ABSTRACT

Background: The characteristic clinical presentation of glomus tumors and the low negative predictive value of an MRI, raise the question whether MRI improves their management. The purpose of this study was to address this question.

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

Results: Patients who are treated by orthopaedic surgeons are more likely to have an MRI during the management of a glomus tumor.

Conclusions: The role of MRI in the management of a glomus tumor is unclear. Orthopaedic surgeons are more likely to request an MRI. Visible lesions with characteristic symptoms probably don’t benefit from MRI. It may help to be sure that the highest quality MRI is used with the best possible coil for the finger.

KEY WORDS: Diagnosis, Glomus Tumor, Magnetic Resonance Imaging, Soft Tissue Neoplasms, Upper Extremity

LEVEL OF EVIDENCE: IV
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 also used to refer to a tumor called paraganglioma 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). Seventy-five percent of all glomus tumors occur in the hand, of which half are subungual (6), but they can occur in other sites such as the nose, lung, gastrointestinal (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 physicians (range 0-7) evaluate a patient before the diagnosis of a glomus tumor is confirmed (14). Regardless of location, complete surgical excision provides 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). Variation in clinical presentation and nonspecific symptoms makes diagnosing 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 see (13). Therefore, glomus tumors are often evaluated with magnetic resonance imaging (MRI). The glomus tumors have a slightly hypo-intensive to slightly hyper-intensive signals on T1-weighted MRI and a hyper-intensive on T2-weighted images. In
particular, the T1-weighted image after gadolinium injection shows a strong enhancement (11, 19, 20).

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

This retrospective study addresses the primary null hypothesis that there are no factors – including clinical presentation or location of the tumor– associated with obtaining an MRI during the management of glomus tumor. Secondarily, we 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. To identify adult patients with a histopathologically confirmed glomus tumor, a computerized search was performed in the Massachusetts General Hospital (Boston, United States of America) pathology database from January 1990 until February 2015, using key words “glomus”, or “glomus tumor” or “glomangioma” (n = 240 adult patients).

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); patients with a recurrent and/or persistent glomus tumor (n = 34), and patients who were treated outside of one of our institutions (n = 52) were excluded. This resulted in a final cohort of 87 patients with a primary presentation of a glomus tumor for further analyses. The mean age of the patients was 49 years (range 20 to 86, SD 15) and 52% were men (Table 1).

Sixty-two percent of all glomus tumors (n = 54) were located in the upper extremity, of which 55% (n = 30) were subungual. Thirty-three 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, non-discolored palpable spot, nodule or mass (38 patients, 44%); a painful, discolored (blue, red, purple or grey), palpable nodule or mass (36 patients, 41%); a non-painful, discolored, mass or swelling (9 patients, 10%). The patient with a penile glomus tumor had increasing urinary frequency, urgency, and incontinence. The patient with a tracheal glomus tumor had intermittent hemoptysis. In two patients, the
glomus tumor was an asymptomatic incidental finding identified on evaluation of a pathology specimen: one stomach tumor and one ovarian tumor.

Statistical analysis

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

The response variable was the number of glomus tumors that were managed with or without MRI.

Patient characteristics are summarized as frequencies (n) and percentages (%) for categorical variables. Continuous variables are summarized using mean and standard deviation (SD) if normally distributed, otherwise using median and interquartile range (IQR). 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 entered into multivariable logistic regression models to evaluate the independent predictors of an MRI request in the management of glomus tumors. The Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test. For subgroup analysis we used exact logistic regression. A two-tailed p-value of < 0.05 was considered statistically significant. All analyses...
were performed using STATA 13 (StataCorp LP, College Station, Texas, United States of America).
RESULTS

Patients who are treated by orthopaedic surgeons are more likely to have an MRI during the management of a glomus tumor than patients treated by other specialists (p < 0.001, Table 1) no matter the presentation or location. Using logistic regression an orthopedic surgeon provider, was the only factor independently associated with requesting an MRI in 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, women (n = 31, 57%, p = 0.034), patients without paroxysmal pain (n = 7, 13%, p = 0.019), and patients having 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 for the management of a glomus tumor, when adjusted for sex, visible tumor and paroxysmal pain (Table 3).
DISCUSSION

