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Early View

Research letter

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Catherine Boily-Daoust, Alexandre Plante, Cedrick Adam, Marc Fortin

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Performance and Safety of Diagnostic Procedures in Superior Vena Cava Syndrome

Catherine Boily-Daoust[1], Alexandre Plante[1], Cedrick Adam[1], Marc Fortin*[1]

[1] Department of Pulmonary Medicine, Institut Universitaire de Cardiologie et de Pneumologie de Québec, Université Laval, Québec, QC, Canada

*Corresponding Author

Catherine Boily-Daoust

Department of Pulmonary Medicine

Institut Universitaire de Cardiologie et de Pneumologie de Québec, Université Laval

2725 Chemin Ste-Foy, Quebec City, Canada, G1V 4G5

boilydaoust.c@gmail.com

P: 1-418-656-8711 #5504

F: 1-418-656-4762

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Introduction

Superior vena cava syndrome (SVCS) is an uncommon condition resulting from extrinsic compression or intraluminal blockade of the superior vena cava. The increased upper body venous pressure results in distended subcutaneous vessels and edema of the head, neck and arms. SVCS can be a medical emergency if associated with laryngeal or cerebral edema. The most common SVCS etiologies are intrathoracic malignancies, accounting for 60 to 86% of cases [1-3].

Promptly obtaining a tissue diagnosis before performing therapeutic interventions is the preferred approach in most cases [3, 4] as the majority of patients present without a prior cancer diagnosis [5]. Invasive procedures, such as bronchoscopy and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), may be required to obtain a histologic diagnosis. Rigid bronchoscopy may also be indicated in cases of concomitant malignant central airway obstruction [6]. Endoscopic procedures are generally performed in recumbent position increasing intracranial pressure [7, 8], and could potentially be at high risk of complication in a population presenting subclinical cerebral edema. Impaired venous return may also cause vascular congestion of the airway leading to an increased bleeding risk [9-11]. Impaired venous return may be further decreased in the supine position [12] with a potential for hemodynamic consequences, especially in the context of the sedations administered [10, 13, 14].

The performance and safety of endoscopic procedures in SVCS patients has not been well studied [9, 15-20]. The objectives of the present study are to evaluate the safety and

performance of different diagnostic and therapeutic procedures in SVCS, with a particular focus on endoscopic procedures.

Methods

We performed a retrospective chart review of all patients who received a diagnosis of SVCS in our institution from 4/1/2012 to 3/31/2017. We included all patients with a superior vena cava occlusion on contrast computed tomography (CT-scan), including those who were initially asymptomatic. Patients were included if they were older than 18-years old and had a diagnostic or a therapeutic procedure, including standard bronchoscopy, EBUS-TBNA, transthoracic needle biopsy (TNB) and rigid bronchoscopy.

SVCS severity was stratified according to the grading system described by Yu et al. (2008) [4]. Central airway lumen obstruction was measured on CT-scan as the ratio of the most narrowed point of the involved airway (trachea or main bronchi) versus its estimated normal diameter, and was considered significant if > 50 percent. The presence of an association between SVCS severity or central airway obstruction and procedural complications was explored.

Bronchoscopies and EBUS-TBNA were performed under conscious sedation using fentanyl and midazolam in the recumbent position while rigid bronchoscopies were performed under general anesthesia. Minor complications, comprising mainly minor hemorrhages and hypoxemias, were respectively defined as bleedings requiring local treatments and hypoxemia

extending more than an hour after the procedure. Complications were considered major if they led to an escalation of care.

Results

Forty-three patients underwent 73 procedures. Diagnostic procedures included 16 bronchoscopies, 23 EBUS-TBNA and 9 TNB. Nineteen bronchoscopies were performed for non-diagnostic purposes, including anatomic evaluation before stent placement (n = 3, 15.8%), stent revision (n = 8, 42.1%) and bronchial cleaning (n = 8, 42.1%). Six therapeutic bronchoscopies were performed, including five for stent placement and one for tumor debulking.

Mean age was 57.2 ($\pm$ 16.0) and the vast majority of patients had a malignant diagnosis (n = 40, 93%), the most frequent being non-small cell lung cancer (n = 23, 53.5%). Twelve (19%) endoscopic procedures were performed while the SVCS severity score was elevated ($\geq$ 3/ 4) and 22 (40%) while the central airway lumen was obstructed more than 50%. Mean procedural time for EBUS-TBNA, diagnostic and therapeutic bronchoscopy were respectively 18.0, 13.1 and 52.3 minutes.

Diagnostic yield of bronchoscopy, EBUS-TBNA and TNB were respectively 81.3%, 87.0 and 100.0%. Regarding EBUS-TBNA, 31 stations were sampled in 23 patients (average 1.3 stations $\pm$ 0.6 per patient). Either the primary lesion or the 4R station were sampled in 20 (87%) patients.

