Anatomic Variations and Malformations as Rare Causes of Median Nerve Compression in Adults

A Narrative Review

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Objective: The median nerve can become compressed at multiple points in the arm, causing carpal tunnel-, pronator-, anterior interosseous-, or lacertus syndrome. Anatomical variations are potential reasons of persisting or recurrent symptoms of median nerve compression and are often recognized late. The objective of this study is to provide a comprehensive list of rare anatomical variations and malformations causing median nerve compression.

Methods: A total of 62 studies describing median nerve compression due to an anatomical structure in adults published from 2000 in English were included. The findings were: 35 tenomuscular, 16 vascular causes, and 4 cases with nerve involvement. Only 1 osseous and 18 combined anomalies caused compression. In 18 cases, the anomaly was found in the proximal forearm.

Results: In 44 cases, the median nerve was surgical released and 35 anomalies were completely resected. Persistent or recurrent symptoms were present in 13 cases. During follow-up, 1 case of recurrence was reported.

Standard operative option for median nerve compression consists of an open median nerve release.

Conclusions: In case of persistent or recurrent carpal tunnel syndrome, unilateral symptoms, the presence of a palpable mass, manifestation of symptoms at young age and pain in the forearm or upper arm, the surgeon has to rule out the presence of an anatomical anomaly. Complete resection of the anomaly is not always necessary. The surgeon should be aware of potential anomalies to avoid inadvertent damage at surgery.

Key Words: anatomic variances, anterior interosseous syndrome, carpal tunnel syndrome, lacertus syndrome, median nerve compression, pronator syndrome

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The most common form of median nerve compression is compression of the nerve at the carpal tunnel, causing carpal tunnel syndrome (CTS). However the median nerve can become compressed more proximal in the arm, mostly at sites of fibroosseous or fibromuscular tunnels causing pronator syndrome, anterior interosseous syndrome, or Lacertus syndrome.[1] Symptoms include paresthesia, pain, and (thenar) weakness in the course of the median nerve, depending on the site of compression. Pronator syndrome manifests in most cases with pain in the volar forearm, aggravated by repetitive pronation.[2,3] Isolated weakness of the thumb and index finger, the inability to form an "okay sign" is pathognomic for anterior interosseous syndrome.[4,5] Lacertus syndrome is also a proximal median nerve compression syndrome whereby the median nerve becomes compressed under the lacertus fibrosus, a ligamentous sheet arising from the biceps tendon, dissipating in the medial forearm fascia. Lacertus syndrome is commonly misdiagnosed. Hagert (2013)[6] and Lalonde (2015)[7] stated if someone is still having symptoms after carpal tunnel release, Lacertus syndrome must be suspected.

Anatomical variations or malformations are other potential reasons of persisting or recurrent symptoms of median nerve compression. For instance accessory carpal bones, supernumerary structures or hypertrophic or anomalous muscles. These uncommon causes of median nerve compression are often recognized late. In case of misdiagnosis, irreversible damage to the median nerve may occur.[8] This narrative review presents an overview of structures, which can cause median nerve compression and may help to avoid a diagnostic delay and unnecessary surgery. The objective of the study is to provide an organized, comprehensive and time-saving list of rare anatomical variations causing median nerve compression. Furthermore, this review can be used as a guide to distinguish idiopathic median nerve compression from (proximal) median nerve compression as a result of an anatomic variation or malformation by presenting clinical work-up findings.

PATIENTS AND METHODS

A review of the literature was performed using PubMed, Embase and Web-of-Science databases. An additional search was conducted to complete the results. The first search was performed at May 11, 2020. The last update of the searches took place at May 25, 2020. A detailed electronic search strategy is described in Appendix A. The results of the search were imported to Endnote (X8; Clarivate Analytics, Philadelphia, PA). After deleting duplicates, the remaining articles were screened for title and abstract. Disagreements were resolved by discussion or a third reviewer.

The following criteria have been used to include a study to this review: studies describing a case, cause or etiology of median nerve compression due to anatomical variations, year of publication from 2000, patients 18 years or older, and studies written in English. All structures involving the median nerve, which cause compression along the full length of the median nerve, were included.

