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Anatomic variations of cervical part of thoracic duct: a systematic review

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SUMMARY

The thoracic duct is the largest lymphatic channel of the human body, and presents with great anatomical variation at its cervical segment. Injury of the thoracic duct can result in local or systemic severe complications. In order to identify the prevalence of the anatomical variations of the terminal portion of the thoracic duct, this study was performed according to PRISMA guidelines. The I-square was used to assess heterogeneity. A wide search was conducted in PubMed/ Embase/ Medline until September 2019.

Out of 28 potentially relevant studies identified by literature search, 14 studies comprising 751 patients were included in the final analysis. The prevalence of thoracic duct ending with a single terminal duct was found at 63% (37%-85%) of the patients. Left internal jugular vein, left subclavian vein, left jugulosubclavian angle, or another vein, was found to receive at least one terminal branch of the thoracic duct in 32% (18%-47%), 27% (13%-43%), 32% (16%-51%) and 7% (0%-19%) of the cases, respectively. Each time the thoracic duct drained into the left internal jugular vein, the left subclavian vein and the left jugulosubclavian angle, a single terminal branch pattern was observed in 58% (21%-92%), 49% (6%- 93%) and 76% (49-96%) of the cases respectively.

The thoracic duct emptied into the left internal jugular vein, the left subclavian vein and the left jugulosubclavian angle in the majority of cases. Patients with a terminal branch at the left jugulosubclavian angle showed higher prevalence of single terminal branch pattern, whereas patients with a terminal branch at the left internal jugular vein or the left subclavian vein presented with similar prevalence of single- and multiple-branch patterns. This information should prove useful in order to reduce iatrogenic thoracic duct lacerations.

Key words: Thoracic duct – Anatomic variations – Thoracic duct injury – Chylous leak prevention

INTRODUCTION

The thoracic duct is the largest lymphatic channel of the human body (Cramer et al., 2014). It mainly drains chyle consisting of lymph and emulsified fat into venous circulation (Wang et al., 2018). Although the anatomy of the thoracic duct has been well defined in the last decades, the thoracic duct is identified in only 50% of cases (i.e. cavaderic studies or surgeries of the thorax) (Hematti and Mehran, 2011). Anatomic variations of the thoracic duct are mainly divided into three categories: variations in origin, variations of the path and va-

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Table 1. Studies included in our research (N/R=Not reported)

S/N	Authors	Year	No of	Specimen studied	Epidemiologic	Number of	Study technique
1	Parsons & Sargent	1909	40	Cadavers	N/R	N/R	Gelatin injection & dissection
2	Davis	1914	22	Cadavers	N/R	N/R	Gelatin injection & dissection
3	Gottlieb & Green-field	1956	75	Cadavers	N/R	N/R	Dissection
4	Shafiroff	1958	30	Cadavers	N/R	N/R	Dissection
5	Kinnaert	1973	49	Patients with terminal CKD	N/R	N/R	Surgical procedure
6	Cha & Sirijintakarn	1975	243	Patients who had lymphograms	N/R	N/R	Bipedal lymphograms
7	Zorzetto et al.	1977	51	Cadavers	Brazilian	N/R	Colored latex-Neoprene injection & dissection
8	Shimada & Sato	1997	100	Cadavers	Japanese	57	Immunohistochemical analysis
9	Langford et al.	1999	24	Cadavers	Caucasian	N/R	Dissection
10	Langford	2002	10	Cadavers	N/R	N/R	Dissection under loupe magnification
11	Akcali et al.	2006	9	Cadavers	N/R	N/R	Dissection
12	Thirupathirao & Srinivasarao	2013	45	Cadavers	N/R	30	Dissection
13	Louzada et al.	2015	25	Cadavers	Caucasian (14/25)	16	Dissection
14	Amore et al.	2016	28	Cadavers	N/R	8/12	Colored latex injection &

Table 2. Prevalence of thoracic duct varieties

Characteristic studied	ES	95% CI	I^2	P
TD not found on left side	0.0	0.00, 0.01	0.00%	0.88
Single terminal ducts	0.63	0.37, 0.85	97.22%	0.00
Multiple terminal ducts	0.37	0.15, 0.63	97.22%	0.00
Internal jugular vein prevalence	0.32	0.18, 0.47	89.80%	0.00
Internal jugular vein single end	0.58	0.21, 0.92	94.65%	0.00
Internal jugular vein multiple end	0.42	0.08, 0.79	94.65%	0.00
Jugulosubclavian angle prevalence	0.32	0.16, 0,51	93.51%	0.00
Jugulosubclavian angle single end	0.76	0.49, 0.96	87.25%	0.00
Jugulosubclavian angle multiple end	0.24	0.04, 0.51	87.25%	0.00
Subclavian vein prevalence	0.27	0.13, 0.43	89.59%	0.00
Subclavian vein single end	0.49	0.06, 0.93	93.06%	0.00
Subclavian vein multiple end	0.51	0.07, 0.94	93.06%	0.00
Other vein prevalence	0.07	0.00, 0.19	92.62%	0.00

riations of the terminal part. The greatest of them are the anatomical variations seen at its cervical portion (Smith et al., 2013). Moreover, the thoracic duct can show patterns of unique or multiple terminal branches, ending into one or more cervical veins. Cases of these branches reuniting before they empty into the venous circulation have also been described (Hematti and Mehran, 2011). Although rare, surgeons carrying out neck dissections may ultimately deal with complications of thoracic duct injury. Hereby chylous leakage occurs in 1% to 2.5% of radical neck dissections, with the majority being on the left side (75% to 92%), particularly during the dissection of the lower part of the internal jugular vein (level IV) (De Gier et al., 1996).