The mean procedural time for diagnostic bronchoscopies, EBUS-TBNA, and therapeutic bronchoscopies were respectively 13.1 minutes ($\pm$ 6.8), 18.0 minutes ($\pm$ 4.9) and 52.3 minutes ($\pm$ 48.9).

There were no complications following TNB. Minor complications were reported in 8 (13%) endoscopic procedures, 4 (6%) hemorrhages requiring topical treatments and 6 (9%) transient hypoxemias extending more than an hour after the procedure but not requiring escalation of care (table 1). Two procedures were associated with two complications. There were significantly more transient hypoxemias following EBUS compared to standard bronchoscopies (5 [21.7%] vs 1 [2.9%], p = 0.03).

Three patients suffered major complications, two of which occurred during therapeutic bronchoscopies. One patient with a tracheoesophageal fistula developed a tension pneumothorax during positive pressure ventilation. Another patient with a tracheal tumor could not be ventilated or intubated following general anesthesia induction and needed an emergent cricotomy. The third patient developed hemodynamically unstable atrial fibrillation during a standard bronchoscopy, in the setting of a neoplastic pericardial effusion. No deaths related to the complications were recorded.

SVCS severity or presence of significant central airway obstruction were not associated with more frequent complications. There were three (25%) minor complications in procedures performed with a SVCS score $\geq$ 3/4 compared to five (9.6%) amongst procedures with a SVCS

score $\leq$ 2 /4 (p = 0.70), and there were four (18.3%) minor complications in procedures performed with a central airway obstruction > 50% compared to four (12.1%) in those with a lesser degree of airway obstruction (p = 0.16).

Discussion

Timely establishment of a histologic diagnosis is required in order to provide optimal treatment for patients with SVCS. In our cohort, endoscopic procedures and TNB proved to have a good diagnostic yield in patients with SVCS, which is consistent with existing literature [16, 18, 19].

The mean procedural time for EBUS-TBNA (18.7 minutes [$\pm$ 20.4]) was consistent with the mean procedural time reported in the literature for EBUS-TBNA done for various indications under conscious sedation [21]. No major complications were observed with EBUS-TBNA, even if 87% patients had punctures in the vicinity of their compressed superior vena cava. Our results suggest that EBUS-TBNA in the setting of SVCS is safe.

Minor complications during endoscopic procedures, consisting of bleeding requiring topical treatments and transient hypoxemia were not uncommon, but did not alter patient trajectory. Minor adverse events occurred in 8.6% of flexible bronchoscopies, which is consistent with other series [22-25]. The EBUS-TBNA complications rate observed in our series (21.7%) may seem higher than in previous reports. The systematic review by M.B. von Barthled et al [26] looked at 16,181 patients and reported an overall complication rates (minor and serious adverse events) of 0.35% for EBUS-TBNA and endoscopic ultrasound (EUS), whereas the

American College of Chest Physicians Quality Improvement Registry, Evaluation, and Education (AQuIRE) reported an EBUS-TBNA complication rate of 1.44% [27]. This difference can be explained by the different definitions, mainly the definition of hypoxemia, used for complications leading to the inclusion of events which would not have been included in previous studies.

Finally, we observed complications in 2/6 (33.3%) therapeutic procedures, which seems higher than what was reported in previous studies than what is reported in the literature [28-33]). We previously reported in a multicentric retrospective study a 6.7% rate of non-lethal complications and the AQuiRe registry reported a complication rate of 3.9% [30]. However, the limited samples of these subgroups analysis prevent any firm conclusions.

Major complications occurred in three endoscopic procedures (4.7%), including two therapeutic bronchoscopies. We feel that major complications in our cohort were not directly related to the SVCS itself, but rather to the underlying malignancy and its proximity to central vital structures. Similarly, Schraufnagel and colleagues reported no complication from the superior vena cava obstruction itself nor the procedures, but rather from other tumor-associated complications, such as cardiac tamponade or airway obstruction [5].

In conclusion, TNB, standard bronchoscopy and EBUS-TBNA have good diagnostic yield and are relatively safe procedures in the setting of SVCS. However, when selecting the best diagnostic

procedure, clinicians should bear in mind the comorbid conditions associated with central lesions.

Table 1. Procedural complications

	Endoscopic procedures (n = 64)				
	Diagnostic		**Therapeutic (n = 6)**	**Other* (n = 19)**	**Total (n = 64)**
	Diagnostic bronchoscopy (n = 16)	**EBUS (n = 23)**			
Minor complications – no. (%)	2 (12.5)	5 (21.7)	0 (0)	1 (5.3)	8 (13)
Major complications – no. (%)	1 (6.3)	0 (0)	2 (33.3)	0 (0)	3 (4.7)
Total – no. (%)	3 (18.8)	5 (21.7)	2 (33.3)	1 (5.3)	11 (17.2)

*Other bronchoscopies: Stent revision (n = 8), anatomic evaluation before stent placement (n 3) and bronchial cleaning (n = 8).

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