12%), arm (9%), and toe (3%). However, the proportion of the classic subungual presentation is lower than that previously published (i.e., 55% in our cohort, 75-90% in other studies, such as Al-Qattan et al., 2005; Carroll and Berman, 1972; Trehan et al., 2015) perhaps due to the referral nature of our pathology department and the inclusion of incidental lesions.

The role of MRI during the management of a glomus tumor is probably unclear. Visible lesions with characteristic symptoms do not benefit from MRI. The dilemma is what to do with characteristic symptoms and examination and a normal MRI. One option is exploration which seems potentially destructive and harmful if one does not know where to look. Another option is monitoring and symptomatic management. Over time, glomus tumors may become visible or detectable on MRI. It may help to be sure that the highest-quality MRI is used with the best possible coil for the finger. Additional studies are necessary to include patients who did not have surgery and assess the quality of the utilized MRI to determine the true value and cost-effectiveness of MRI in order to diagnose a glomus tumor.

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