Chylous leakage has been associated with great systematic complications, whereas if left uncontrolled it may lead to necrosis of the skin flap and carotid damage (Smoke and Delegge, 2008). Moreover, the need for additional procedures in order to treat chylous leak and the intense surveillance imaging, increase significantly the overall health care costs. Therefore, as the exact anatomy of the thoracic duct is not always easily identified before a procedure, the aim of this systematic review was to assess the existing literature, and provide information about known anatomical variations of the terminal portion of the thoracic duct in order to improve clinical awareness for better surgical outcomes by preventing thoracic duct injury.

MATERIALS AND METHODS

Search strategy and selection criteria

This systematic review was performed according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines (Shamseer et al., 2015). Systematic searches were conducted in PubMed/ Embase/ Medline until September 2019. The keywords used, were: “thoracic duct anatomy”, “lymphatic anatomical variations” and “thoracic duct anatomic variations”. Two independent investigators conducted a comprehensive search of the literature (NT, SG). Disagreements were discussed and the final decision was reached by consensus with the addition of a third reviewer (IT) (Giannopoulos et al., 2018). Retrospective or prospective real-world analyses as well as cadaveric studies were included in this systematic review, as long as anatomic variations of the thoracic duct were reported. The references of the included studies were also manually reviewed in order to identify further potentially eligible articles.

Data extraction

Two reviewers (NT, SG) independently and blindly to each other extracted the relevant data from the eligible studies. All disagreements were discussed and the final decision was reached by consensus with the addition of third reviewer (IT) (Giannopoulos et al., 2018). The data that were extracted included the first author, title of article, publication date, study design, epidemiologic characteristics, number of male patients, technique used and information regarding the anatomic variation of the terminal thoracic duct. The cases identified were categorized into groups according to the vein that received the terminal thoracic duct branch.

Statistical synthesis and analysis

The prevalence (%) identified for every anatomical variation of the thoracic duct, with its corresponding 95% confidence intervals (CIs) was synthesized. Heterogeneity was assessed with the Higgins I-square (I2) statistic. I2 greater than 75% indicated significant heterogeneity (Higgins et al., 2003). A forest plot was used to graphically display the effect size in each study and the pooled estimates. A p value <0.05 was considered significant. STATA 14.1 (StataCorp, College Station, Texas) was used as statistical software.

RESULTS

Search Results

The electronic and printed literature research yielded 463 articles. After screening of the titles and abstracts, 28 articles were retrieved for full-text evaluation. Case reports were excluded from this study, in order to avoid any publication bias and incorrect estimation of prevalence. After full text evaluation, 14 studies eventually fulfilled the predefined inclusion criteria (Parsons and Sargent, 1909; Davis, 1915; Gottlieb and Greenfield, 1956; Shafiroff and Kau, 1959; Kinaert, 1973; Cha and Sirijintakarn, 1976; Zorzetto et al., 1977; Merrigan et al., 1997; Langford et al., 1999; Langford, 2002; Akcali et al., 2006; Vishnumukkala, 2013; Louzada et al., 2016; Amore et al., 2016), as shown in the PRISMA flow diagram (Fig. 1). The 14 included studies enrolled overall 751 cases. Twelve of these studies were cavaderic and two studies were based on living human species. Epidemiologic details of the specimen studied were provided in 4 out of 14 studies, and the sex of the patients was included in 4 out of 14 studies. Detailed study characteristics are presented in Table 1.

Prevalence of the different thoracic duct variations

The thoracic duct was not found on the left side in a minimal number of cases (N=6/751) (14 studies; 751 patients; 0%-1%; I2= 0.0%). A single terminal duct was identified at 63% of the patients (10 studies; 639 patients; 37%-85%; I2= 97.22%), while multiple terminal ducts were observed in 37% of the patients (10 studies; 639 patients; 15% -63%; I2= 97.22%) (Fig. 2). The thoracic duct presented with at least one terminal branch draining into the left internal jugular vein, left subclavian vein and the left jugulosubclavian angle, in 32% (12 studies; 463 patients; 18%-47%; I2= 89.80%) (Fig. 3A), 27% (11 studies; 388 patients; 13%-43%; I2= 89.59%) (Fig. 3B) and in 32% of the cases (12 studies; 463 patients; 16%-51%; I2= 93.51%) (Fig. 3C), respectively (Fig. 4). The prevalence of at least one thoracic duct terminal branch emptying into a vein other than the previously mentioned, was found to be 7% (12 studies; 463 patients; 0%-19%, I2= 92.62%) (Fig. 5). When the thoracic duct drained into the left internal jugular vein, left subclavian vein and the left jugulosubclavian angle, a single terminal branch pattern was observed in 58% (9 studies; 396 patients; N=93/160; 21%-92%; I2= 94.65 %) (Fig. 6A), 49% (9 studies; 330 patients; N=40/92; 6%- 93%; I2= 93.06%) (Fig. 6B) and 76% (8 studies; 371 patients; N= 82/120; 49-96%; I2= 87.25%) (Fig. 6C) of the cases, respectively. Detailed information