Excluded studies involved cadavers, animals, and cases of other causes of median nerve compression (among which: idiopathic CTS, pregnancy, edema, rheumatoid arthritis, gout, diabetes mellitus, hypothyroidism, tenosynovitis, acromegaly, repetitive tasks, traumatic neuropathy, and infectious causes).

Data Extraction

Information about patient characteristics, side of compression, unilateral or bilateral compression, cause of compression, symptoms at presentation, duration of symptoms at presentation, physical examination, diagnostics, treatments, location of the compression, results of treatment, complications, follow-up, and recurrence were extracted.

Data were analyzed in SPSS (IBM SPSS Statistics version 26). In case of missing data, studies were excluded from that particular part of statistical analysis.

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Data Analysis

All included studies were analyzed together for the general characteristics. In addition, groups are formed based on compressive structure and site of compression. The formed groups were analyzed for similarities, indications, and distinctive information.

RESULTS

Study Selection

A total of 2205 studies were found and after deduplication, using Endnote, 534 duplicates were removed and 1671 titles and abstracts were left to be screened for inclusion. On the basis of title and abstract, 1592 studies were excluded. A total of 79 articles were assessed for eligibility on the base of full text of which 30 articles were excluded. There were 13 additional studies found in the reference lists. A total of 62 articles were included for full text analysis of which the earliest study is from the year 2000 and the most recent study of 18th of April 2020. Appendix B presents a flow diagram of this study selection process.

General Characteristics

Full text analysis revealed 62 studies describing 74 cases of median nerve compression due to an anatomic variation or malformation. The mean age of the patients was 44.55 years (range, 18–90 years), 36 were men and 38 women. Table 1 describes the general characteristics of the cases.

The mean duration of symptoms before visiting a doctor was 15.63 months. In 54 patients, symptoms were unilateral (20 left, 26 right, 8 unknown), and in 20 patients, bilateral. In 13 cases (17.6%), the patient presented for the second time after initial carpal tunnel release. A total of 70 patients (96%) had sensory symptoms, 47 patients reported pain (64%) and only 19 patients experienced a motor deficit. In 14 patients a swelling was found during physical examination (19%). Triggering of the wrist was present in 11 patients. Preoperative imaging took place in 51 cases (75%), varying from ultrasound, radiography, computed tomography, angiography, and magnetic resonance imaging, whether or not combined.

Treatment consisted in 44 cases (64%) of an open release of the compressed nerve, among which 1 endoscopic procedure converted to an open carpal tunnel release. In 35 cases (51%), it was possible to perform complete resection of the anomaly or malformation. Partial resection was performed in 5 cases (7.2%) and 8 patients received nonsurgical treatment (12%).

The anatomic variation was in 53 cases found at the level of the carpal tunnel. Other median nerve compression occurred more proximal at the (distal) upper arm (7 cases), forearm (6 cases), elbow (5 cases), and in 3 cases, the anatomic variation extended from the forearm to the carpal tunnel or even to the hand, as shown in Figure 1. A total of 16 (76%) of 21 patients with a proximal median nerve compression or malformation, complained of pain the forearm in contrast to only 3 (5.7%) of 53 patients with CTS.

The anatomic variation or malformation was found through imaging before treatment in 44 (60%) of 74 cases and in 25 (34%) of 74 the anomaly was found intraoperatively. For 5 cases, the moment of diagnosis remains unknown

After treatment, 38 patients reported complete recovery of symptoms. In 23 cases, improvement was achieved, and in 1 case, the operative treatment did not relieve symptoms. Mean follow-up was 19.31 months (ranging from 1 to 132 months). During follow-up, 1 case of recurrence was reported in a patient with an arteriovenous malformation (AVM) in the palm of the hand.

A total of 35 tenomuscular causes were found, followed by 16 vascular causes and 4 median nerve involvement. Only 1 osseous anomaly causing median nerve compression was found and 18 combined anomalies. Table 2 provides an overview of these anatomic variations found in this review.