The role of MRI in the management of a suspected glomus tumors could be considered an area of debate. We found that orthopaedic surgeons are more likely to request an MRI in the management of a primary glomus tumor, perhaps in part because tumors at other sites are often palpable or in other ways more obvious, but also in part from 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, it is based off the database of the department of pathology of our institute at one of the largest hospitals in the region and a quaternary referral center. To some degree including only patients that were treated at our institution should improve generalizability, although many of those patients might have been referred for unusual tumors. Secondly, since we used surgical pathology to identify patients, we don’t have any information on patients with suspected glomus tumors that were determined not to have a glomus tumor, which might have lead to a selection bias. Third, we relied on retrospective review of the electronic medical record and some variables may not have been reported consistently. Therefore, we could not analyze hand dominance in the upper extremity and cold hypersensitivity, point tenderness, and paroxysmal pain outside the upper extremity. The characteristics of the MRI equipment and technique were not reported. We considered a symptom absent if not reported, which might introduce some inaccuracies.

Our observation that orthopedic surgeons are more likely to order MRI in the management of a glomus tumor is in accordance with the existing data on the current use of MRIs. This is consistent with observed unwarranted variation of discretionary services (23, 24). Cammisa et al. (23) reported a rate of 1.09 increase in use of MRI per month in 34 high-volume practice sites between 2007 and 2008. 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 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. (21) reported a PPV of 97% for MRI in the diagnosis of glomus tumors as small as 2 mm among 42 patients, while Ham et al. (11)(2013) reported a PPV of a 100% for finding small mass lesions among 21 patients (Ham et al., 2013). Al-Qattan et al. (21) excluded patients with an atypical clinical presentation or other leading diagnosis. Specifically including 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 (21) reported that 10% of all patients had a non-diagnostic MRI. Since the majority of those patients had small size (all 2-3 mm in diameter) glomus tumors, it can be related to the lack of detection of the smaller tumors on MRI (3). Consequently, both 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 (26), or for ruling out multifocality of the lesion (17). Since the absence of relevant clinical history was associated with lack of true diagnosis by the radiologist (17), it is important to communicate a clinical suspicion of a glomus tumor during consultation.

In our review of 87 cases, the patient characteristics of glomus tumors are consistent with previous case series (12, 15, 17, 20). We did not find any symptoms of cold hypersensitivity and paroxysmal pain in glomus tumors outside the upper extremity. This is in line with Shiefer et al. (27), who reported cold hypersensitivity as being present in only one out of fifty-six patients with
extra digital glomus tumors (1.8%) and did not take paroxysmal pain into consideration. Chou et al. (15) reported 42% of cold hypersensitivity in his digital glomus tumor cohort (n = 33) which is comparable to the 31% (n = 18) we found. Furthermore, the majority of glomus tumors in our study were located in the upper extremity. This is in accordance with Mravic et al., who reported that 52% of all glomus tumors were located in the hand, 14% in the arm, 13% in the leg, and 4% in the toe. We found a total of 60% in the hand, 9% in the arm, 12% in the leg (including the ankle and knee) and 3% in the toe. The proportion of the classic subungual presentation is however lower than previously published (55% in our cohort, 75 – 90% in others (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.
CONCLUSION

The role of magnetic resonance imaging in the management of a glomus tumor is unclear. Visible lesions with characteristic symptoms probably don’t 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 that include patients that did not have surgery and assess the quality of the utilized MRI are necessary to determine the true value and cost-effectiveness of MRI in diagnosing a glomus tumor.
STATEMENTS

Conflict of Interest

- Dr. C.A. Bargon has nothing to disclose.
- Dr. A. Mohamadi has nothing to disclose.
- Dr. M. Talaei-Khoei has nothing to disclose.
- Dr. D.C. Ring reports grants from Skeletal Dynamics, other from Wright Medical, personal fees from Biomet, personal fees from Acumed, other from Illuminos, personal fees from Deputy Editor for Journal of Hand Surgery, personal fees from Deputy Editor for Clinical Orthopaedics and Related Research, personal fees from Universities and Hospitals, personal fees from Lawyers, outside the submitted work.
- Dr. C.S. Mudgal has nothing to disclose.

Conflict of Human and Animal Rights

This study was approved by our Institutional Review Board. The Partners Human Research Committee (PHRC) is the Institutional Review Board (IRB) of Partners HealthCare.

Conflict of Informed Consent

Institutional review board of Massachusetts General Hospital has approved the data repository research protocol. The IRB approval number is 2009P001019

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