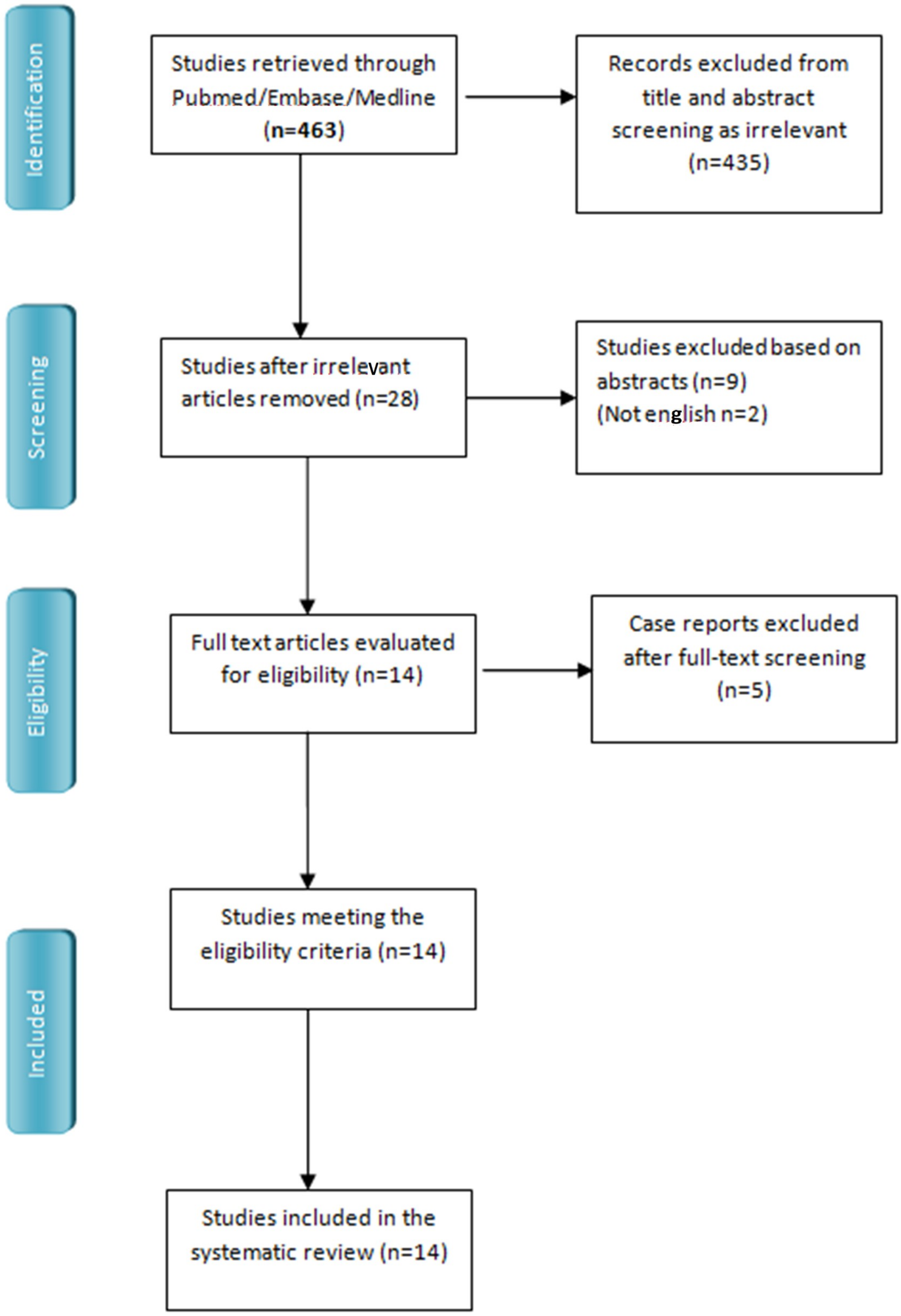

Fig 1. PRISMA Flow Diagram.

about the prevalence of each anatomic variation of the thoracic duct is presented in Table 2.

DISCUSSION

This systematic review demonstrated that in almost all cases the thoracic duct was found on the left hemithorax, draining into the venous circulation with a single terminal duct in 63% of the cases. Terminal branches of the thoracic duct were identified in the left internal jugular vein, left subclavian vein and the left jugulosubclavian angle in 32%, 27% and in 32% of the cases respectively. In addition, patients with a terminal branch at the left jugulosubclavian angle showed higher prevalence of the single terminal branch pattern (76%), whereas