TABLE 1. Characteristics of Cases

		Frequency (n)	Percentage (%)
Sex	Male	36	49
	Female	38	51
Side*	Left	20	30
	Right	26	39
	Bilateral	20	30
Symptoms†	Sensory	70	96
	Motor	19	26
	Pain	47	64
	Swelling	14	19
	Triggering	11	15
Preoperative imaging‡		51	75
Treatment§	Release of median nerve	44	64
	Complete resection of compressive structure	35	51
	Partial resection	5	7.2
	No operative treatment	8	12
Treatment outcome	Recovery	38	51
	Improvement	23	31
	No improvement	1	1.4
	Not described	12	16
Recurrence	Yes	1	1.4
	No	44	60
	Not described/unknown	29	39

* For 8 cases missing data.
† For 1 case missing data.
‡ For 6 cases missing data.
§ For 5 cases missing data.

DISCUSSION

The majority of causes of median nerve compression were due to a tenomuscular variation as well as a bifid median nerve, whether or not combined with other anatomic variations. In only 14 of 74 patients a swelling was found during physical examination. This result shows the difficulty of diagnostics in the absence of a distinct mass. In this review, 13 patients already received treatment for median nerve compression but experienced persisting or recurrent symptoms. Only 1 article mentioned a case of recurrence as outcome. In the remaining cases, the anatomic variation or malformation was most likely recognized and subsequently adequately treated. The recurrence rate in this review is not reliable because of the amount of missing data. In 51 cases imaging took place, which might be a reason for high number of preoperative diagnosis. In case of less frequent application of imaging modalities, anatomic variations could be missed.

This study is limited by publication bias. We realize only rare causes of compression are published and other rare causes can be missed. Besides, all included studies were case reports or case series. This study consists of a heterogeneous group of many different causes of median nerve compression. Therefore no conclusions about incidence and prevalence can be made. However, this was not the intention of the study.

In 5 cases, partial resection of the structure was performed. In 1 case, a combination of 3 anomalies or malformations caused the median