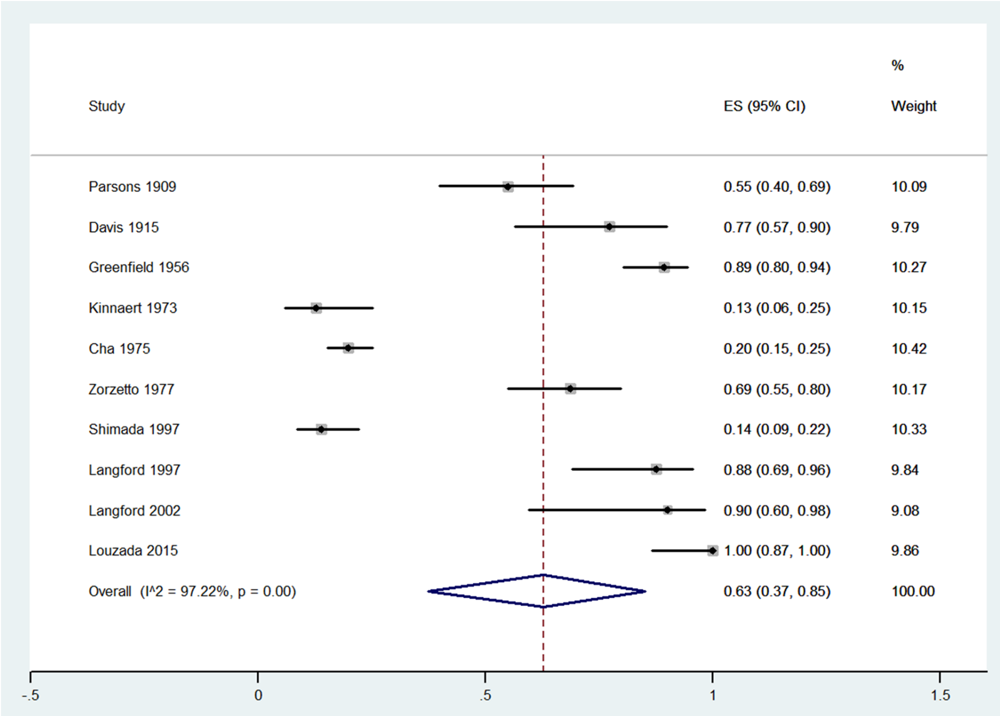

Fig 2. Prevalence of single thoracic terminal duct.

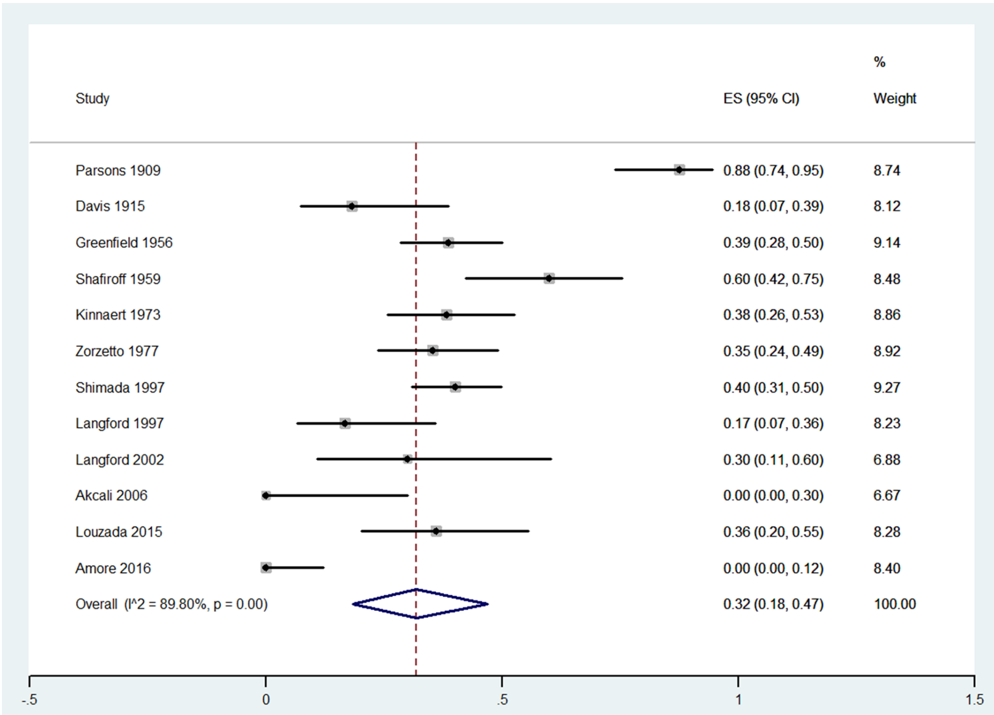

Fig 3A. Prevalence of at least one terminal thoracic duct branch draining into the internal jugular vein.

patients with a terminal branch at the left internal jugular vein or the left subclavian vein presented with almost similar prevalence of single- and multiple-branch patterns (58% and 49% respectively).

The thoracic duct may empty through one or multiple terminal branches to the venous system. Patterns of terminating branches that reunite before the final end at the venous system have also been described (Phang et al., 2014). As shown by our review, most frequently the thoracic duct drains into the left internal jugular vein, left jugulosubclavian angle and left subclavian vein. Cases of thoracic duct emptying in a vein other than these three have also been reported across literature, although such cases are quite rare (Davis, 1915; Shimada and Sato, 1997). In Table 3 a list of the veins that received terminal thoracic duct branches is included. However, awareness of the anatomical

Table 3. Veins that were found to receive a thoracic duct terminal branch

Internal jugular vein
Jugulosubclavian angle
Subclavian vein
Brachiocephalic vein
Vertebral vein
External jugular vein
Transverse cervical vein
Angle of internal jugular vein with left posterior jugular vein
Cervical lymphatic chain
Jugulovertebral angle
Suprascapular vein
Brachiocephalic vein

variations of the thoracic duct is essential for every surgeon or interventionalist performing a therapeutic or diagnostic procedure involving the thoracic duct or its branches, in order to prevent chylous leak due to iatrogenic thoracic duct injury (Smith et al., 2013).

In general, an accidental laceration of the thoracic duct occurs in 1%-2.5% of radical neck dissections, although it can be of 4.5% to 8.3% after thyroidectomy and lateral neck dissection (Roh et al., 2008a; Roh et al., 2008b). Most commonly it occurs on the left side (75-92%) involving the final segment of the thoracic duct, which drains into the veins of the neck (De Gier et al., 1996). It is well associated with lateral neck dissection and operations taking place at the level IV cervical lymph nodes, which correspond to the lower jugular lymph nodes located around the lower third of the internal jugular vein (De Gier et al., 1996; Gregor, 2000; Louzada et al., 2016). Preoperative radiation therapy and cervical nodal metastasis (i.e., head and neck squamous cell cancer, differentiated thyroid cancer) impose greater danger of thoracic duct laceration (Spiro et al., 1990; Roh et al., 2008a; Roh et al., 2008b; Teymoortash et al., 2010).

Thoracic duct injury after neck dissection can result in chylous leaks, which can eventually present as chylous fistulae, chylothoraces, or rarely, cervical chylomas. Although thoracic duct laceration is uncommon after neck dissection, it is a significant complication (Kimura et al., 2017). Chylous leak may cause local complications, like dehiscence, inflammation, secondary infection, delayed wound healing and skin necrosis of the surgical wound, as well as damage to the carotid artery (Gregor, 2000; Smoke and Delegge, 2008; Brennan et al., 2012). Furthermore, chyle leakage has been associated with more tremendous systemic complications, including but not limited to severe electrolyte, metabolic and immunologic complications (Gregor, 2000; Pillay and Singh, 2016). Therefore, the thoracic duct injury not only increases the hospitalization duration and costs but also has a bad prognosis for the patient, generally.

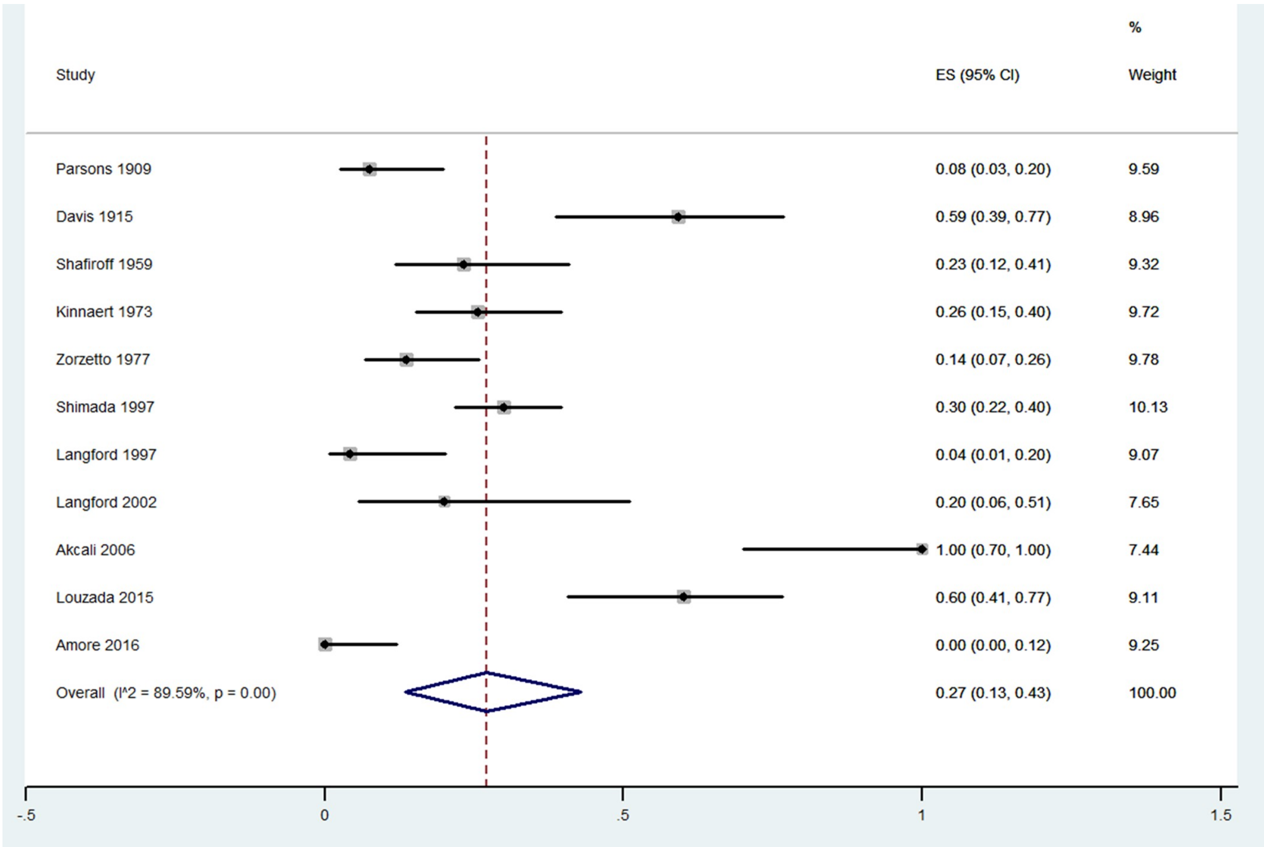

Fig 3B. Prevalence of at least one terminal thoracic duct branch draining into subclavian vein.