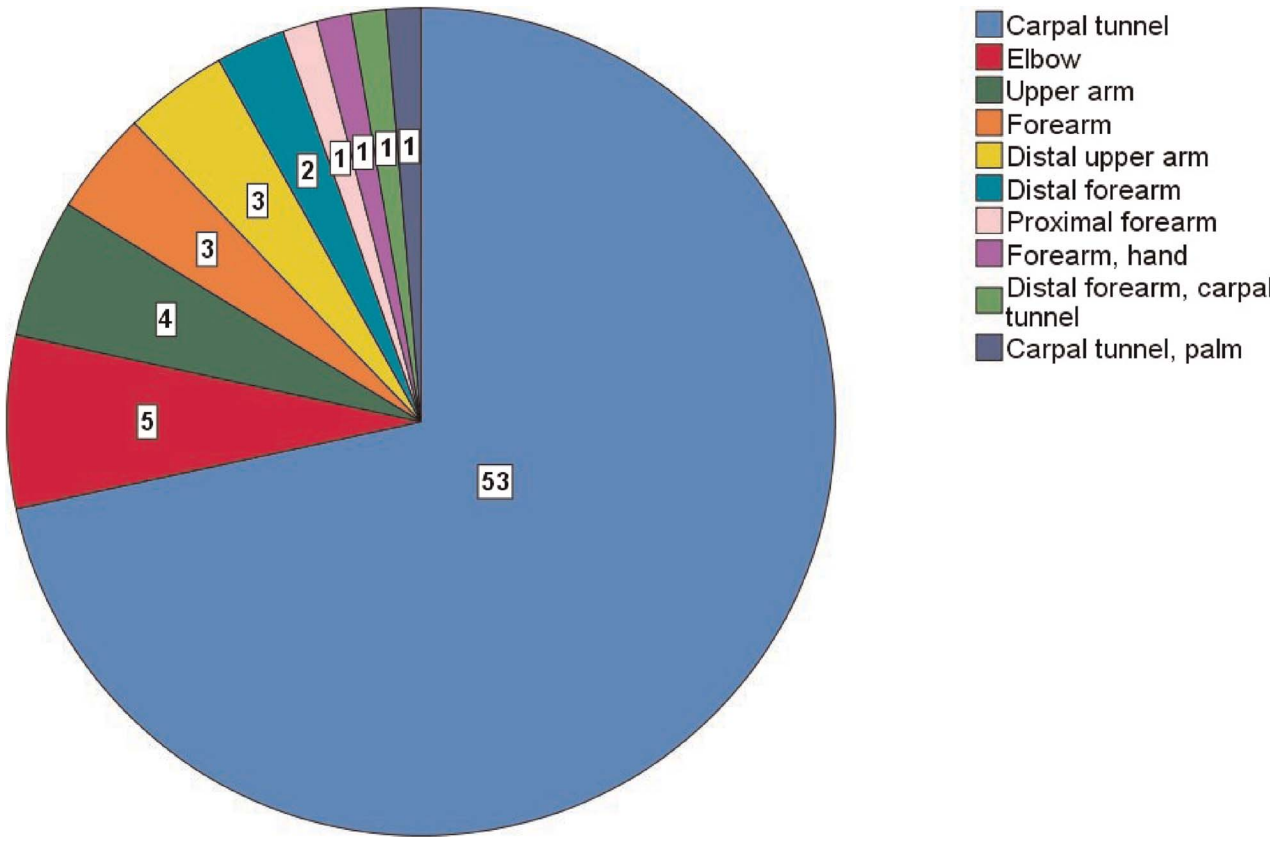

FIGURE 1. Pie chart of localization of median nerve compression. full color online

nerve compression, among which a digastric FDS. The surgeon decided not to sacrifice the digastric FDS. Therefore, only the muscle belly was debulked. Recurrence was reported in 1 case involving an AVM, written by Patiniott et al.[9] Complete resection was not possible, because of the risk of ischemia to the hand. Therefore, aneurysmal sacs were coiled and the feeding vessels were embolized. After 9 months, the symptoms became worse and a high-risk surgical treatment consisting of resection of the AVM and multiple vascular grafts was proposed but declined by the patient because of perioperative risks.

As a result of anatomic variations of malformations, complications can occur during surgery. For example prohibiting endoscopic release, damage to the median nerve, or injury to an unsuspected artery. The surgeon should be aware of these potential anomalies to avoid inadvertent damage at surgery.

No case of Lacertus syndrome was found in this review, most likely because of the unrecognized nature and therefore the lack of published articles. Hagert (2013) described 44 patients with proximal median nerve entrapment. Diagnosis of Lacertus syndrome was based on muscle weakness distal to lacertus fibrosus, pain upon pressure over the median nerve at the level of lacertus fibrosus and a positive scratch collapse test. Hagert advocates minimal invasive surgery to release the median nerve at the level of lacertus fibrosus using only local anesthesia. In a series of Gessini et al (1983)[10], 2 cases of lacertus fibrosus (1%) and only 1 (0.4%) case of Struthers ligament syndrome of 228 cases of median nerve compression were reported.

Tenomuscular

Various tenomuscular structures can compress the median nerve against the surrounding tissue, altering its normal course and narrowing the space in both the forearm and upper arm.[11] Normal muscle bellies can become hypertrophic and thence compress the median nerve. Supernumerary, accessory muscles or fibrous structures, like arches and fascia of muscles, the Lacertus fibrosus or ligament of Struthers, are also known to cause median nerve compression, in particular in the upper arm (pronator syndrome and anterior interosseous syndrome).

Standard operative options for median nerve compression consist of an open or minimal invasive release of the transverse carpal ligament to relieve pressure on the median nerve.[12] Resection of the muscle is not always necessary when the median nerve is released tension free. If this is not the case, the anomalous muscle or tendon should be resected to resolve the compression.[13–15]

Osseous

Besides the pisiform-hamate coalition found in this review, the presence of supernumerary bones of bony deformities is also described in older literature. A supracondylar process is present in 0.1% to 2.7% and is associated with the ligament of Struthers.[16] The ligament of Struthers is located in the cubital fossa and originates usually at the supracondylar process, running to the medial epicondyle.