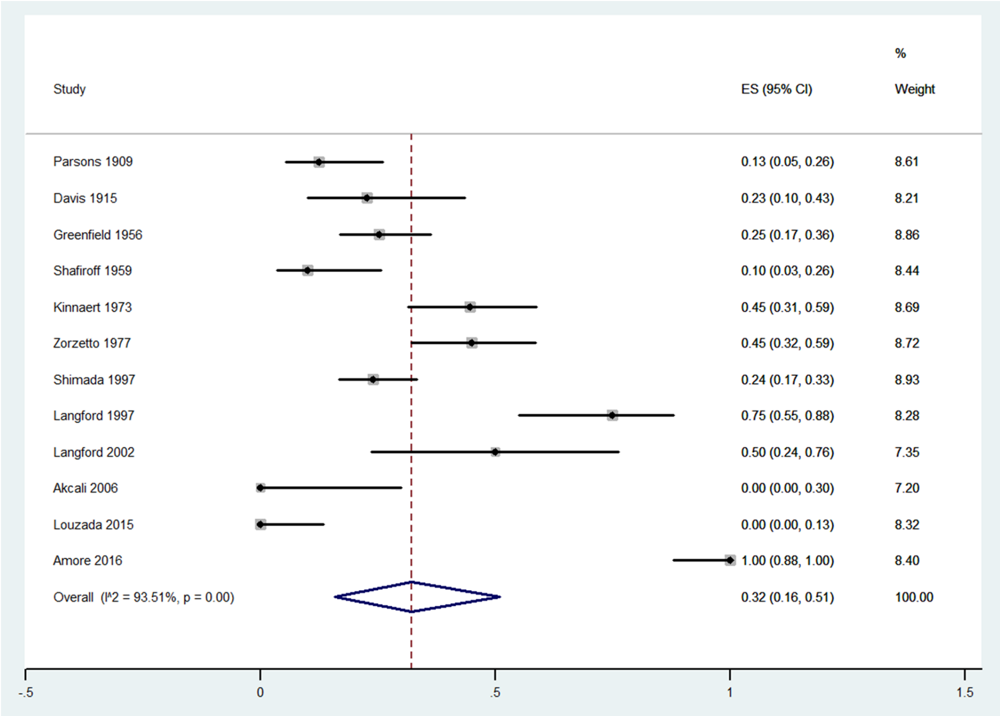

Fig 3C. Prevalence of at least one terminal thoracic duct branch draining into the jugulosubclavian angle.

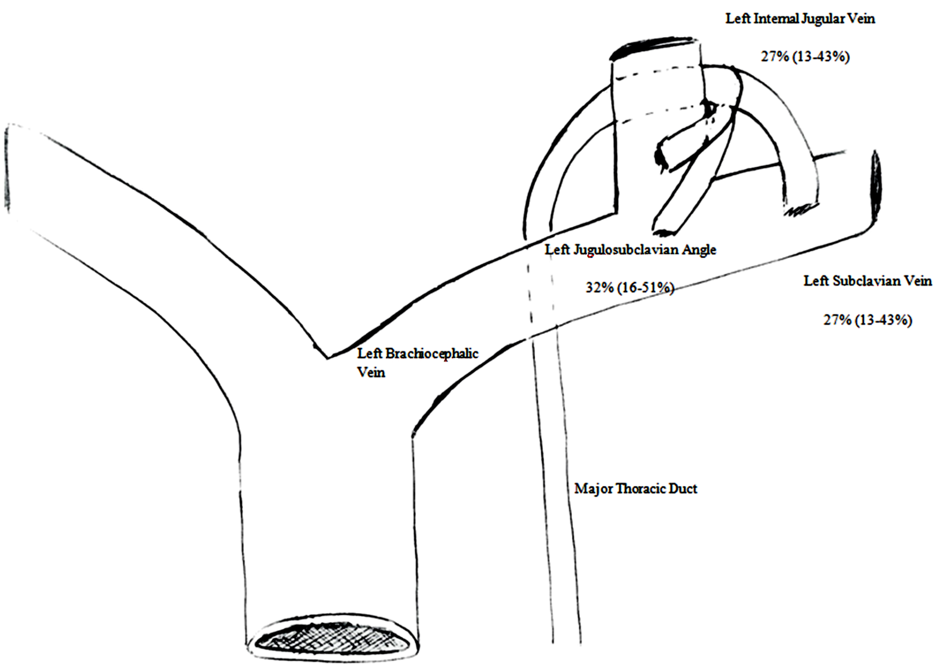

Fig 4. Thoracic duct terminal branch draining into the internal jugular vein, subclavian vein and the jugulosubclavian. The prevalence and the 95% corresponding confidence intervals of its anatomic variation are also provided.

The best treatment for chylous leak is to avoid it at first place (Gregor, 2000). This signifies the importance of knowing and being familiar with the surgical anatomy of the thoracic duct, its surrounding structures, and their multiple variances (Spiro et al., 1990; Langford et al., 1999). However, if chylous leak occurs and is not observed and treated during the operation, then it will be diagnosed clinically, during the first postoperative days (Nussenbaum et al., 2000; Kumar et al., 2004). Diagnostic imaging plays a less important role in the diagnosis of chylous leakage, and is performed when the patient's chylous leak does not improve despite conservative therapeutic measures, or in cases with severe systemic manifestations complicating the patient's periprocedural course (Scorza et al., 2008). Lymphangiography and lymphoscintigraphy are the two classic tests used both in the

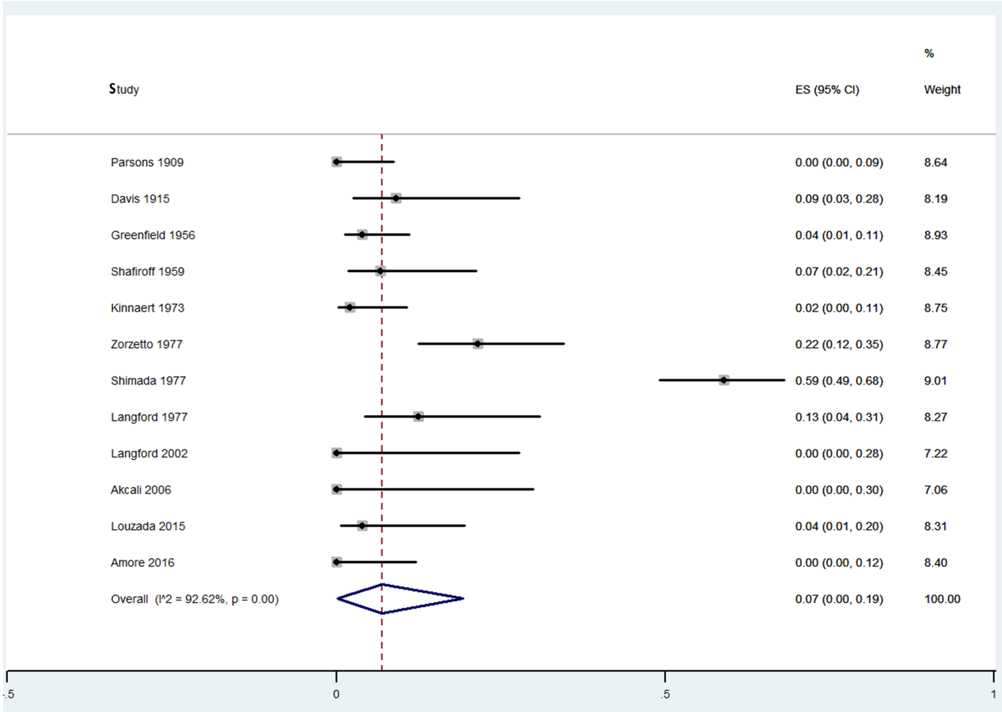

Fig 5. Prevalence of at least one terminal thoracic duct branch draining into a vein other than the internal jugular vein, the jugulosubclavian vein, or the subclavian vein.

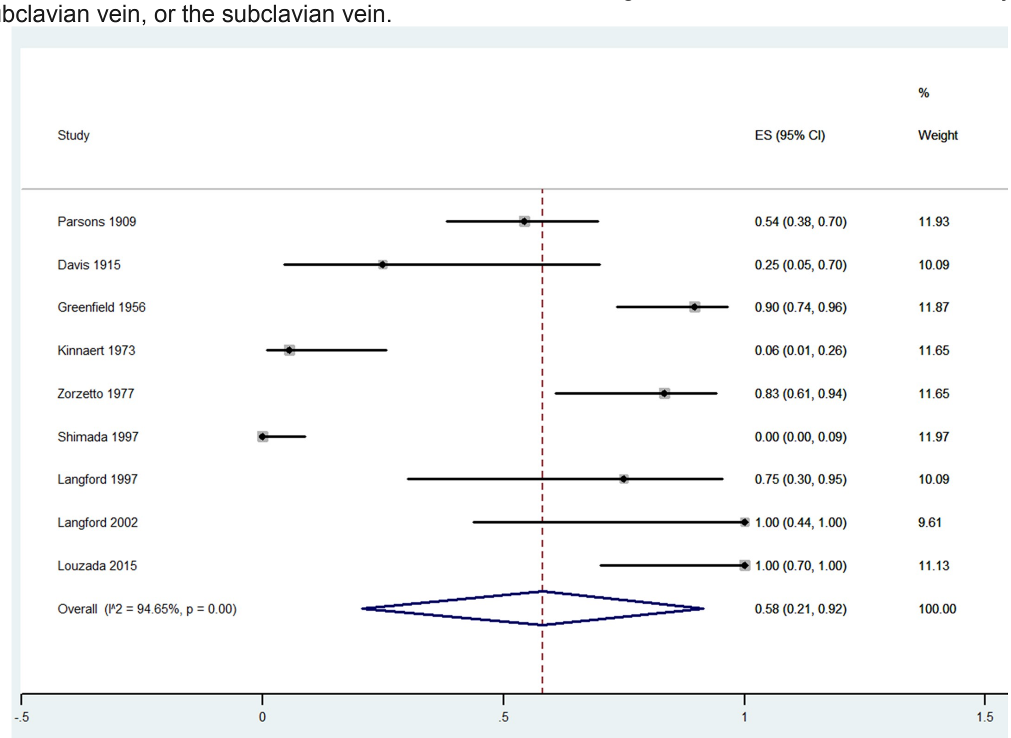

Fig 6A. Prevalence of single terminal branch pattern, when thoracic duct drained into internal jugular vein.

diagnosis and localization of chylous leaks (Bourgeois et al., 2008; Deso et al., 2012; Kim et al., 2018). In addition, magnetic resonance lymphangiography, multidetector row computed tomography (CT) and high resolution ultrasonography have also shown satisfying results on the visualization of morphological and functional features of the thoracic duct lately (Brennan et al., 2012; Gao et al., 2017). However, imaging is rarely used during preoperative planning of surgical treatment. Thus, acknowledgement of the several anatomic variations of the thoracic duct is of high clinical significance, as it could help reduce the risk for iatrogenic injury of the thoracic duct (Phang et al., 2014). Future, large anatomic studies are needed to evaluate the results of this systematic review and to further determine the anatomy of the thoracic duct. The optimal goal would be to develop uni-