Median Nerve

Bifid median nerve is an anatomic variation that occurs frequently, in about 18% of patients with symptoms suggestive of CTS and in about 15% of symptom-free subjects and is often accompanied with a persistent median artery.[17,18] Normal decompression surgery is not always sufficient. A thorough exploration is necessary to relieve

TABLE 2. Anatomical Variances Causing Median Nerve Compression

Category	Subcategory	Anatomical variance	n	%	Site of Compression
Muscular (n = 35)	FDS	Hypertrophied	7	9.8	CT
		Anomalous muscle belly	5	7	CT
		Accessory muscle belly	1	1.4	CT
		Digastric FDS combined with transverse muscle fiber band	1	1.4	From distal forearm to CT
		Hypertrophied and anomalous muscle belly	1	1.4	CT
	Palmaris Longus	Dual tendon	1	1.4	Forearm
		Hypertrophic	1	1.4	Forearm
		Epifascial accessory	1	1.4	CT
		Reversed and 2-headed	1	1.4	Distal forearm
	Lumbrical	Anomalous muscle belly	2	1.4	CT
		Supernumerous muscle	1	1.4	CT
		Anomalous origin*, combined with hypertrophy lumbricals	1	1.4	CT
		Palmaris profundus	3	4.1	CT
		Brachial and biceps brachii fascia	1	1.4	Distal upper arm
		FDP penetrating median nerve	1	1.4	CT
		Pronator teres	1	1.4	Proximal forearm
		Ligament of Struthers	1	1.4	Elbow
		Transverse carpal muscle	4	5.4	CT
		Anomalous palmaris longus (L) and anomalous FDS (R) belly	1	1.4	CT
Ossal (n = 1)		Pisiform-hamate coalition	1	1.4	CT
Nerve (n = 4)		Bifid	2	2.7	CT
		Superficial to transverse carpal ligament	1	1.4	CT
		Anomalous intramuscular course	1	1.4	Upper arm
Vascular (n = 16)		(Arterio)venous malformation	4	5.4	CT (n = 2) CT to palm (n = 1) Forearm to hand (n = 1)
		Intraneural hemangioma	2	2.7	Elbow (n = 1) CT (n = 1)
		Hemangioma tendon sheath	1	1.4	CT
		Radial artery within carpal tunnel	3	4.1	CT
	Persistent median artery	Interposed persistent median artery†	1	1.4	CT
		Thrombosed persistent median artery	1	1.4	CT
		Penetrating median nerve	1	1.4	Forearm
		Aneurysm spurium brachial artery	1	1.4	Upper arm
		Tortuous axillary artery aneurysm	1	1.4	Upper arm
		Venous aneurysm (brachial vein)	1	1.4	Upper arm
Combination (n = 18)	Bifid median nerve combined with	(Thrombosed) persistent median artery	8‡	11	CT
		Reversed palmaris longus	2	2.7	CT
		Palmaris profundus	2	1.4	CT
	Supracondylar process combined with	Ligament of Struthers§	4	5.4	Distal upper arm (n = 2) Elbow (n = 2)
		Accessory humeral head PT	1	1.4	Elbow
		Reversed palmaris longus, accessory abductor minimi, and persistent median artery	1	1.4	Distal forearm

FDS, flexor digitorum superficialis; FDP, flexor digitorum profundus; L, left; R, right, PT, pronator teres; CT, carpal tunnel.

* Origin proximal to carpal tunnel arising from FDP and FDS tendons.

† Between palmar aponeurosis and flexor retinaculum.

‡ 4 of 7 thrombosed.

§ In 1 case neurovascular bundle superior to the ligament of Struthers.

symptoms.[3] The median nerve variations can be divided in 4 groups, as described by Lanz[18]:

I. Variations in the course of the thenar branch
II. Accessory branches at the distal portion of the carpal tunnel
III. High divisions of the median nerve
IV. Accessory branches proximal to the carpal tunnel

Vascular

A persistent median artery has a prevalence of 1.1% to 16% and can cause acute CTS in case of thrombosis.[19] This artery plays a major

role in the vascularization of the hand. Segmental arterectomy can relieve the symptoms but microsurgical vessel reconstruction may be necessary in case of insufficient vascularization of the radial 3 fingers.[3,20]

Vascular malformations usually become symptomatic at a young age because of mechanical compression or as a result of a steal phenomenon.[9,21] Low flow malformations can be treated with coiling and embolization, but care has to be given to prevention of spill to the nerve. Treatment of high flow malformations has lower success rates among others because of collateral feeding vessels.

Complete excision can resolve the symptoms in patients with a hemangioma. In some cases, excision under loupe magnification is required and surrounding tissue must be excised as well to prevent recurrence.[22]

Combination

The simultaneous presence of multiple anatomical anomalies has been very rarely described.[23]

CONCLUSIONS

In the majority of the cases, the anatomical variation was most likely recognized and subsequently adequately treated. In 17.6%, an anatomic variation was found after recurrent or persisting symptoms. Therefore, recurrence or persisting symptoms after initial release may be a result of an unrecognized anatomical variation.

Based on the data presented, one can conclude that in case of persistent or recurrent CTS, unilateral symptoms, the presence of a swelling, and manifestation of symptoms at young age, the surgeon has to rule out the presence of an anatomical anomaly or malformation. A thorough physical examination of the entire arm is necessary to recognize any swelling. Furthermore, in 76% pain in the forearm or upper arm was a symptom of proximal median nerve compression as a result of an anatomical variation of malformation. Therefore, we suggest early imaging diagnostics in case of the presence of one of the factors stated above. Ultrasound is useful in diagnosing anomalies and has the advantage of dynamic imaging.

If the anatomical structure is recognized, the selected treatment is usually adequate and in that case, recurrence is unlikely. A thorough knowledge of all anatomic variations is very important to prevent iatrogenic damage to unsuspected anatomic variations, in particular in redo surgery. Classic carpal tunnel release is usually sufficient, but in specific cases, the treatment must be adapted to the anatomic anomaly, including excision of the anomaly or in vascular cases embolization, coiling or arterectomy.

In treating CTS, it is essential to become familiar with the anatomical variations causing median nerve compression to perform the adequate additional procedure, to prevent possible recurrence.

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Appendix A: Electronic search strategy Pubmed:

1. ((median nerve compression[tiab] or carpal tunnel syndrome[tiab] or carpal tunnel syndrome[mesh] or median nerve neuropathy[tiab] or median neuropathy[tiab] or median neuropathy[mesh] or compression neuropathy[tiab] or entrapment neuropathy[tiab] or median nerve entrapment[tiab] or pronator syndrome[tiab] or anterior interosseous nerve syndrome[tiab] or proximal median nerve entrapment[tiab] or proximal median nerve compression[tiab]) and (rare[tiab] or unique[tiab] or uncommon[tiab] or unfrequent*[tiab] or unusual[tiab] or infrequent*[tiab] or less common[tiab]) and (causality[mesh] or "carpal tunnel syndrome/etiology"[mesh:noexp] or "median neuropathy/etiology"[mesh:noexp] or pathogenesis[tiab] or causes[tiab] or caus*[tiab] or cases[tiab] or case[ti]))
2. Publication date from 2000

Additional search:
1. Lacertus OR bicipital aponeurosis[All fields]
2. Publication date from 2000

Embase:
1. ((exp carpal tunnel syndrome/ or (Median nerve compression or carpal tunnel syndrome or median nerve neuropathy or median neuropathy or compression neuropathy or entrapment neuropathy or median nerve entrapment or pronator syndrome or anterior interosseous nerve syndrome).ti,ab,kw.) and (rare or unique or uncommon or unfrequent or unusual or infrequent or less common).ti,ab,kw. and (causality/ or carpal tunnel syndrome/et or (pathogenesis or causes or caus* or cases).ti,ab,kw. or case.ti.))
2. limit 1 to conference abstract status
3. 1 NOT 2
4. Publication year from 2000

Additional search:
1. Lacertus or bicipital aponeurosis
2. limit 1 to conference abstract status
3. 1 NOT 2
4. Publication year from 2000

Web of Science:
1. (AB = (median nerve compression or carpal tunnel syndrome or median nerve neuropathy or median neuropathy or compression neuropathy or entrapment neuropathy or median nerve entrapment or pronator syndrome or anterior interosseous nerve syndrome or proximal median nerve entrapment or proximal median nerve compression)) AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article OR Abstract of Published Item)
2. (AB = (rare or unique or uncommon or unfrequent* or unusual* or infrequent* or less common*)) AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article OR Abstract of Published Item)
3. (AB = (causality or etiology or pathogenesis or causes or caus* or case*)) AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article OR Abstract of Published Item)
4. #1 and #2 and #3, timespan 2000 to 2020

Additional search:
1. Lacertus or bicipital aponeurosis, timespan 2000–2020

Appendix B: Flow diagram of study selection