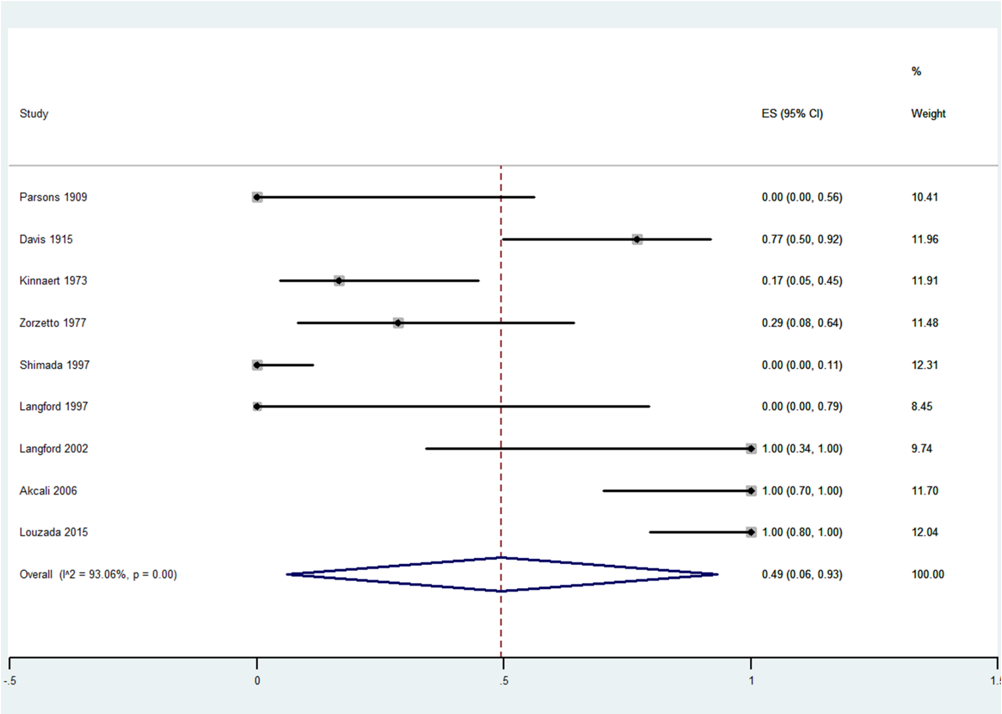

Fig 6B. Prevalence of single terminal branch pattern, when thoracic duct drained into subclavian vein.

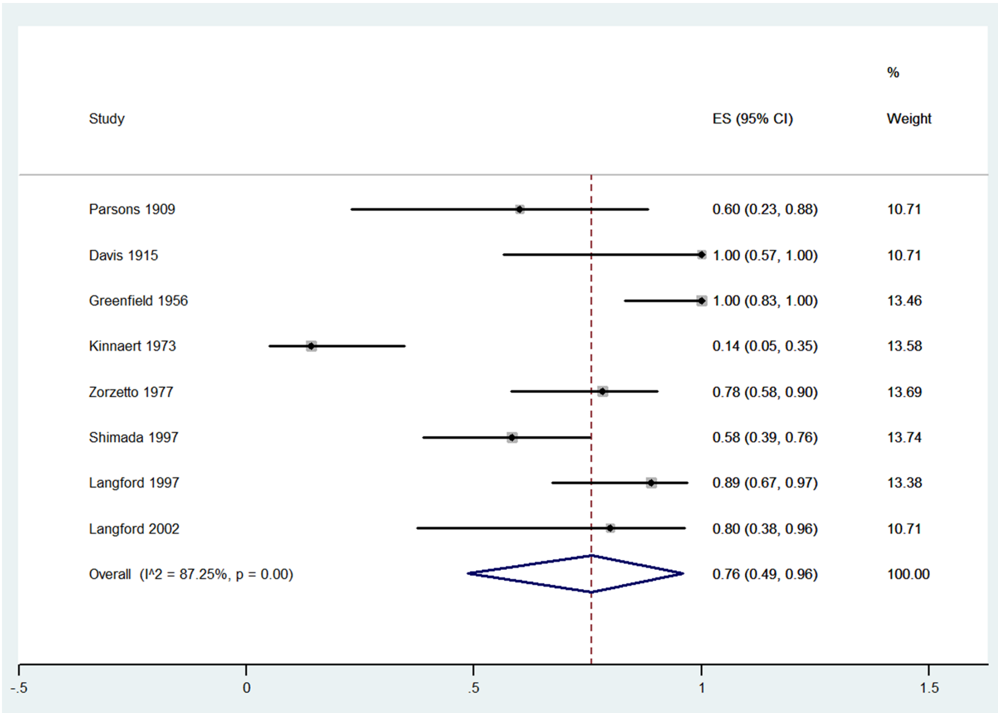

Fig 6C. Prevalence of single terminal branch pattern, when thoracic duct drained into internal jugulosubclavian angle.

versal classification systems for thoracic duct anomalies and their associated risk of thoracic duct injury in specific types of surgical procedures.

Limitations

The results of the present study should be interpreted in the context of two main limitations. First, data about baseline characteristics of the included patients (e.g. race, sex, age etc.), were limited and therefore sensitivity analysis regarding the thoracic duct's anatomic variations among different populations was not possible. Second, the results of the current systematic review are based on a small number of studies, which could limit the generalizability of our results. Determination of the incidence of the most common anatomical variations of the terminal portion of the thoracic duct, identified by our systematic review, warrants further investigation, in order to relate populations and procedures with a potentially high risk for thoracic duct injury in neck operations.

Conclusions

In this systematic review, the most commonly presented anatomic variations of the final portion of the thoracic duct were identified and their corresponding prevalence was estimated. We believe that the excluded results of this study will be very useful in order to minimize iatrogenic thoracic duct injuries and their associated sequelae. Further studies are needed in order to identify populations and procedures placed at a high risk for thoracic duct injury in order to lower the complication rates and keep the costs of hospitalization low.

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